BADAN POM

World Health Organization Indonesia

80 Bersatu Berdaulat Rakyat Sejahtera Indonesia Maju

BerAKHLAK
Berorientasi Pelayanan Akuntabel Kompeten Harmonis Loyal Adaptif Kolaboratif

#bangga melayani bangsa

KUMPULAN MATERI

Capacity Building and Workshop on Quality Standardization of Extracts and Quality Control Assessment in Traditional Medicine Products



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standar-otskk.pom.go.id

Regulation of Natural Medicines in Indonesia

Mohamad Kashuri

Deputy for Traditional Medicine, Health Supplement, and Cosmetic Control

The Indonesian Food and Drug Authority

August 19, 2025





Definition of Natural Medicines

> Substances derived from plants, animals, microorganisms, or minerals, used traditionally or scientifically proven, for maintaining and restoring health.

This definition recognizes both our cultural roots and the importance of modern scientific validation.

Example: *Sambiloto* (Andrographis paniculata), traditionally used for fever, is now standardized for immune system support through modern research–showing the transition from empirical heritage to evidence-based medicine.

Types of Natural Medicines

Jamu

Traditional herbal remedies used for generations, proven mainly through empirical use

Obat Herbal Terstandar (OHT)

Standardized Herbal Medicines requiring preclinical studies to confirm safety and efficacy

Fitofarmaka

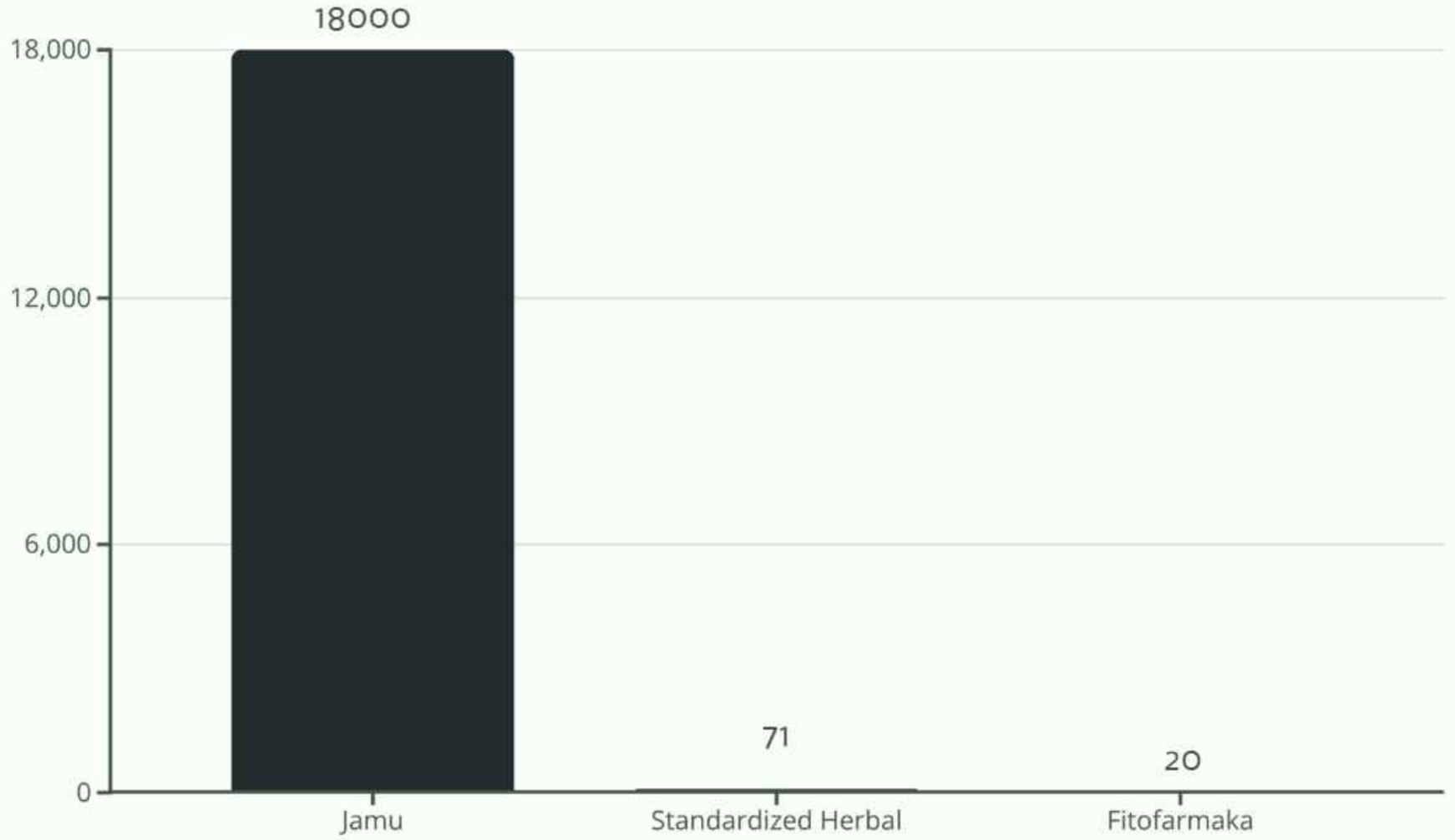
Highest category, equivalent to modern medicines, supported by both preclinical and clinical trials

Other Categories

Imported, licensed, and innovative herbal medicines

Example: Turmeric-based jamu for digestive problems can be upgraded to OHT or Fitofarmaka through standardization and clinical testing, enabling wider acceptance in hospitals and insurance schemes.

Legal Classification (Health Law No. 17/2023)



This growth demonstrates a significant shift toward evidence-based herbal products. Yet, compared to our biodiversity potential, the number is still small–indicating both a challenge and an opportunity.

Potential and Opportunities



Sales of jamu and herbal medicines are expected to surpass **23 trillion rupiah by 2025**

Beyond economics, integrating natural medicines into the national health system is a strategic move to ensure resilience and independence in healthcare.

During COVID-19, ingredients like ginger experienced surging demand both domestically and globally, proving natural medicines are cultural heritage and economic assets.

Challenges in Developing Natural Medicines

Safety, Efficacy, Quality

Ensuring consistent standards across all products

Clinical Trials

Conducting robust preclinical and clinical studies

Standardization

Of raw materials and finished products

Technological Gaps

In extraction and formulation processes

Example challenge: Standardizing poly-compositions (mixtures of multiple herbs) is scientifically complex and requires advanced analytical methods.

Criteria for Safety, Efficacy, and Quality

Manufacturing Standards

Products must be manufactured under **Good Manufacturing Practices (CPOTB)**

Efficacy Evidence

Must be supported by empirical use or scientific evidence

Raw Material Quality

Must meet pharmacopoeia standards or internationally recognized references

Example: An herbal capsule for liver health must cite traditional use, prove active compounds, safety levels, and consistent manufacturing quality.



Key Aspects in Development

Standardization

Guarantees reproducibility of herbal extracts

Preclinical Studies

Ensure basic safety and pharmacological effects



Clinical Trials

Provide ultimate evidence for doctors, patients, and global markets

Without clinical trials, a herbal product will remain jamu. With clinical trials, it can become a fitofarmaka, recognized at the same level as modern medicines.

Principles and Challenges of Standardization

The Principle

Consistent, high-quality products

The Challenges

- Herbal mixtures with multiple components
- Differences in solvents used in traditional texts versus laboratory methods
- Need for validated parameters for both extracts and finished products



Example: An extract prepared traditionally with water might show different chemical

Regulations Governing Natural Medicines

Safety and Quality

PerBPOM No. 29/2023

Preclinical Toxicity

PerBPOM No. 10/2022

Clinical Trial Approval

PerBPOM No. 8/2024

Manufacturing (CPOTB)

PerBPOM No. 14/2021 and updates

Labeling and Claims

PerBPOM No. 10/2024 and No. 30/2023

This regulatory ecosystem ensures that every product on the market, whether jamu or fitofarmaka, is accountable to safety, efficacy, and transparency.

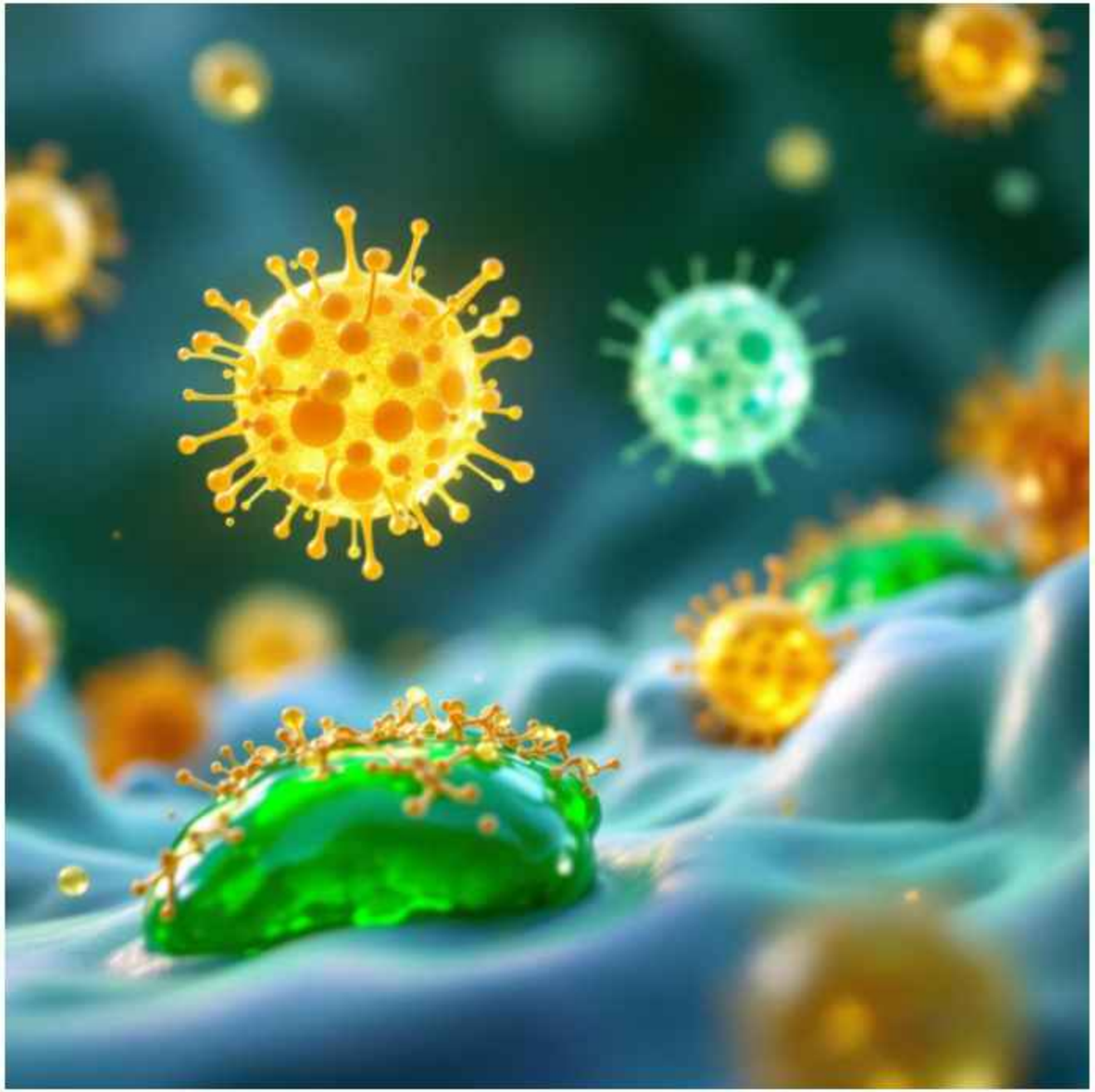
Nanotechnology and Irradiation

Nanotechnology Benefits

Allows better delivery of active herbal compounds, increasing bioavailability and effectiveness

Irradiation Applications

Helps ensure microbial safety of raw materials



Example: Nano-formulated curcumin has been shown to enhance absorption significantly



Guidelines for Raw Materials (Draft)

We are currently developing guidelines for preparing extracts and fractions as standardized raw materials. This will give industry clearer directions to produce consistent, high-quality inputs, not just for domestic markets but also for exports.

These guidelines will help standardize the production process from raw plant material to finished extract, ensuring consistency across the industry.

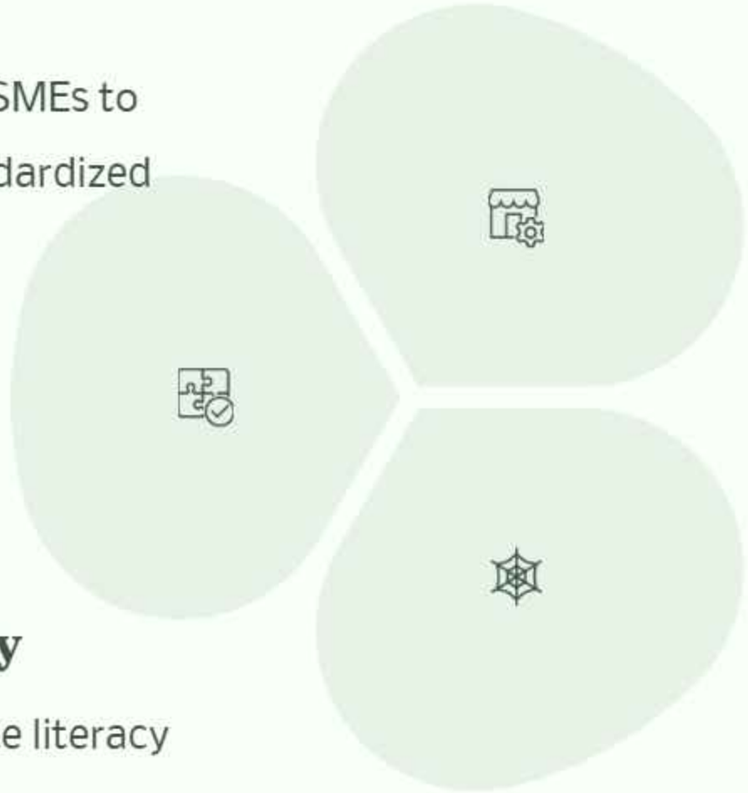
BPOM's Real Action and Collaboration

Industry Support

Technical guidance for SMEs to upgrade jamu into standardized products

Academic Collaboration

Joint clinical trials with universities



Goverment

- Regulatory and research facilitation
- Promoting utilization

International Cooperation

Work with WHO and ASEAN to harmonize standards

Society

Adequate literacy

Regulation alone is not enough. BPOM actively collaborates with stakeholders–universities, industries, international organizations, and local communities.

Thank You



Keterkaitan Ekstraksi dan Kualitas Obat Bahan Alam

Dr.rer.nat. apt. Yosi Bayu Murti

Fakultas Farmasi Universitas Gadjah Mada

Pendahuluan



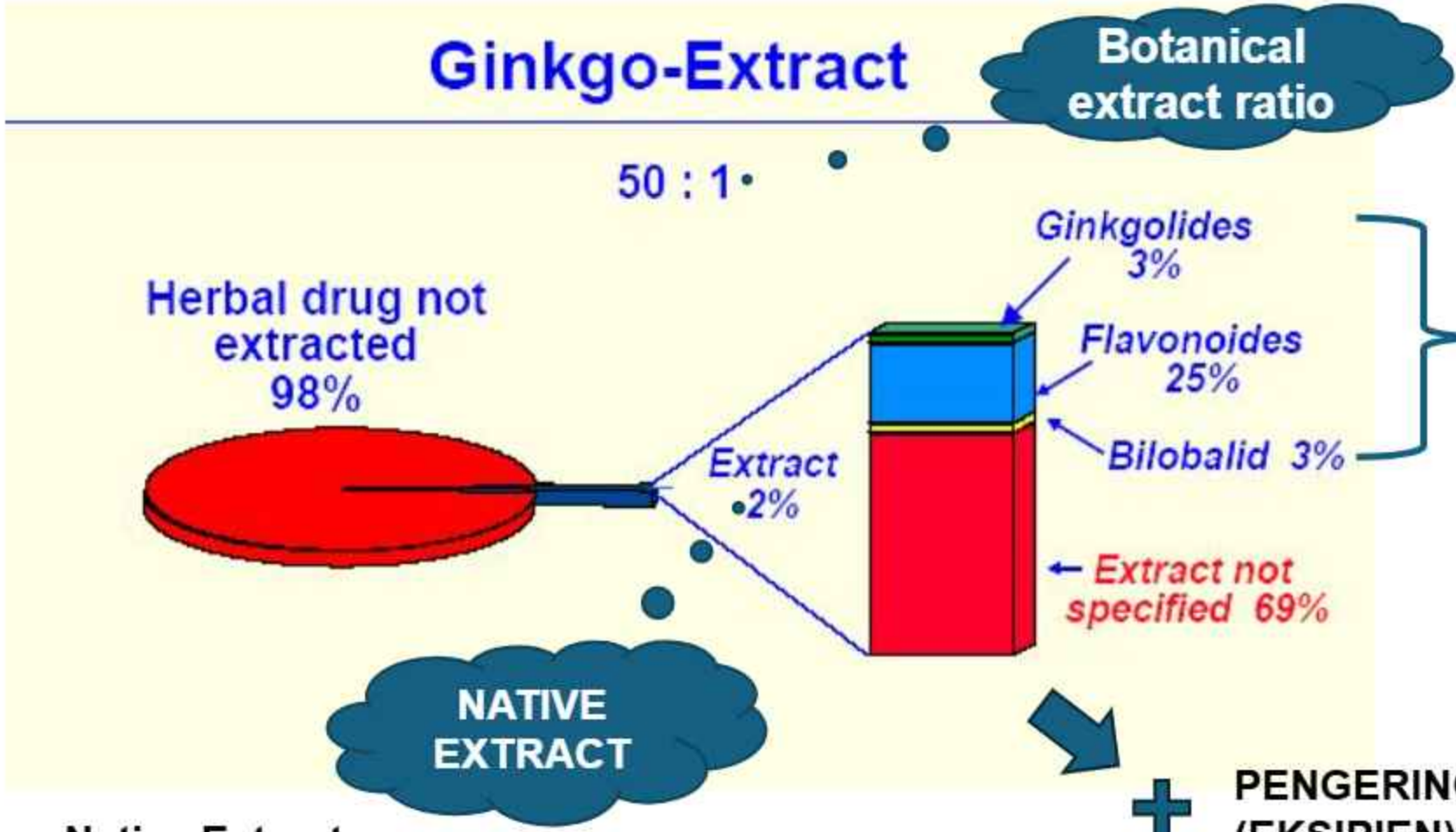
- Kontrol kualitas tanpa standardisasi
- Keamanan dan Khasiat
  - Bersifat empiris



- Kontrol kualitas dilengkapi standardisasi standardisasi berbasis marker aktif, marker analitik atau kadar golongan senyawa
- Keamanan dan Khasiat berdasarkan Uji Praklinik (OHT) dan disertai uji Klinik (Fitofarmaka)

Ekstrak

- **Ekstrak** adalah hasil penyarian dalam bentuk cair, kental atau kering yang dibuat dengan menyari bahan aktif dari simplisia nabati atau hewani menggunakan pelarut dan cara yang sesuai sehingga memenuhi baku yang telah ditetapkan. Sering didefinisikan sebagai **native extract**
- **Ekstrak cair** adalah ekstrak berbentuk cair yang diperoleh dari hasil penyarian dengan atau tanpa proses penguapan penyari, hingga memenuhi persyaratan yang ditetapkan.
- **Ekstrak kering** (Dry extract = DE) adalah ekstrak berbentuk kering, yang diperoleh dari proses penguapan penyari dengan atau tanpa bahan tambahan, hingga memenuhi persyaratan yang ditetapkan.
  - **DE (Dry extract)** : Native extract + Bahan pengisi/pengering
  - Contoh DE 75 = 75 bagian Native extract + 25 bagian pengisi



Botanical Extract Ratio:
Perbandingan Jumlah simplisia dengan ekstrak yang dihasilkan
= Drug Extract Ratio (DER)

Marker aktif / kuantitatif

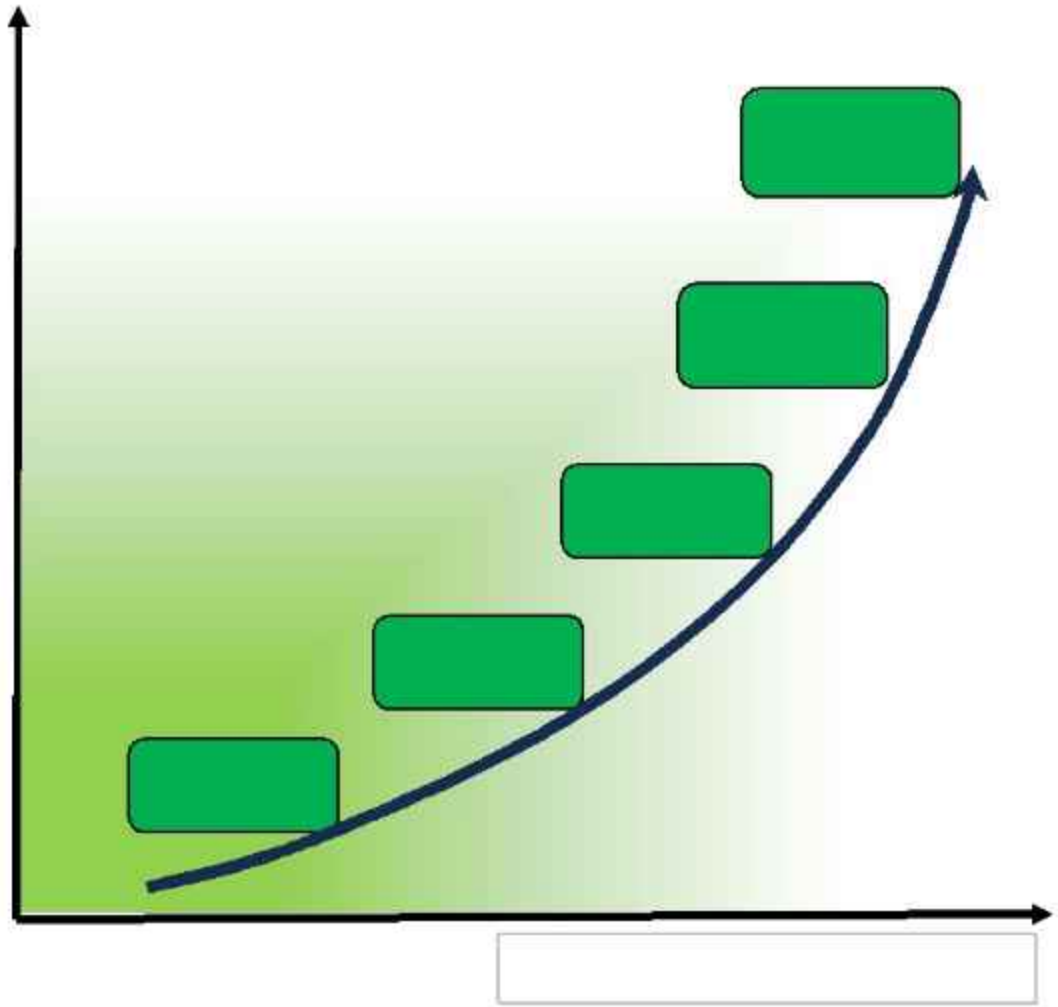
Native Extract:
Ekstrak Bahan Alam tanpa zat tambahan baik eksipien maupun pelarut

PENGERING (EKSIPIEN) → **DRY EXTRACT (DE#)**

DE (Dry extract) : Native extract + Bahan pengisi/pengering
Contoh DE 75 = 75 bagian Native extract + 25 bagian pengisi

(modifikasi dari Calixto, 2000)

Korelasi Pengembangan OBA berdasarkan Kemurnian senyawa vs Kompleksitas Pengembangan



√ ISOLASI DAN PEMURNIAN
√ SINTESIS ORGANIK → NON OBA

√ EKSTRAKSI DAN FRAKSINASI DIPANDU UJI AKTIVITAS

√ EKSTRAKSI DAN FRAKSINASI

√ TEKNOLOGI EKSTRAKSI SELEKTIF

√ EKSTRAKSI

√ PENGERINGAN

OBA

Fraksi

- Fraksinasi adalah proses pemisahan ekstrak bahan alam menjadi sejumlah bagian dengan komposisi senyawa yang berbeda. Fraksinasi ditujukan untuk meningkatkan senyawa-senyawa aktif terapetik atau marker aktif.
- Fraksi adalah hasil dari pemisahan ekstrak bahan alam yang memiliki komponen lebih sederhana dari ekstrak asalnya.
- Dasar pemisahan ekstrak bahan alam menggunakan perbedaan sifat fisika kimia senyawa-senyawa bahan alam yang meliputi
  - Asam – basa dan penggaraman
  - Polaritas relatif
  - Kelarutan dalam pelarut tertentu
  - Tekanan uap parsial (khusus minyak atsiri)
  - Kemampuan membentuk kristal

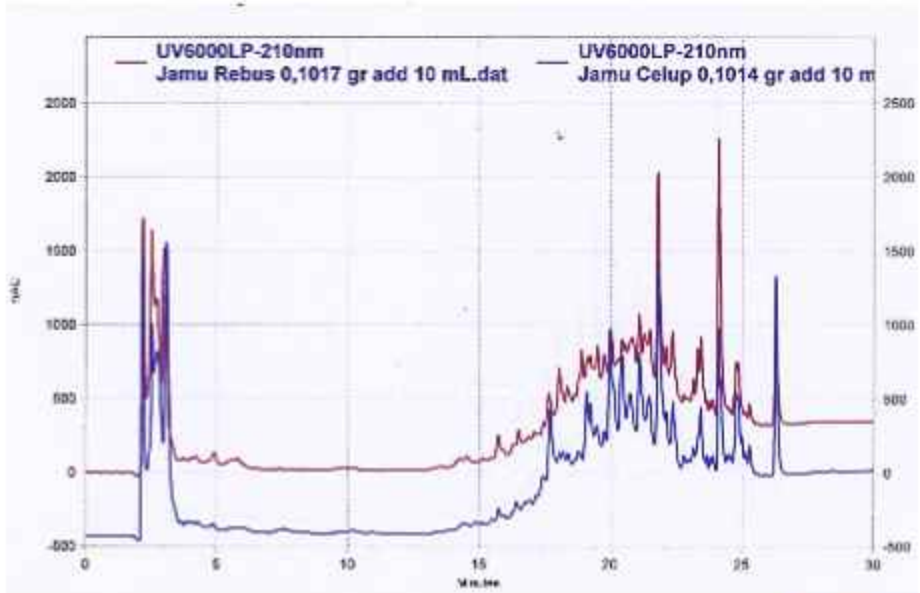
Isolat

- Isolat merupakan hasil pemurnian dari ekstrak melalui proses pemisahan/fraksinasi yang dilanjutkan dengan serangkaian proses pemurnian seperti perlakuan kimiawi untuk menghilangkan matriks (cth. hidrolisis, salting in-salting out), kromatografi preparatif dan kristalisasi.
- Isolat dan senyawa murni hasil sintesis tidak bisa dimasukkan sebagai OBA.

Ekstraksi: Titik Kritis

Titik Kritis

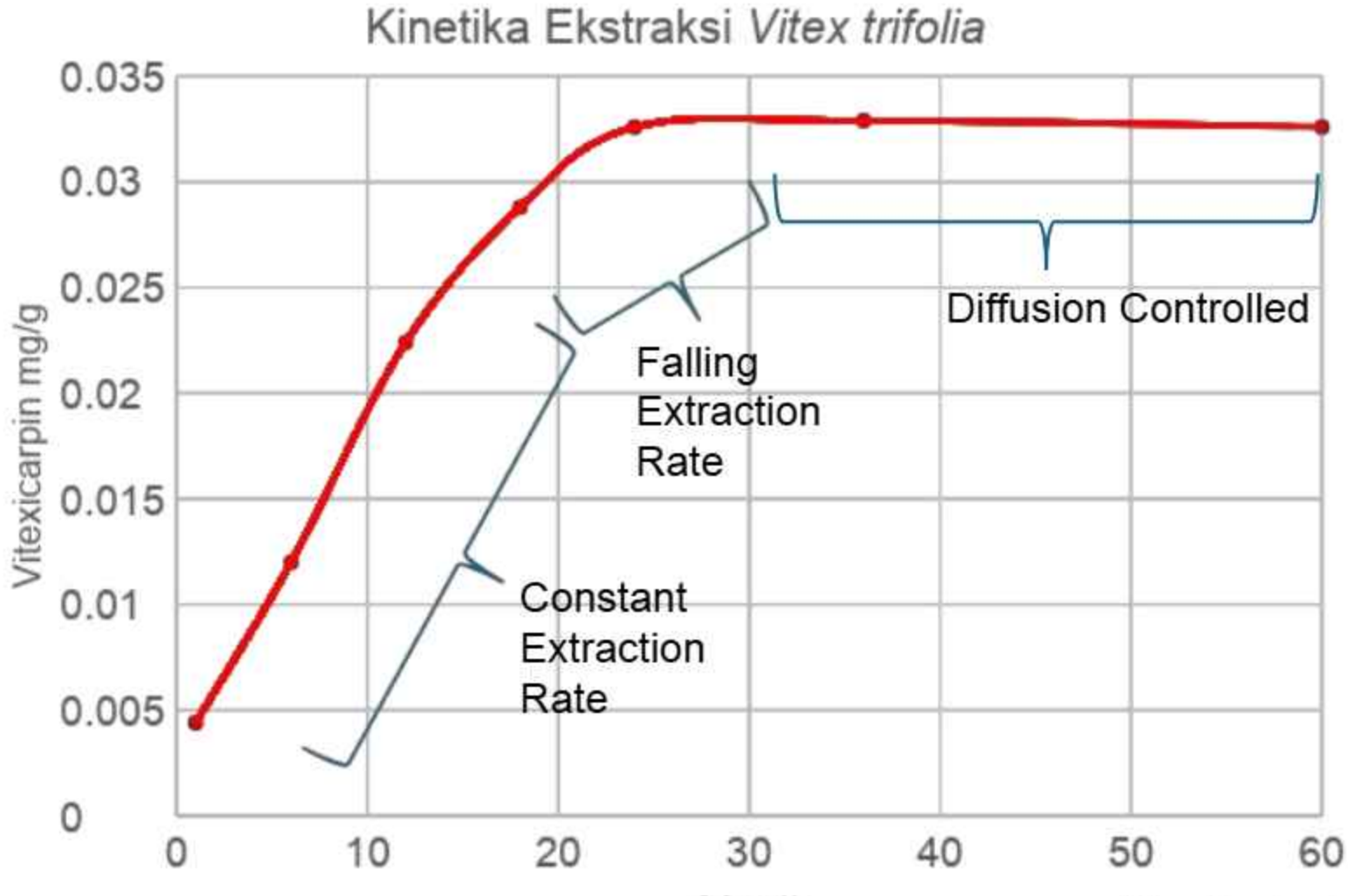
- Metode ekstraksi
- Pemilihan pelarut
- Ukuran partikel, agitasi dan suhu serta kondisi ekstraksi lainnya



Note

- Metode menentukan efisiensi ekstraksi
- Tumbuhan berisi campuran kompleks bahan alam dengan polaritas bervariasi polaritas pelarut mempengaruhi jenis dan jumlah senyawa efikasi berbeda
- Partikel makin halus ekstraksi meningkat tetapi tingkat kehilangan senyawa juga meningkat, agitasi meningkatkan transfer massa, dan suhu meningkatkan solubilitas dan kemampuan difusi pelarut

Kinetika Ekstraksi



(Murti, et.al., 2012)

Faktor-faktor penentu optimasi ekstraksi

Pelarut : Polaritas dan kisaran polaritas

Perbandingan Pelarut penyari dengan simplisia (Solvent to Feed Ratio)

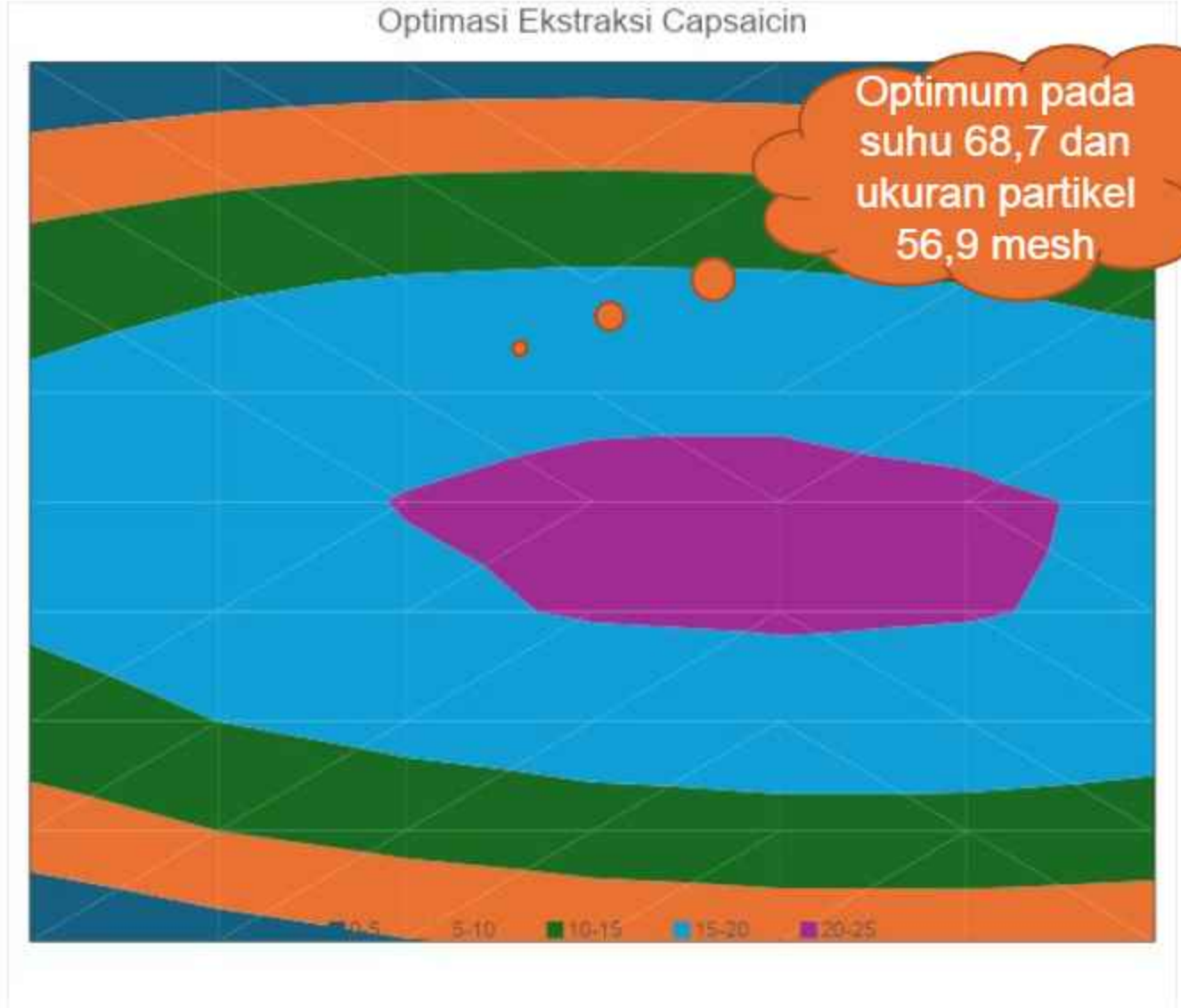
Suhu

Ukuran Partikel

Agitasi (pengadukan, bantuan ultrasonic atau microwave)

RSM dalam optimasi ekstraksi multiparametrik

Aplikasi statistik dalam optimasi ekstraksi memungkinkan analisis multiparameter secara simultan



(Triska, et.al., 2012)

Exhaustik vs non exhaustik

Exhaustic

- Umum dipakai untuk tujuan analisis
- Diperoleh dengan memperpanjang fase DC (penambahan solvent dan waktu) dan rasio S/F lebih tinggi
- Memperoleh total komponen lebih banyak
- Pembatas dari ekstraksi adalah kelarutan senyawa dalam pelarut yang digunakan

Non exhaustic

- Umum dipakai untuk ekstraksi industrial
- Memotong fase DC atau bahkan sebelum memasuki fase DC untuk memperoleh waktu lebih pendek dan batch lebih banyak
- Lebih ekonomis, menggunakan waktu-pelarut lebih sedikit, memperbanyak batch ekstraksi

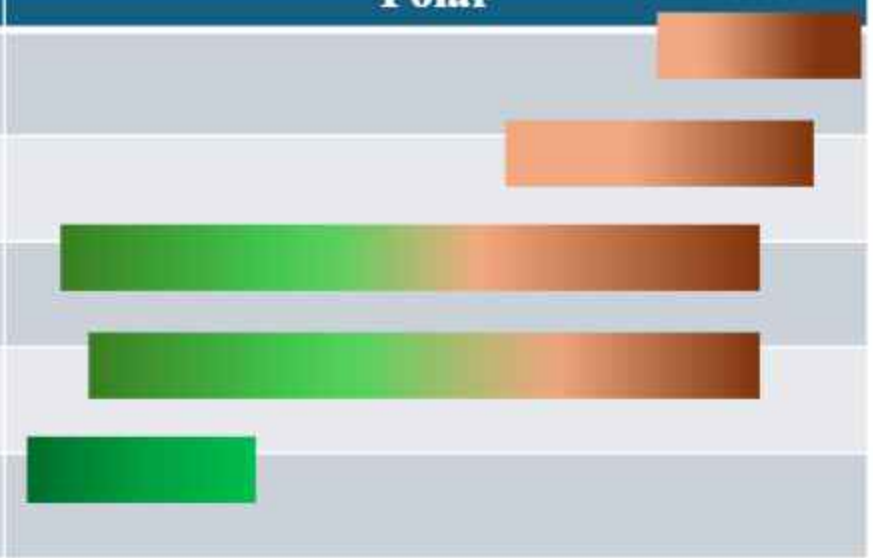
Pemilihan pelarut

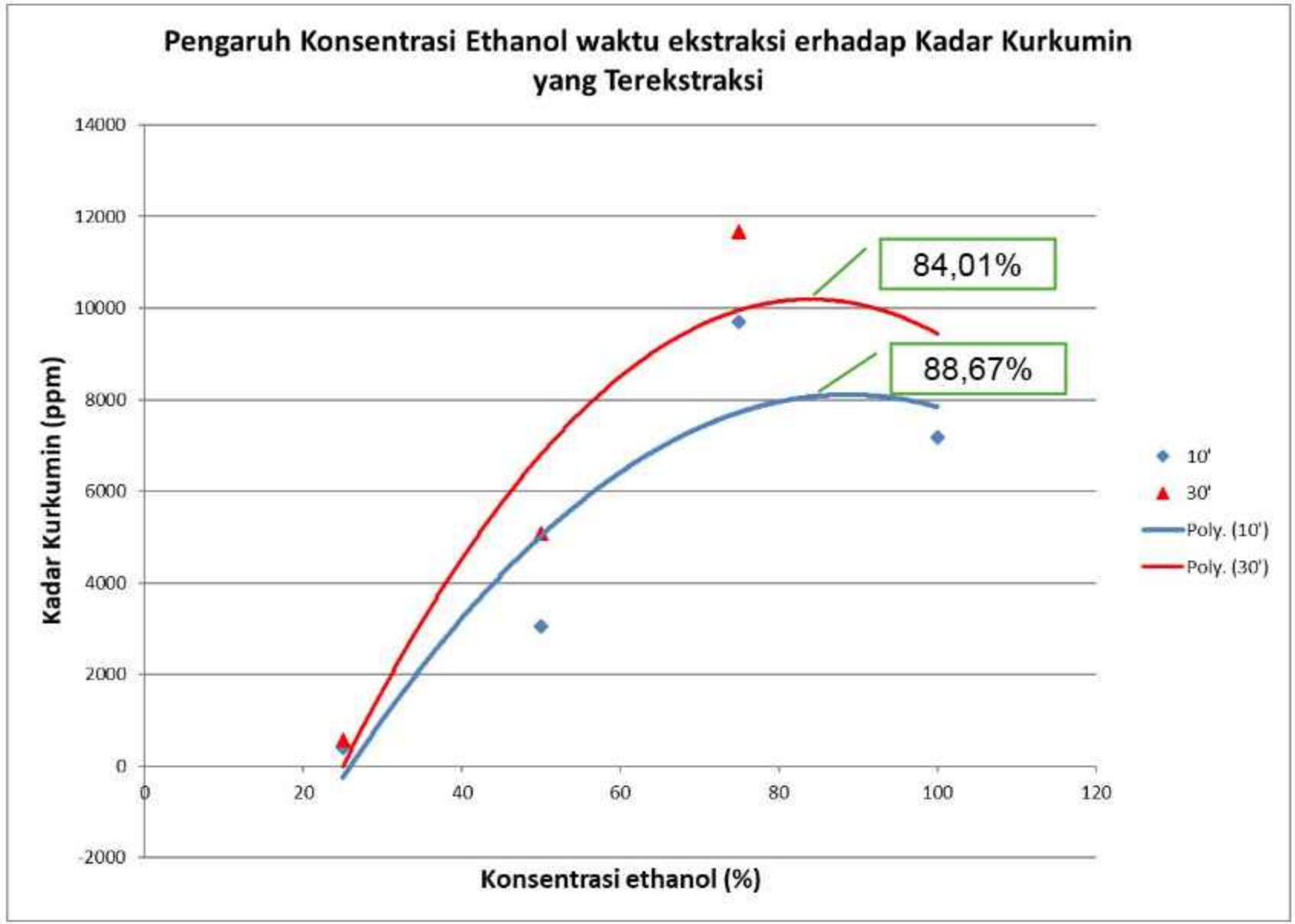
1. Kelarutan senyawa yg diharapkan: mampu melarutkan sebanyak mungkin zat berkhasiat dan sesedikit mungkin zat yg tdk diharapkan
2. Kemudahan kerja penguapan mudah (makin tinggi kadar etanol makin mudah diuapkan)
3. Tidak merusak zat berkhasiat (inert)
4. Viskositas rendah, stabil kimiawi, titik didih rendah, toksisitas rendah atau sesuai regulasi
5. Ekonomis

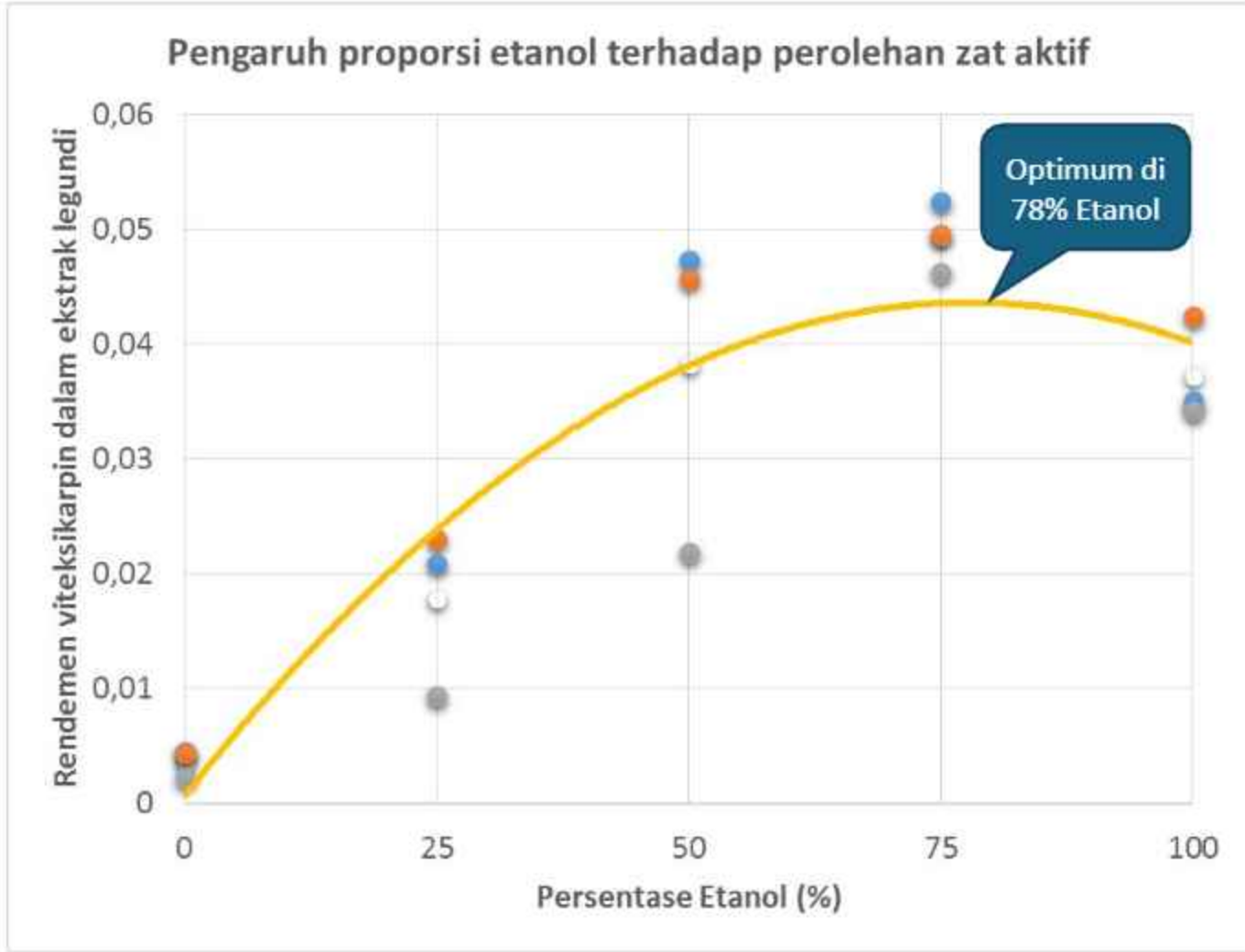
Polaritas dan kisaran polaritas

Pelarut	Polaritas	Titik Didih (°C)	Viskositas (cPoise)	Kelarutan dalam air (% b/b)
n-Heksan	0,009	69	0,33	0,001
Etil asetat	0,228	77	0,45	8,7
Metanol	0,762	65	0,60	100
Etanol	0,654	78	1,20	100
Air	1,000	100	1,00	100

Pelarut	Ilustrasi Kisaran polaritas
	Polar □ Non Polar
n-Heksan	
Etil asetat	
Metanol	
Etanol	
Air	




Pengaruh Konsentrasi Ethanol waktu ekstraksi erhadap Kadar Kurkumin yang Terekstraksi
Kadar Kurkumin (ppm)
14000
12000
10000
8000
6000
4000
2000
0
-2000
0
20
40
60
80
100
120
Konsentrasi ethanol (%)
84,01%
88,67%
10'
30'
Poly. (10')
Poly. (30')


Pengaruh proporsi etanol terhadap perolehan zat aktif
Rendemen viteksikarpin dalam ekstrak legundi
0,06
0,05
0,04
0,03
0,02
0,01
0
0
25
50
75
100
Persentase Etanol (%)
Optimum di
78% Etanol

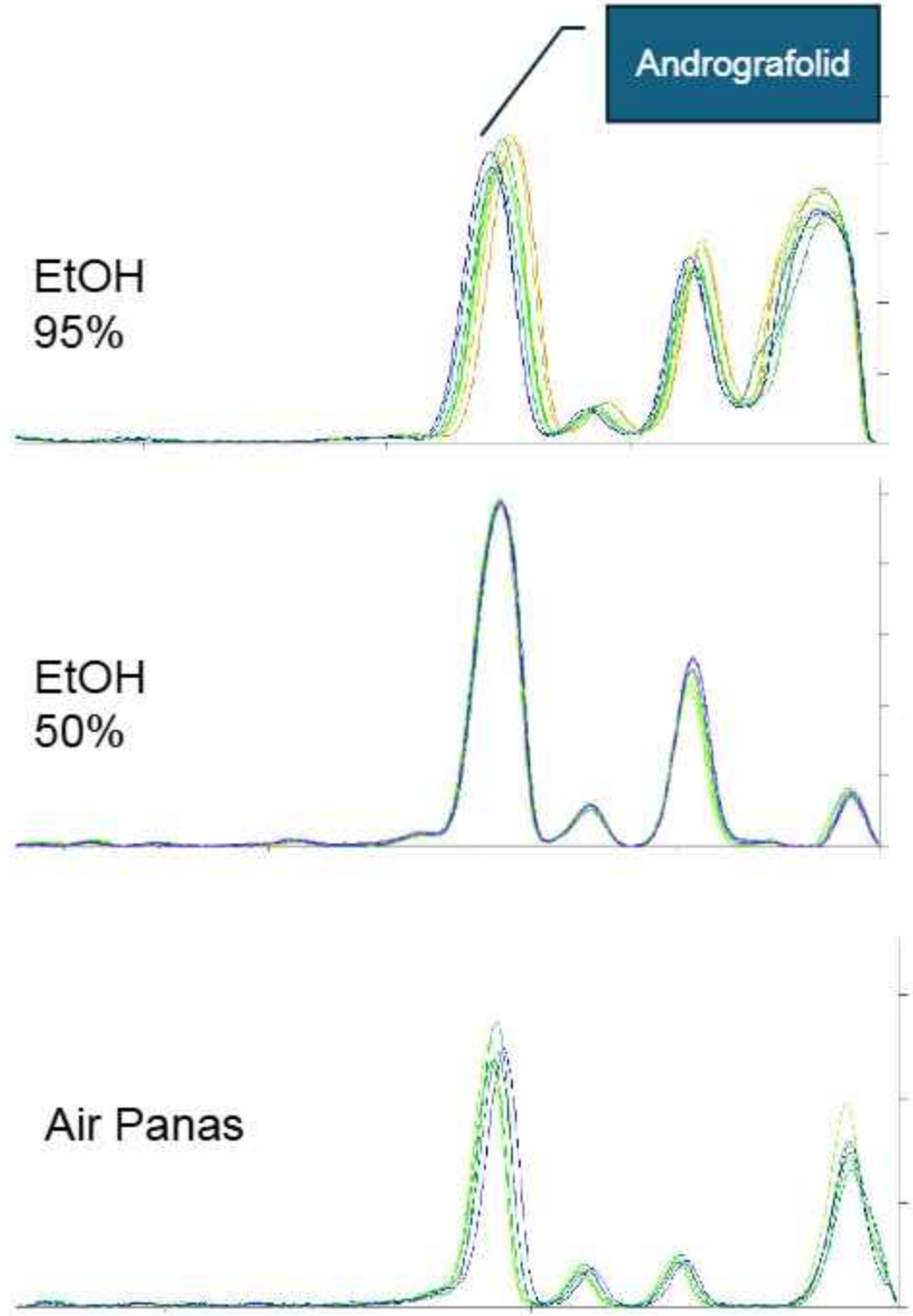
Pengaruh pelarut penyari terhadap profil kimiawi

Andrografolide merupakan diterpene yang secara struktur bersifat nonpolar, meski demikian ekstraksi dengan air panas memungkinkan untuk mendapatkannya dalam ekstrak.
Kadar andrografolid dalam ekstrak

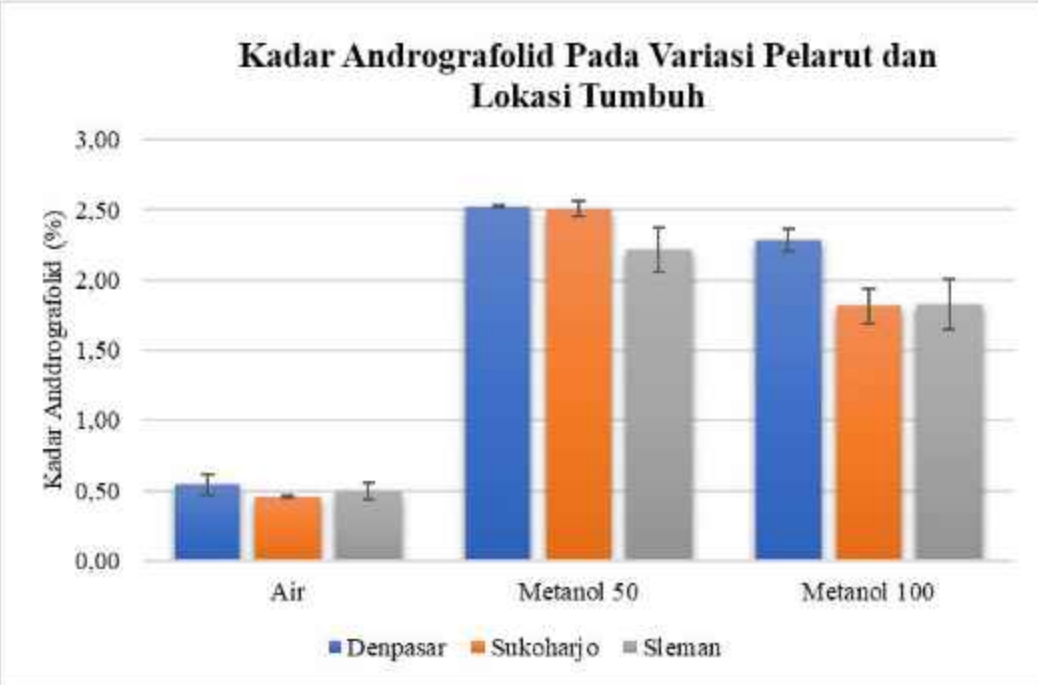
1. Air panas 0,48-0,62%
2. Etanol 50% 2,50-2,53%
3. Etanol 95% 2,21-2,37%

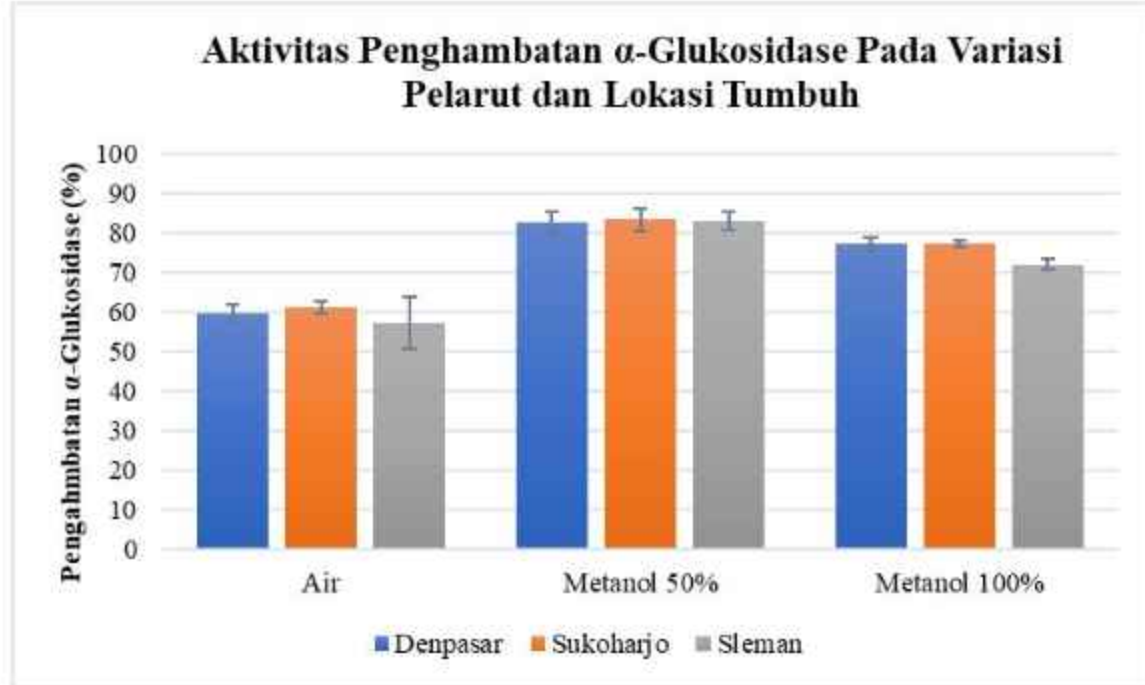
Selain itu terdapat perbedaan profil kromatogram hasil ekstraksi (gambar)

(Priyasana, 2023)



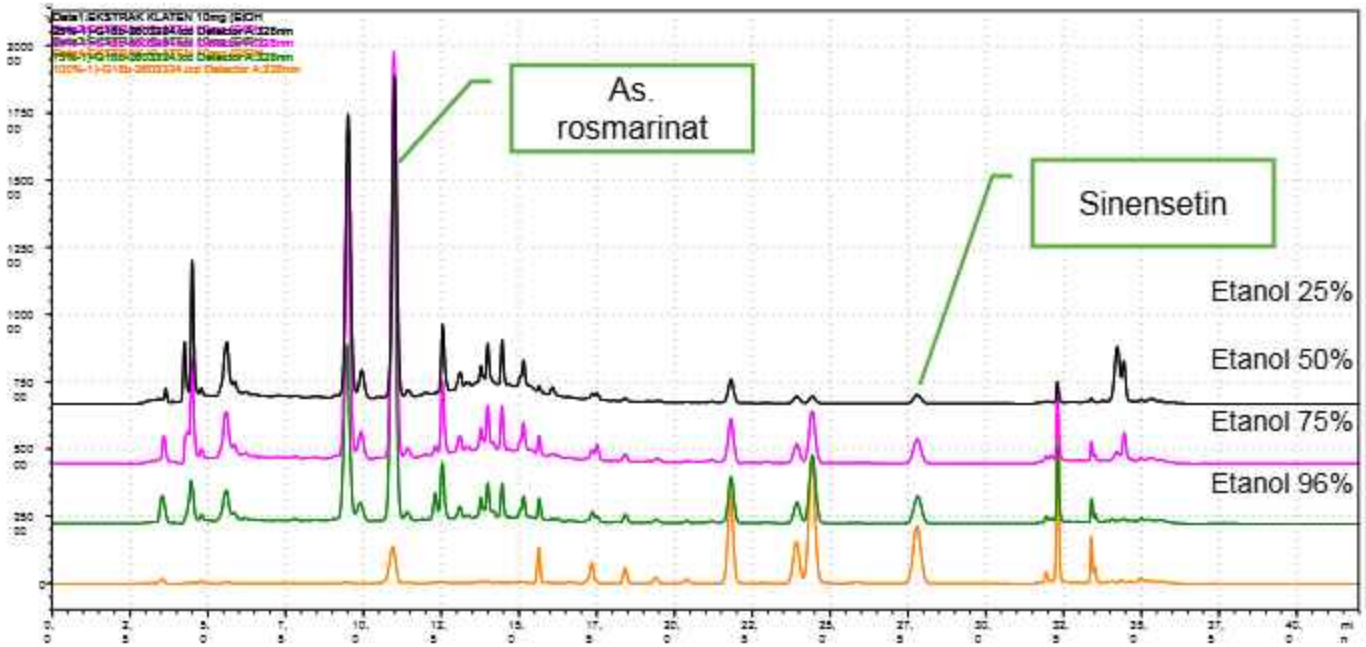
Keterkaitan pelarut ekstraksi, kadar marker dan aktivitas

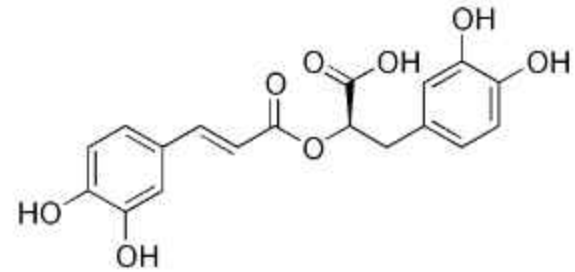


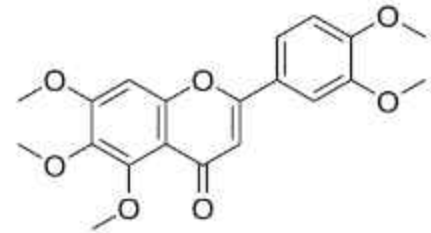


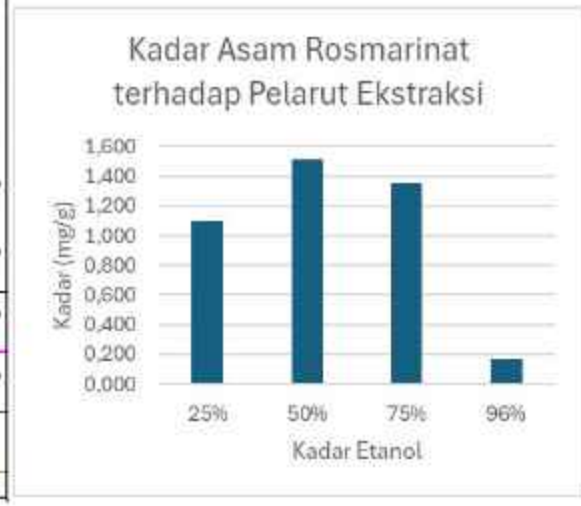
Priyasana dkk, 2023

Pengaruh konsentrasi etanol terhadap profil senyawa ekstrak *Orthosiphon aristatus*











Perbedaan kualitas pelarut menentukan komposisi senyawa dalam ekstrak dan selanjutnya berkaitan dengan efikasi dan keamanan.

Ramadhani, 2024

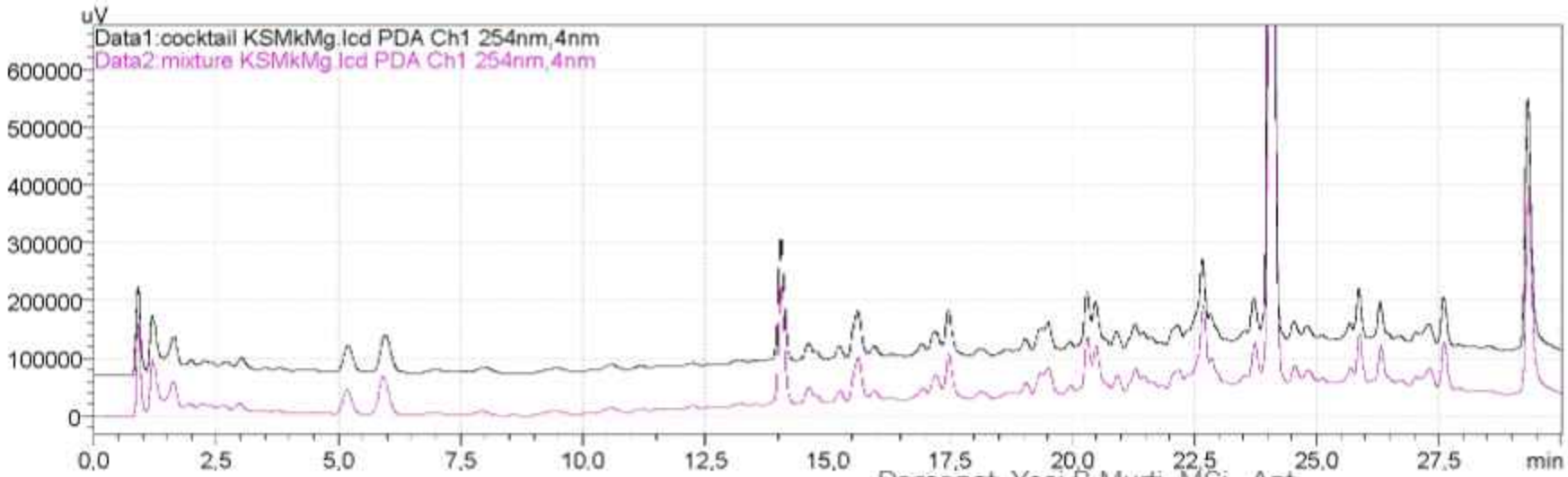
Ekstraksi Campuran simplisia (“cocktail”)

Kelebihan

- Efisien Waktu dan biaya
- Memudahkan proses produksi terkait dengan ketersediaan ekstraktor

Kekurangan

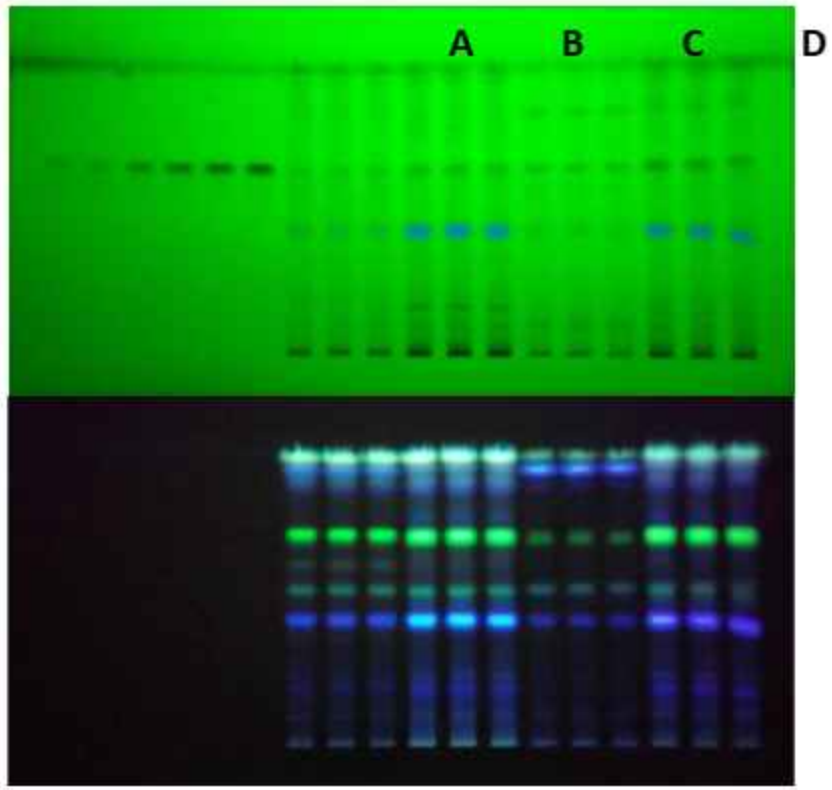
- Ekstraksi masing-masing komponen tidak optimal. Tidak dimungkinkan optimalisasi kadar zat aktif per bahan baku
- Variasi hasil ekstraksi lebih besar terkait dengan variasi bahan baku
- Tidak dimungkinkan standardisasi ekstrak dalam arti ke ajegan zat aktif perbahan baku



Ekstraksi Koktail

- Ekstraksi Koktail dapat dilakukan dengan asumsi bahwa zat aktif dari masing-masing penyusun ekstrak memiliki polaritas / kelarutan yang mirip.
- Standardisasi kualitas ekstrak bersandar kepada standardisasi bahan baku dan protocol produksi yang baik dan tetap.
- Kontrol kualitas idealnya mengacu kepada kadar marker masing-masing bahan baku penyusun ekstrak kesulitan akan terjadi jika polaritas marker yang digunakan berbeda serta adanya *sharing* marker (marker yg sama untuk spesies berbeda)

Variasi Profil Fitokimia Ekstrak Antar Produsen



Tiap IEBA mengembangkan dan mengoptimasi ekstraksi berdasarkan sumberdaya dan kesesuaian peralatan yang tersedia serta sumber bahan baku yang berbeda, sehingga terjadi variasi komposisi kimiawi dan kadar marker produknya.

Disamping adalah contoh perbandingan ekstrak pasak bumi dari 4 IEBA. Dapat di lihat dari perbandingan profil dan analisis kadar bahwa

1. Terjadi variasi kadar marker antar produk
2. Terjadi variasi profil/komposisi kimiawi

Murti (unpublished)

Hal-hal yang perlu diperhatikan terkait perubahan bahan baku

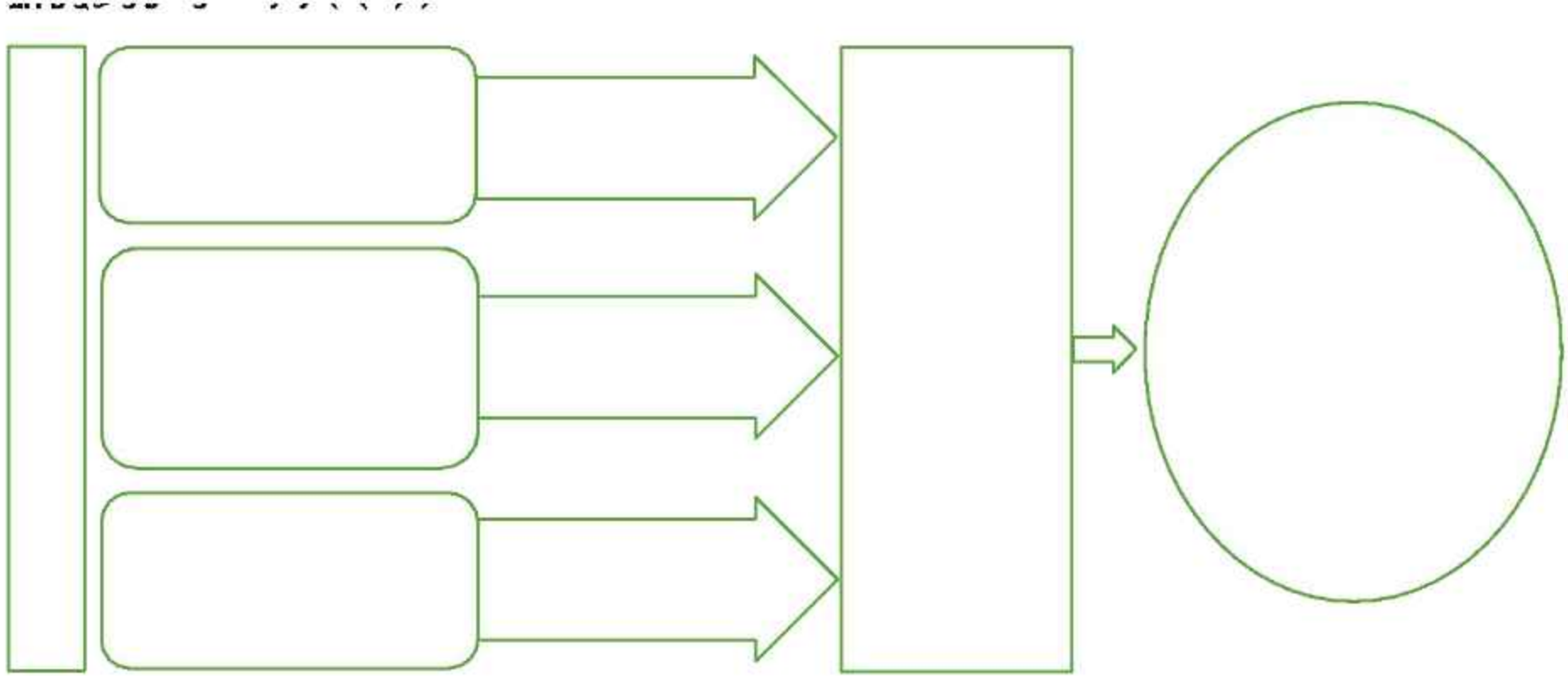


Konsep fitoekuivalen dikembangkan pertama kali di Jerman pertengahan 1990 untuk menunjukkan kesetaraan satu sediaan OBA dengan sediaan lainnya atau bahkan terhadap produk yang sudah teruji klinik.

Pengujian fitoekuivalensi ekstrak sulit dilakukan akibat kompleksitas senyawa dalam tumbuhan, akan tetapi perkembangan teknologi kromatografi dan spectroskopi dikombinasikan dengan pendekatan statistic multivariat (kemometrika) memungkinkan konsep ini dilaksanakan.

Martinelli, 2022

Standardisasi dan Fitoekuivalensi



Modifikasi dari:
Martinelli, 2022

Langkah analisis fitoekuivalensi

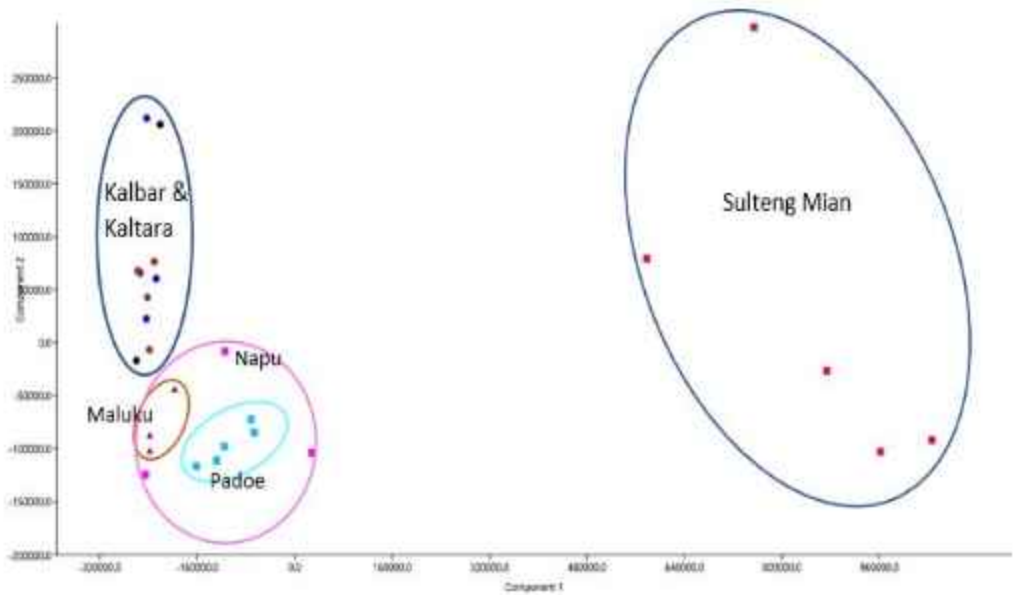
PENGUMPULAN DAN EKSTRAKSI SAMPEL

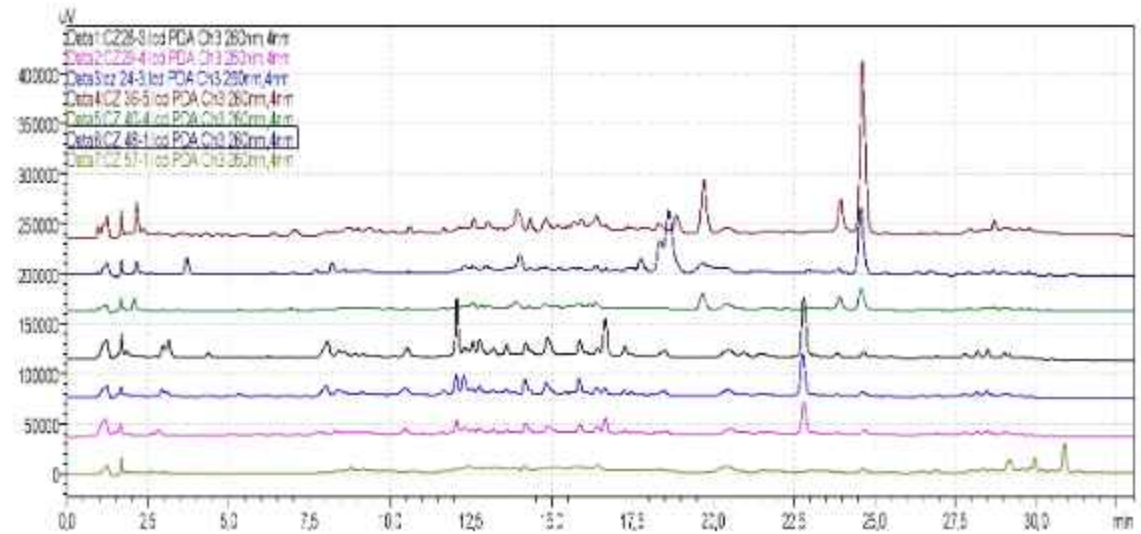
ANALISIS CHROMATOGRAFI /SPECTROSKOPI

ANALISIS KEMOMETRI

INTERPRETASI KEMOMETRIK

PCA of HPLC Fingerprint of *C. zedoaria* dari berbagai daerah





Murti (unpublished)

Standardisasi vs Fitoekuivalensi

- Standardisasi berbasis kadar marker yang biasanya hanya senyawa tunggal tidak menggambarkan keseluruhan senyawa dalam satu sediaan.
- OBA secara alamiah merupakan campuran kompleks yang bervariasi tergantung faktor-faktor intrinsik dan ekstrinsik, sehingga kadar marker yang setara (ekuivalen) antara dua produk belum tentu setara (ekuivalen) komposisi (jenis dan kadar) kimiawinya.
- Fitoekuivalensi menggambarkan kesetaraan (ekuivalensi) antar batch produksi sediaan atau antara satu produk dengan produk lain dengan bahan baku yang sama.

Martinelli, 2022

Penutup

Ekstraksi Bahan Alam memungkinkan penyederhanaan komponen obat bahan alam

Banyak Faktor yang berpengaruh terhadap efektivitas, selektivitas dan efisiensi ekstraksi

Pustaka

- Calixto, J.B. (2000) Efficacy, Safety, Quality Control, Marketing and Regulatory Guidelines for Herbal Medicines (Phytotherapeutic Agents). Brazilian Journal of Medical and Biological Research, 33, 179-189. http://dx.doi.org/10.1590/S0100-879X2000000200004
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- Kaggwa B, Anywar G, Munanura EI, Wangalwa R, Kyeyune H, Okella H, Kamba FP, Engeu OP. Application of the herbal chemical marker ranking system (Herb MaRS) to the standardization of herbal raw materials: a case study. BMC Complement Med Ther. 2023 Sep 30;23(1):348. doi: 10.1186/s12906-023-04178-3. PMID: 37777721; PMCID: PMC10542261.
- Pace R, Martinelli EM. The phytoequivalence of herbal extracts: A critical evaluation. Fitoterapia. 2022 Oct;162:105262. doi: 10.1016/j.fitote.2022.105262. Epub 2022 Aug 6. PMID: 35940385.
- TGA, Guidance on equivalence of herbal extracts in complementary medicines, https://www.tga.gov.au/resources/resource/guidance/guidance-equivalence-herbal-extracts-complementary-medicines#topofpage
- Dewi, Triska H. H. C., et al. "Optimasi Ekstraksi Oleoresin Cabai Rawit Hijau (Capsicum Frutescens L.) Melalui Metode Maserasi." *Jurnal Teknosains Pangan*, vol. 1, no. 1, 1 Oct. 2012.



Penjaminan Mutu Bahan Baku Ekstrak dan Produk Jadi Obat Bahan Alam (Quality Assurance of Extracted Raw Material and Finish of Natural Medicines Products)

Peningkatan Kapasitas dan Lokakarya tentang Standardisasi Mutu Ekstrak dan Penjaminan Mutu Produk Obat Bahan Alam

(Capacity Building and Workshop on Standardization of Extract Quality and Quality Control Assessment in Natural Medicines Products)

Badan POM Republik Indonesia
Jakarta, 19-21 Agustus 2025

Elfahmi

- Lecturer, Researcher of The School of Pharmacy, ITB
- Director of Research and Innovation – ITB
- Chairman of Excellence Center for Nutraceutical, ITB
- Founder and Owner Markherb
- Chairman of ASASI

MarkHerb Products of ebmiscitech

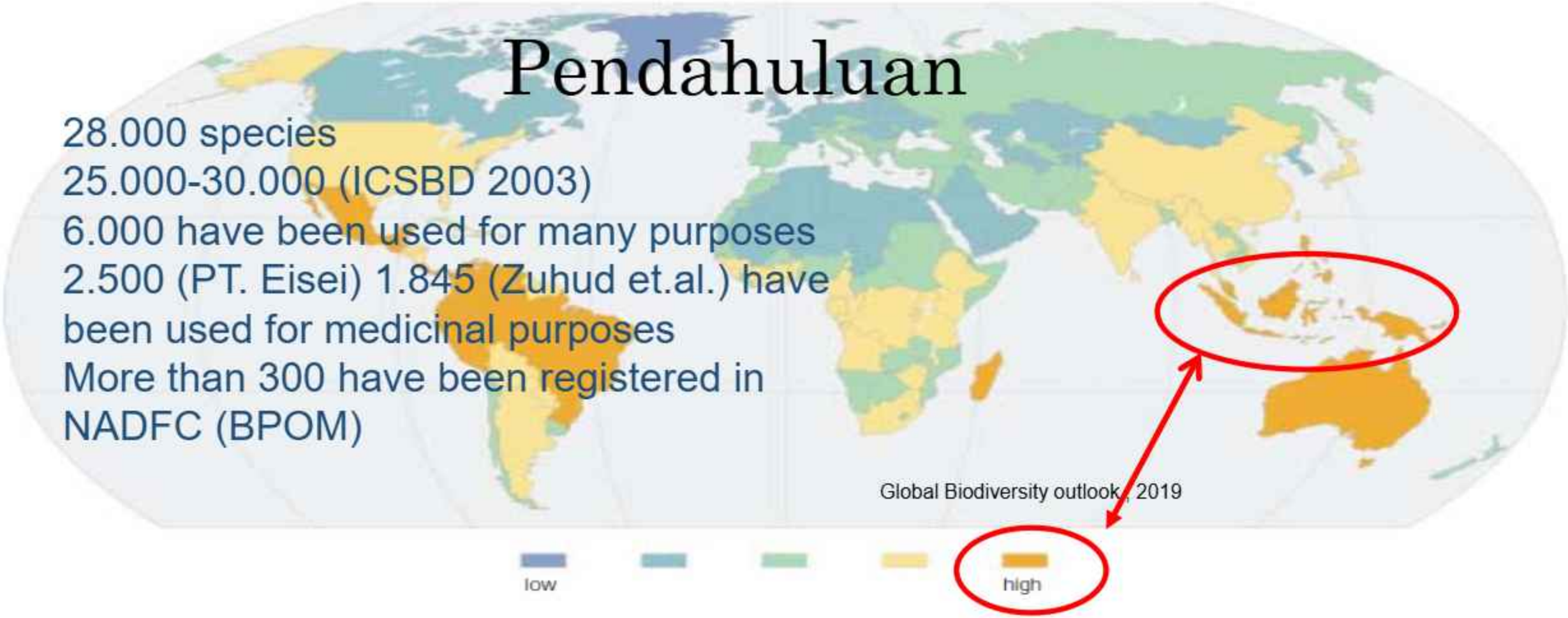
PUSAT PENELITIAN BIOSAINS & BIOTEKNOLOGI INSTITUT TEKNOLOGI BANDUNG

PUI-PT nutrasetikal

School of Pharmacy

Pendahuluan

28.000 species
25.000-30.000 (ICSBD 2003)
6.000 have been used for many purposes
2.500 (PT. Eisei) 1.845 (Zuhud et.al.) have been used for medicinal purposes
More than 300 have been registered in NADFC (BPOM)



Biodiversity at country level

- **Indonesia is 2nd biggest country on Biodiversity**
- **Including marine biodiversity and microbe, Indonesia become the nr. 1 in the world**
- **Estimation of 25% medicines contain chemical compounds from plants**
- **Jamu, Javanese/Indonesian Traditional Medicines is one of popular traditional medicines in the world, like TCM, Ayurveda, Kampo**

Obat Bahan Alam

Penjaminan Mutu :

- Safety (Kemanan)
- Efficacy Khasiat
- Quality (Mutu)
- (Cheaper) Murah

Active compounds (Senyawwa Aktif) ???

Penjaminan Mutu Obat Bahan Alam

- Penjaminan Mutu adalah metode sistematis yang digunakan untuk memastikan bahwa suatu produk atau layanan memenuhi persyaratan dan standar yang ditentukan
- Meliputi semua aspek yang terkait dengan manajemen kualitas, termasuk perencanaan, pelaksanaan, dan evaluasi.
- Tujuannya adalah menjamin bahwa sistem manajemen kualitas yang diterapkan efektif dan efisien, serta mampu menghasilkan produk atau layanan yang berkualitas tinggi.
- Biasanya dilakukan sebelum produk atau layanan tersebut diserahkan kepada pelanggan, agar masalah kualitas dapat diidentifikasi dan diatasi sejak awal

Penjaminan Mutu Obat Bahan Alam

- Menetapkan standar kualitas yang harus dipenuhi oleh produk atau layanan.
- Menyusun dan mengimplementasikan sistem manajemen kualitas yang sesuai dengan standar yang telah ditetapkan.
- Menetapkan prosedur dan instruksi yang harus diikuti dalam proses produksi atau layanan.
- Mengawasi proses produksi atau layanan untuk memastikan bahwa standar kualitas yang ditetapkan dipenuhi.
- Menganalisis data kualitas dan mengambil tindakan yang diperlukan untuk mengatasi masalah kualitas yang terjadi.
- Menyusun laporan hasil pengawasan dan menyampaikannya kepada pihak yang berwenang.
- Mengembangkan dan mengimplementasikan program pelatihan bagi anggota tim yang terkait dengan manajemen kualitas.
- Mengkomunikasikan dengan pelanggan dan vendor terkait dengan masalah kualitas yang terjadi.
- Membantu dalam menyusun dan mengupdate dokumen-dokumen manajemen kualitas yang relevan.

Variasi kandungan kimia tanaman obat

Kandungan senyawa aktif dipengaruhi oleh banyak faktor:

- Ketinggian tempat tumbuh
- Panen dan pasca panen
- Keaneka ragaman genetik
- Lingkungan tempat tumbuh
- Faktor biotik
- Tanah dan nutrisi
- Air
- Temperatur
- Kualitas, Intensitas,
- Lama pencahayaan

KONTAMINAN

- MIKROBA ATAU TOKSINNYA
- PESTISIDA DAN FUMIGAN
- LOGAM BERAT
- SENYAWA SINTETIS
- PRODUK BINATANG

PROSES

- PEMANASAN
- PELARUT
- SISA PELARUT
- PENANDAAN
- PENYIMPANAN

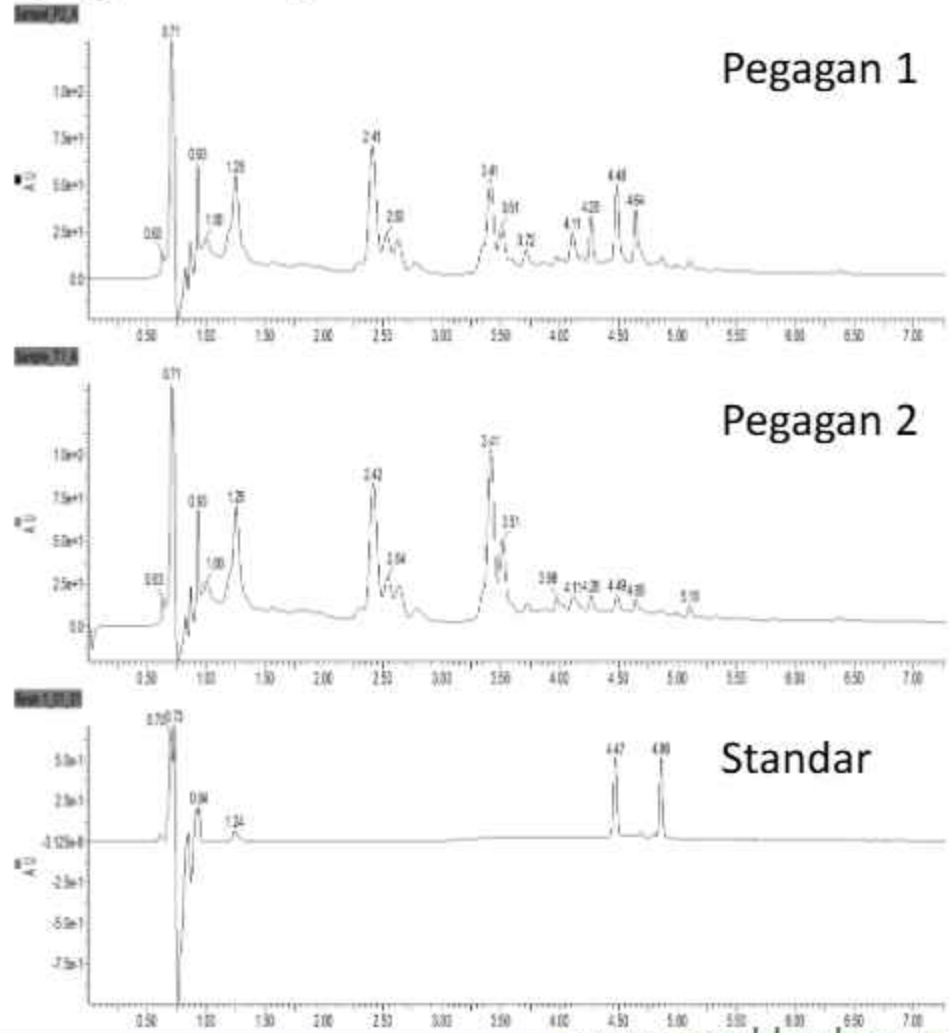
Tanpa kontrol ???

@Suganda

Variasi kandungan kimia tanaman obat

Analisis asiatikosida-madekasosida pada herba pegagan dengan UPLC-UV

Asal Sampel	Kadar CATs (%, b/b kering)		Keterangan
	Asiatikosida (A)	Madekasosida (M)	
Bali	0.0036	0,185	Herba daun campur batang
Jatinangor	0,067	0,234	Herba daun campur batang; tanpa naungan; petak 1
Jatinangor	0,263	0,299	Herba daun campur batang; tanpa naungan; petak 2
Jatinangor	0,190	0,517	Herba daun campur batang; dengan naungan; petak 1
Jatinangor	0,261	0,964	Herba daun campur batang; dengan naungan; petak 2
Tanjungsari	3,152	8,938	Herba daun tanpa batang
Semarang	0,468	1,755	Herba daun campur batang
Surabaya	0,988	1,538	Herba daun campur batang; banyak tanah
Thailand (SNP)	0,800	1,66	Ekstrak serbuk pegagan
Thailand (SNP)	0,592	1,44	Ekstrak cair pegagan



Farmakope Herbal Indonesia
Karakteristik simplisia pegagan mengandung asiatikosida tidak kurang dari 0,07%

Standardisasi

BADAN STANDARDISASI NASIONAL

PERATURAN BADAN STANDARDISASI NASIONAL
REPUBLIK INDONESIA
NOMOR 8 TAHUN 2022
TENTANG
PENGEMBANGAN STANDAR NASIONAL INDONESIA

DENGAN RAHMAT TUHAN YANG MAHA ESA

KEPALA BADAN STANDARDISASI NASIONAL REPUBLIK INDONESIA,

BAB I KETENTUAN UMUM

Pasal 1.

1. **Standardisasi** adalah proses merencanakan, merumuskan, menetapkan, menerapkan, memberlakukan, memelihara, dan mengawasi standar yang dilaksanakan secara tertib, dan bekerja sama dengan semua pemangku kepentingan.
2. Penilaian Kesesuaian adalah kegiatan untuk menilai bahwa barang, jasa, sistem, proses, atau personal **telah memenuhi persyaratan acuan.**
3. **Standar** adalah persyaratan teknis atau sesuatu yang dibakukan, termasuk tata cara dan metode yang disusun berdasarkan konsensus semua pihak, pemerintah, atau keputusan internasional yang terkait dengan memperhatikan syarat keselamatan, keamanan, kesehatan, lingkungan hidup, perkembangan ilmu pengetahuan dan teknologi, pengalaman, serta perkembangan masa kini dan masa depan untuk memperoleh manfaat yang sebesar-besarnya.
4. .....

❖ Pendahuluan: *Milestone* Farmakope Herbal Indonesia (FHI)



Materia Medika Indonesia 1-6, (977-1986)

2008
FHI Edisi 1



70 Monografi

2010
FHI
Supl 1,
Edisi 1



2013
FHI
Supl 2,
Edisi 1



2015
FHI
Supl 3,
Edisi 1



2017
FHI
Edisi 2



253 Monografi
116 Tanaman obat

2022
FHI Supl 1
Edisi 2

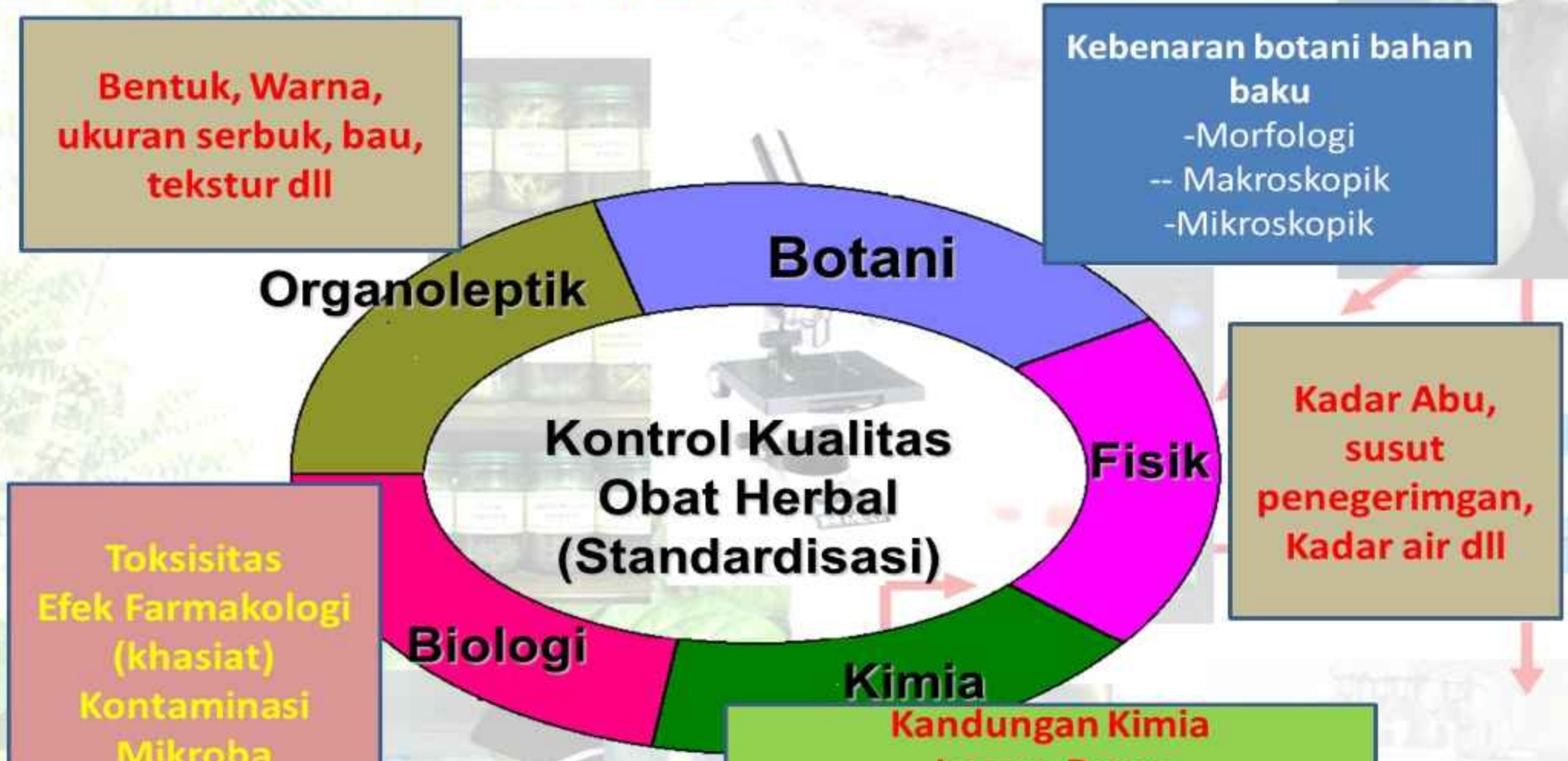
FHI Ed 2
Sup 1
110
Monografi
dari 55
tumbuhan
obat

2023
FHI
Supl 2,
Edisi 2

FHI Ed 2
Sup 2
62
Monografi
dari 62
tumbuhan
obat

Pembaharuan MMI (2006-2007)

Parameter Spesifik dan non Spesifik



STANDARDIZATION

Parameter Pengujian FHI non biologi

Monografi Simplisia

- Senyawa identitas
- Pola Kromatografi
- Susut pengeringan
- Abu total
- Abu tidak larut asam
- Sari larut air
- Sari larut etanol
- Kandungan kimia

Monografi Ekstrak

- Pembuatan ekstrak
- Rendemen
- Pemerian
- Senyawa Identitas
- Kadar air
- Abu tidak larut asam
- Sari larut air
- Sari larut etanol
- Kandungan kimia

Parameter Spesifik dan non Spesifik

Parameter Spesifik

- Identitas simplisia atau ekstrak
- Organoleptis
- Senyawa terlarut dalam simplisia atau ekstrak
- Kandungan Kimia

Parameter non spesifik

- Susut pengeringan
- Bobot Jenis
- Kadar air
- Kadar abu
- Sisa pelarut
- Residu pestisida
- Cemaran logam berat
- Cemaran mikroba

Parameter Mutu Produk jadi obat bahan alam

BADAN PENGAWAS OBAT DAN MAKANAN
REPUBLIK INDONESIA

PERATURAN BADAN PENGAWAS OBAT DAN MAKANAN
NOMOR 29 TAHUN 2023
TENTANG
PERSYARATAN KEAMANAN DAN MUTU OBAT BAHAN ALAM

BAB 1, Pasal 1, ayat 3

Produk Jadi adalah produk yang telah melalui seluruh tahap proses pembuatan.

Pasal 3

(1) Pelaku Usaha wajib menjamin keamanan dan mutu Obat Bahan Alam yang dibuat, diimpor, dan/atau diedarkan di wilayah Indonesia sebelum dan selama beredar.
(2) Untuk menjamin keamanan dan mutu Obat Bahan Alam sebagaimana dimaksud pada ayat (1), Pelaku Usaha wajib memenuhi persyaratan keamanan dan mutu.
(3) Persyaratan keamanan dan mutu sebagaimana dimaksud pada ayat (2) merupakan persyaratan untuk:
    a. Bahan Obat Bahan Alam; dan
    b. Produk Jadi.

Pasal 4

(1) Persyaratan keamanan dan mutu Bahan Obat Bahan Alam sebagaimana dimaksud dalam Pasal 3 ayat (3) huruf a tercantum dalam farmakope herbal Indonesia atau materia medika Indonesia yang diterbitkan oleh menteri yang menyelenggarakan urusan pemerintahan di bidang kesehatan.
(2) Dalam hal persyaratan keamanan dan mutu Bahan Obat Bahan Alam belum diatur dalam farmakope herbal Indonesia atau materi medika Indonesia sebagaimana dimaksud pada ayat (1), persyaratan keamanan dan mutu yang digunakan dapat mengacu:
    a. standar persyaratan keamanan dan mutu Bahan Obat Bahan Alam dalam farmakope Indonesia atau farmakope negara lain;
    b. standar persyaratan keamanan dan mutu Bahan Obat Bahan Alam yang berlaku secara internasional;
    c. referensi ilmiah mengenai standar persyaratan keamanan dan mutu Bahan Obat Bahan Alam yang diakui: dan/atau
    d. data ilmiah mengenai standar persyaratan keamanan dan mutu Bahan Obat Bahan Alam yang sahih.

Parameter Mutu Produk jadi obat bahan alam

- ✓ Produk Jadi : obat dalam; dan obat luar.
- ✓ Bentuk sediaan Obat Bahan Alam berupa kapsul, dapat berisi: ekstrak kering; bahan cair berupa minyak; dan/atau serbuk simplisia tertentu.
- ✓ Bentuk sediaan Obat Bahan Alam berupa tablet/kaplet, dapat berisi:
  a. ekstrak kering; dan/atau
  b. serbuk simplisia tertentu.
- ✓ Dalam hal bentuk sediaan kapsul berisi bahan cair berupa minyak, Pelaku Usaha dalam membuat Obat Bahan Alam wajib menggunakan:
  a. kapsul lunak; atau
  b. kapsul yang dibuat dengan teknologi khusus.
- ✓ Serbuk simplisia tertentu, dilakukan evaluasi berdasarkan pertimbangan ilmiah terkait teknologi pembuatan, dosis, keamanan, dan khasiat.

Parameter Mutu Produk jadi obat bahan alam

- ✓ Dalam hal diperlukan pemastian terhadap pemenuhan persyaratan keamanan dan mutu Produk Jadi selain sebagaimana dimaksud dalam Pasal 8, Pelaku Usaha harus melakukan pengujian terhadap parameter uji Produk Jadi yang meliputi:
  a. kadar senyawa penanda pada Bahan Obat Bahan Alam dan Produk Jadi obat herbal terstandar;
  b. kadar senyawa penanda pada Bahan Obat Bahan Alam dan Produk obat Jadi fitofarmaka;
  c. residu pelarut Bahan Obat Bahan Alam dan/atau Produk Jadi dengan pelarut ekstraksi selain etanol dan/atau air yang ditetapkan penggunaannya berdasarkan persetujuan registrasi
  d. bahan dan/atau produk lain yang berdasarkan kajian membutuhkan uji kualitatif dan/atau kuantitatif.

Pemenuhan persyaratan keamanan dan mutu dibuktikan melalui pengujian di laboratorium yang terakreditasi dan/atau laboratorium internal industri atau usaha Obat Bahan Alam yang diakui oleh Badan Pengawas Obat dan Makanan.

Parameter Mutu Produk jadi obat bahan alam

LAMPIRAN II
PERATURAN BADAN PENGAWAS OBAT DAN MAKANAN
NOMOR 29 TAHUN 2023
TENTANG
PERSYARATAN KEAMANAN DAN MUTU OBAT BAHAN ALAM

JENIS BENTUK SEDIAAN DAN PARAMETER UJI PRODUK JADI

A. DEFINISI

1. Sediaan Galenik yang selanjutnya disebut Ekstrak adalah sediaan kering, kental atau cair dibuat dengan menyari Simplisia nabati atau hewani menurut cara yang sesuai, di luar pengaruh cahaya matahari langsung.
2. Simplisia adalah bahan alam yang telah dikeringkan yang digunakan untuk pengobatan dan belum mengalami pengolahan, kecuali dinyatakan lain suhu pengeringan tidak lebih dari 60°C (enam puluh derajat celcius).
3. Rajangan adalah sediaan Obat Bahan Alam berupa satu jenis Simplisia atau campuran beberapa jenis Simplisia, yang cara penggunaannya dilakukan dengan pendidihan atau penyeduhan dengan air panas.
4. Rajangan Obat Luar adalah sediaan Obat Bahan Alam berupa satu jenis Simplisia atau campuran beberapa jenis Simplisia, yang digunakan untuk obat luar.
5. Serbuk adalah sediaan Obat Bahan Alam berupa butiran homogen dengan derajat halus yang sesuai, terbuat dari Simplisia atau campuran dengan Ekstrak yang cara penggunaannya diseduh dengan air panas.
6. Serbuk Instan adalah sediaan Obat Bahan Alam berupa butiran homogen dengan derajat halus yang sesuai, terbuat dari Ekstrak yang cara penggunaannya diseduh dengan air panas atau dilarutkan dalam air dingin.
7. Efervesen adalah sediaan padat Obat Bahan Alam, terbuat dari Ekstrak dan/atau simplisia tertentu, mengandung natrium bikarbonat dan asam organik yang menghasilkan gelembung gas (karbon dioksida) saat dimasukkan ke dalam air.
8. Pil adalah sediaan padat Obat Bahan Alam berupa masa bulat, terbuat dari serbuk Simplisia dan/atau Ekstrak.
9. Kapsul adalah sediaan Obat Bahan Alam yang terbungkus cangkang keras.
10. Kapsul Lunak adalah sediaan Obat Bahan Alam yang terbungkus cangkang lunak.
11. Tablet/Kaplet adalah sediaan Obat Bahan Alam padat kompak, dibuat secara kempa cetak, dalam bentuk tabung pipih, silindris, atau bentuk lain, kedua permukaannya rata atau cembung, termasuk tablet salut.
12. Granul adalah sediaan Obat Bahan Alam berupa butiran terbuat dari Ekstrak yang telah melalui proses granulasi yang cara penggunaannya diseduh dengan air panas atau dilarutkan dalam air dingin.
13. Pastiles adalah sediaan padat Obat Bahan Alam berupa lempengan pipih, umumnya berbentuk segi empat, terbuat dari Serbuk Simplisia dan/atau Ekstrak.
14. Dodol/Jenang adalah sediaan padat Obat Bahan Alam dengan konsistensi lunak tetapi liat, terbuat dari Serbuk Simplisia dan/atau Ekstrak.
15. Film Strip adalah sediaan padat Obat Bahan Alam berbentuk lembaran tipis yang digunakan secara oral.
16. Cairan Obat Dalam adalah sediaan Obat Bahan Alam berupa minyak, larutan, suspensi atau emulsi, terbuat dari Serbuk Simplisia dan/atau Ekstrak dan digunakan sebagai obat dalam.
17. Cairan Obat Luar adalah sediaan Obat Bahan Alam berupa minyak, larutan, suspensi atau emulsi, terbuat dari Simplisia dan/atau Ekstrak dan digunakan sebagai obat luar.
18. Losio adalah sediaan Cairan Obat Bahan Alam mengandung Serbuk Simplisia, Eksudat, Ekstrak, dan/atau minyak yang terlarut atau terdispersi berupa suspensi atau emulsi dalam bahan dasar Losio dan ditujukan untuk pemakaian topikal pada kulit.
19. Parem adalah sediaan padat atau cair Obat Bahan Alam, terbuat dari Serbuk Simplisia dan/atau Ekstrak dan digunakan sebagai obat luar.

Parameter Mutu Produk jadi obat bahan alam

20. Salep adalah sediaan Obat Bahan Alam setengah padat terbuat dari Ekstrak yang larut atau terdispersi homogen dalam dasar Salep yang sesuai dan ditujukan untuk pemakaian topikal pada kulit, termasuk balsem.
21. Krim adalah sediaan Obat Bahan Alam setengah padat mengandung satu atau lebih Ekstrak terlarut atau terdispersi dalam bahan dasar Krim yang sesuai dan ditujukan untuk pemakaian topikal pada kulit.
22. Gel adalah sediaan Obat Bahan Alam setengah padat mengandung satu atau lebih Ekstrak dan/atau minyak yang terlarut atau terdispersi dalam bahan dasar Gel dan ditujukan untuk pemakaian topikal pada kulit.
23. Oral Gel adalah sediaan Obat Bahan Alam setengah padat mengandung satu atau lebih Ekstrak dan/atau minyak yang terlarut atau terdispersi dalam bahan dasar Gel dan ditujukan untuk pemakaian oral.
24. Serbuk Obat Luar adalah sediaan Obat Bahan Alam berupa butiran homogen dengan derajat halus yang sesuai, terbuat dari serbuk simplisia dan/atau ekstrak dan/atau minyak dan digunakan sebagai obat luar dengan cara penggunaan yang sesuai kecuali luka terbuka.
25. Pilis adalah sediaan padat Obat Bahan Alam, terbuat dari Serbuk Simplisia dan/atau Ekstrak dan digunakan sebagai obat luar yang digunakan di dahi dan di pelipis.
26. Tapel adalah sediaan padat Obat Bahan Alam, terbuat dari Serbuk Simplisia dan/atau Ekstrak dan digunakan sebagai obat luar yang digunakan di perut.
27. Plester adalah sediaan Obat Bahan Alam terbuat dari bahan yang melekat kuat dapat berisi Serbuk Simplisia, Minyak dan/atau Ekstrak, digunakan sebagai obat luar dengan cara penggunaan yang sesuai.
28. Supositoria untuk wasir adalah sediaan padat Obat Bahan Alam, terbuat dari Ekstrak yang larut atau terdispersi homogen dalam dasar supositoria yang sesuai, umumnya meleleh, melunak atau melarut pada suhu tubuh dan cara penggunaannya melalui rektal.
29. Tablet Kunyah adalah sediaan tablet yang dimaksudkan untuk dikunyah, memberikan residu dengan rasa enak dalam rongga mulut, mudah ditelan dan tidak meninggalkan rasa pahit atau tidak enak.
30. *Gummy Chewable* adalah sediaan berwujud padat kenyal yang dibuat dari gelatin dan Bahan Tambahan lain yang sesuai, bertujuan sebagai Obat Bahan Alam dan bukan pangan biasa.
31. Aerosol adalah sediaan yang mengandung Obat Bahan Alam dalam larutan atau dalam suspensi, dikemas di bawah tekanan, dan dilepaskan saat aktivasi dari sistem katup yang sesuai dan digunakan sebagai obat luar kecuali luka terbuka.

Persyaratan mutu lengkap untuk berbagai sediaan jadi bisa dibaca pada Perka BPOM RI

BADAN PENGAWAS OBAT DAN MAKANAN
REPUBLIK INDONESIA

PERATURAN BADAN PENGAWAS OBAT DAN MAKANAN
NOMOR 29 TAHUN 2023
TENTANG
PERSYARATAN KEAMANAN DAN MUTU OBAT BAHAN ALAM

Metode yang dipakai untuk analisis saat ini

- KLT Densitometer: Senyawa spesifik
- Spektrofotometer UV: Flavonoid total, Fenol total, dll
- Destilasi : minyak atisri
- Pola KLT
- Metode khusus seperti gravimetri, dll

HPLC ??????

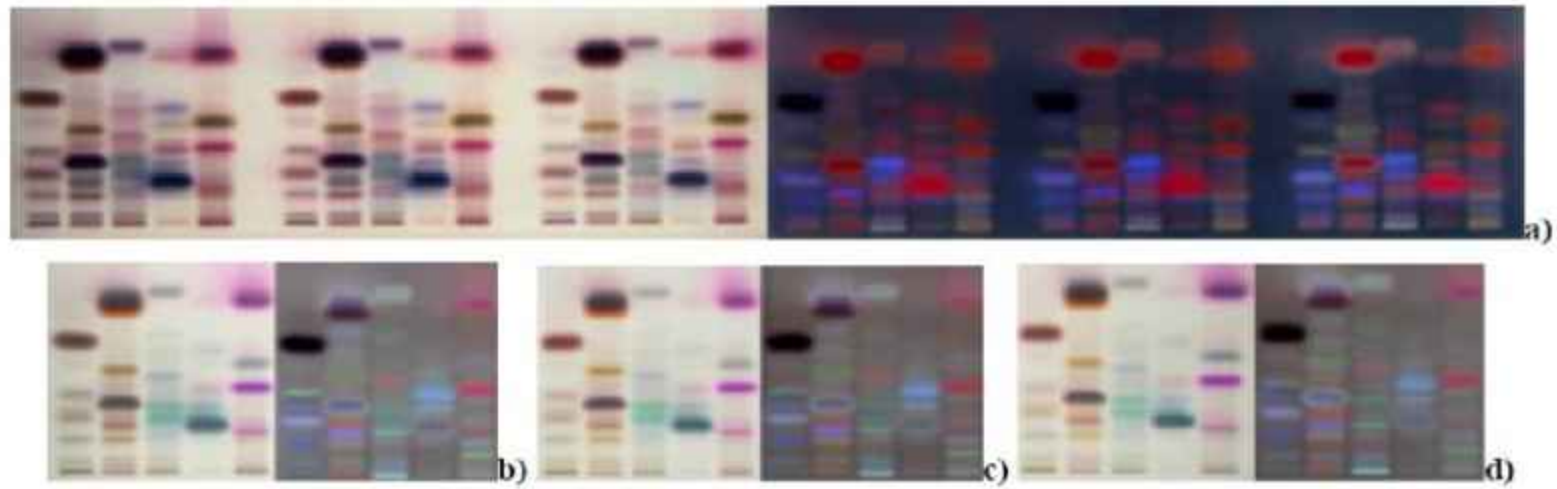


Figure 9 Subsequent treatment

a) Anisaldehyde reagent *R*, detected direct after derivatization; b) stored 120 minutes wrapped in aluminium foil; c) stored 120 minutes covered with a glass plate and wrapped in aluminium foil; d) stored 120 minutes covered with a glass plate

Tantangan untuk standardisasi

- Metode analisis
- Kesiapan laboratorium
- Biaya analisis????
- Senyawa Marker
- *Willingness*
- SDM
- Monografi yang ada adalah simplisia dan ekstrak, tidak ada monografi sediaan
- Dan lain-lain

Standardisasi ------ Kualitas produk obat herbal ----- Kontribusi untuk bangsa

Verifikasi dan Validasi Metode Analisis

Verifikasi dan validasi metode analisis

- Konfirmasi untuk memastikan bahwa metode atau prosedur analisis yang digunakan telah memenuhi persyaratan
- Memastikan metode tersebut menghasilkan hasil, juga data yang valid
- Pada verifikasi metode analisa, parameter minimal yang wajib untuk diuji adalah presisi dan akurasi.
- Parameter lain yang dapat diuji pada verifikasi metode analisa diantaranya adalah linearitas, Limit of Detection (LOD), Limit of Quantification (LOQ), spesifisitas dan *robustness*

Jenis-jenis bahan baku untuk produk obat herbal



Catatan : efek sinergisme dan antagonis???.....perlu dilihat satu persatu

Isolat sebagai senyawa marker

Standardisasi:
Terkait dengan senyawa berkhasiat atau marker



Production of active compounds or markers from medicinal plants

Local Market & Field Cultivation

Selection, Drying & Crushing

Plant Extraction

Plant Extracts Fractionation and Chromatography Separation

Pure Compounds

HPLC

NMR

UV

MS

Purity Determination, Structure Identification, and Product Certification

Product Packaging

Products Marketing



www.markherb.com

MarkHerb

Sharing SF ITB Markherb

Kelor (*Moringa oleifera*)



Moringa leaves

Moringa extractor

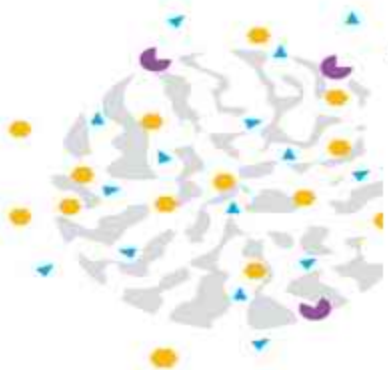
Waste recovery

Ultrafiltration or centrifuge

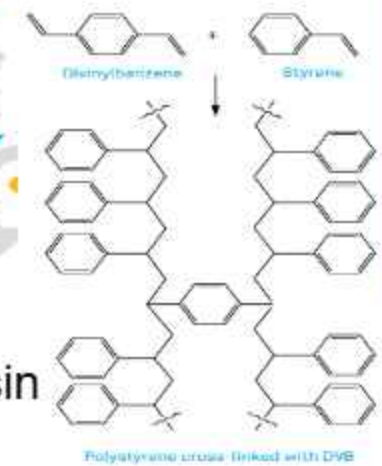
Green extraction and advance fractionations

Scale-up Purification with Reverse-Phase Chromatography

Flavonoid glycosides
(Fractions eluted with 20-50% alcohol)



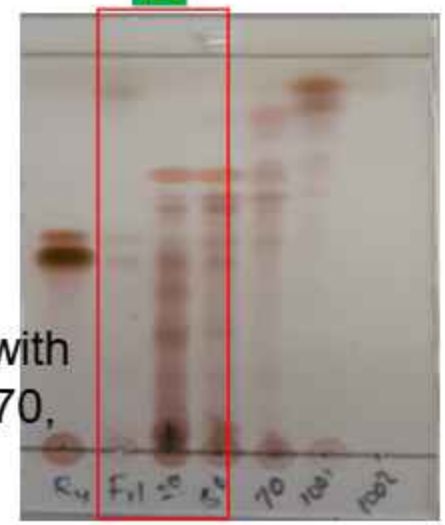
Macroporous resin



Resin-filled column

Nicotiflorin
Rutin

Gradient elution with alcohol (20, 50, 70, 100%)

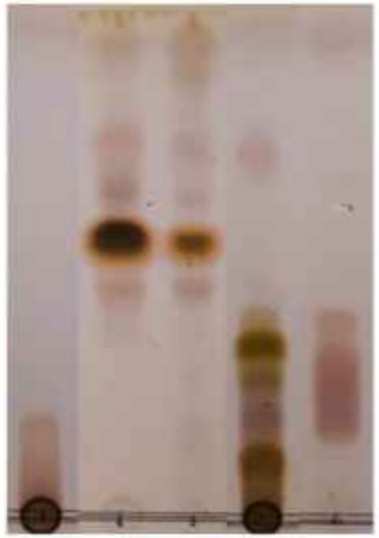


Collector

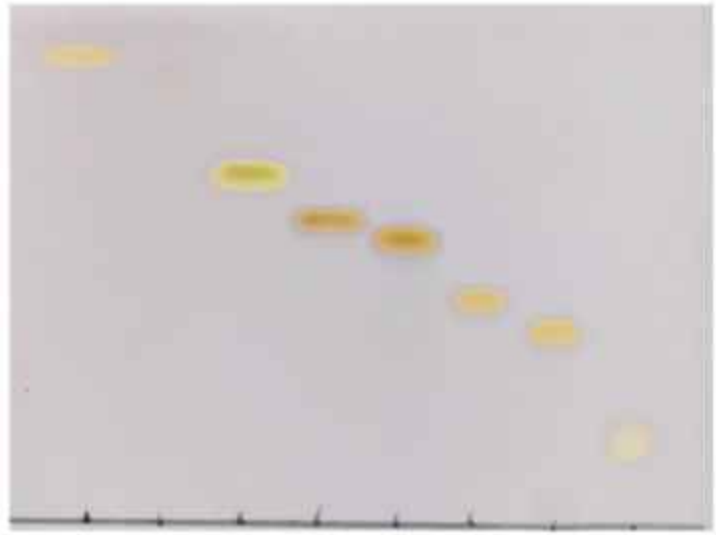
Sharing SF ITB
Markherb

Kelor (*Moringa oleifera*)

Kelor (Ekstrak, Fraksi, Isolat)



Profil KLT setiap subfraksi hasil kromatografi flash



KLT isolat bioflavonoid kelor dari setiap fraksi/subfraksi

Keterangan:

1. Kaempferol (**fraksi 4**)
2. Quercetin (**fraksi 3**)
3. Niazirin (**subfraksi B**)
4. Astragalin (**subfraksi D**)
5. Hyperoside (**subfraksi D**)
6. Nicotiflorin (**subfraksi E**)
7. Rutin (**subrafksi E**)
8. Unknown (**subfraksi C**)





Isolat bioflavonoid dari daun kelor

PUSAT PENELITIAN BIOSAINS & BIOTEKNOLOGI
INSTITUT TEKNOLOGI BANDUNG

School of Pharmacy

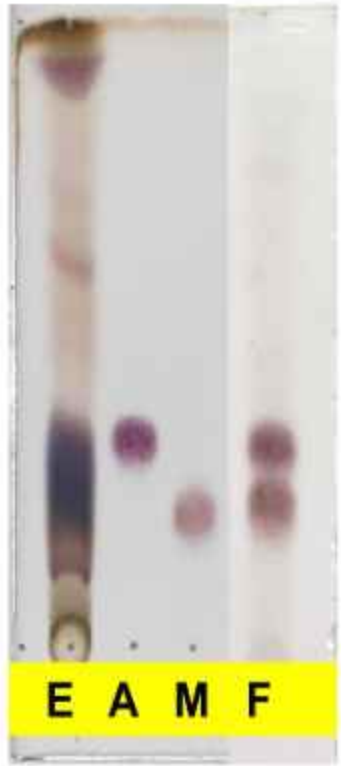
Sharing Markherb

Pegagan (*Centela asiatica*)

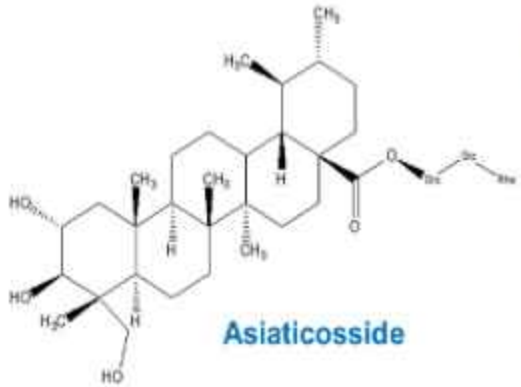
Pegagan (Ekstrak, Fraksi, Isolat)



UV 366 nm

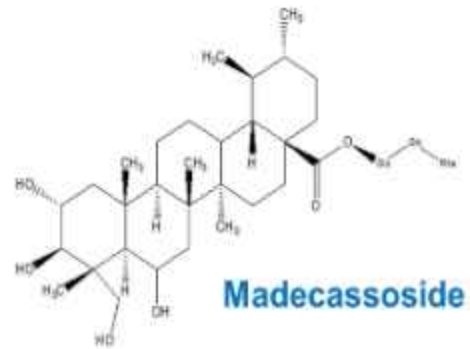


Vis



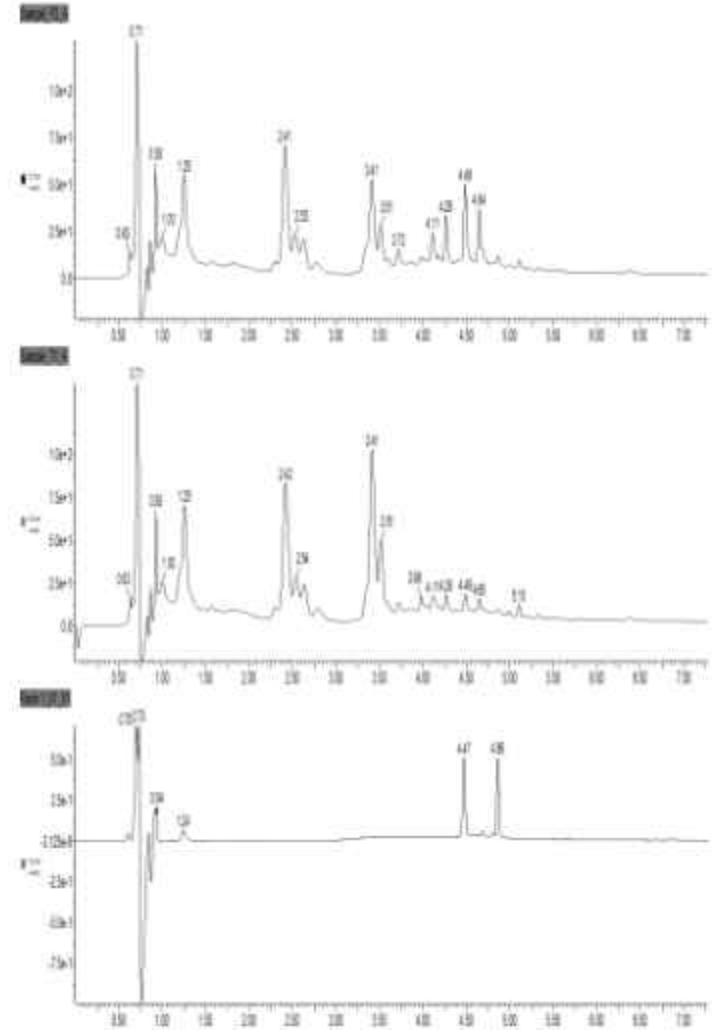
Asiaticosside





Madecassoside

Keterangan:
E: Ekstrak
A: Asiaticoside
M: Madecassoside
F: Fraksi Saponin (Asiatic-/Madecassoside)



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PUI-PT nutrasetikal

PUSAT PENELITIAN BIOSAINS & BIOTEKNOLOGI
INSTITUT TEKNOLOGI BANDUNG

School of Pharmacy

Analisis senyawa marker dari produk jadi (simulasi)

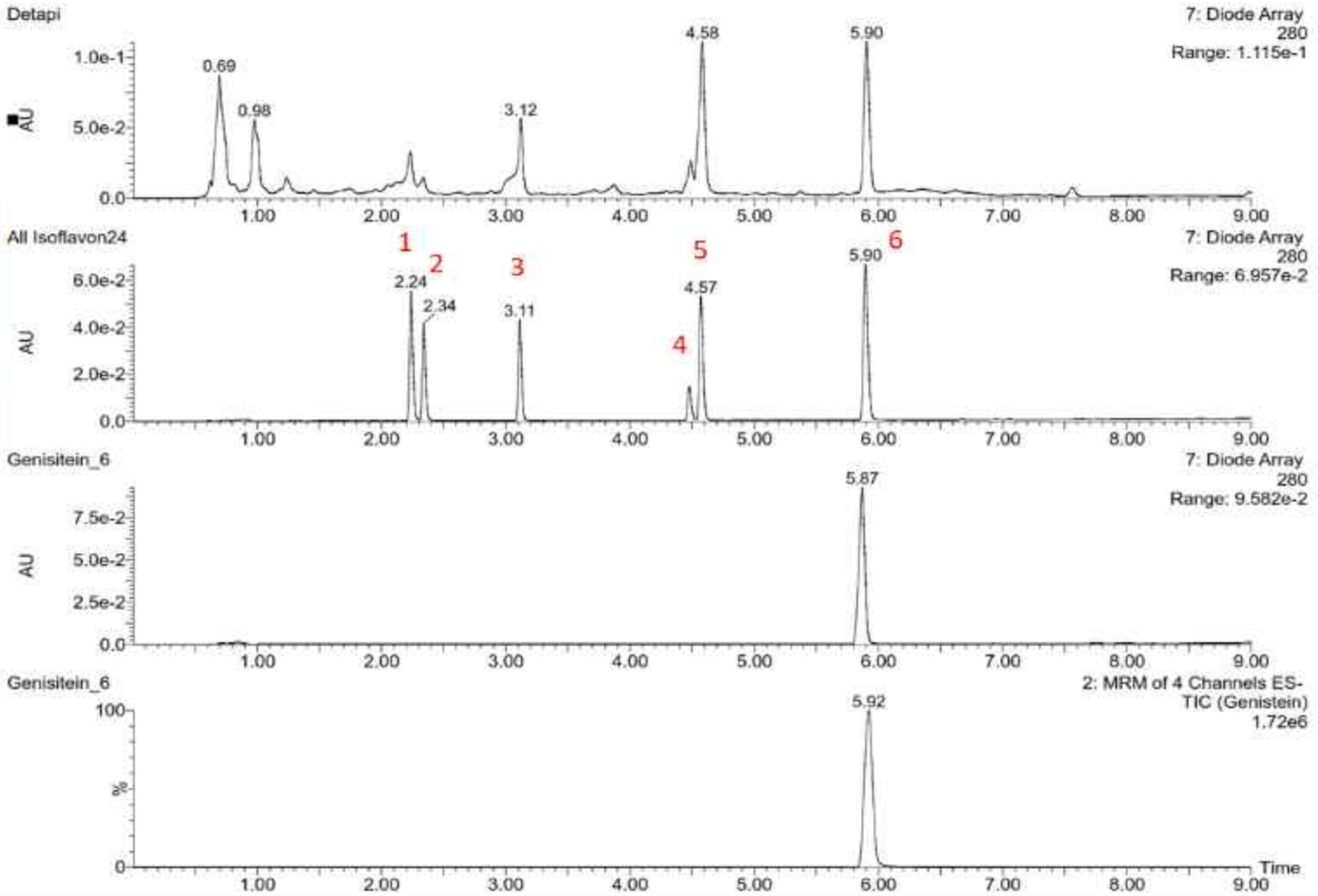
Analisis senyawa marker dalam bahan/produk herbal

Analisa UPLC:



Kedelai

1. Daidzin
2. Glisitin
3. Genistin
4. Glisitein
5. Daidzein
6. Genistein



Sampel Kedelai Varietas Detapi (Detektor UV)

6 Standar Senyawa Isoflavone (Detektor UV)

Standar Genistein (Detektor UV)

Standar Genistein (Detektor MS)

Analisis senyawa marker dari produk jadi (simulasi)

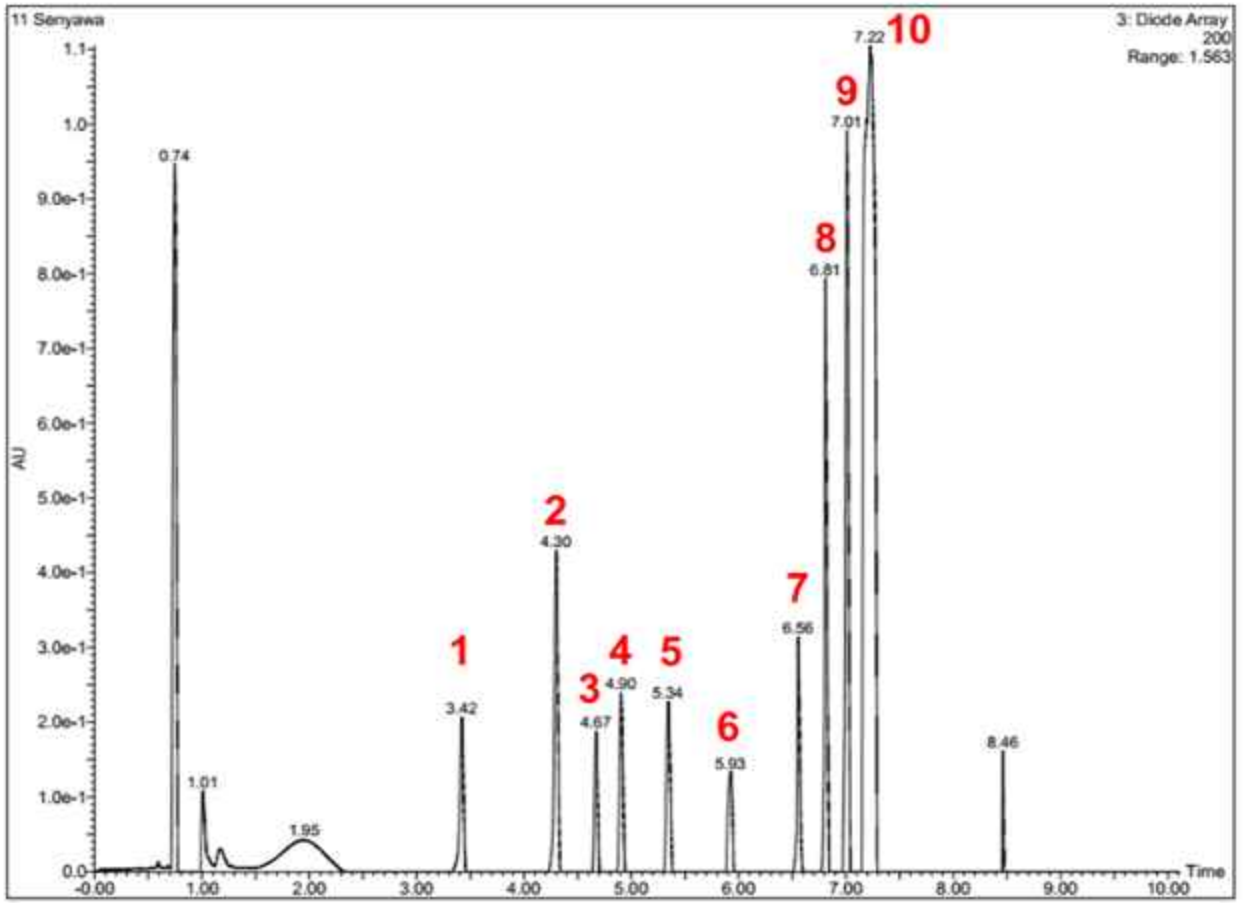
Analisis senyawa marker dalam bahan/produk herbal

Analisa UPLC:

Ekstrak Daun Kelor+Pegagan+Meniran

Senyawa Standar

1. Niazirin (3.42)
2. Hyperoside (4.30)
3. Rutin (4.67)
4. Nicotiflorin (4.90)
5. Astragalin (5.34)
6. Madecassoside (5.93)
7. Asiaticoside (6.56)
8. Quercetin (6.81)
9. Kaempferol (7.01)
10. Phyllanthin-Hypophyllanthin (7.22)



Terima kasih --- Thank you very much

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ebmiscitech

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Founder and Advisor



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Rivai
Laboran



Agus Gian
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Presented on:

"Capacity Building and Workshop on Quality Standardization of Extracts and Quality Control Assessment in Traditional Medicine Products"

National Agency of Drug and Food Control; Jakarta, 19 August 2025

IRRADIATION: PRESERVING TECHNIQE IN RAW MATERIALS AND FINISHED PRODUCTS





Hendig Winarno

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BADAN RISET DAN INOVASI NASIONAL

Outline

1. Introduction
2. Application of Radiation Technology on Raw Materials and Finished Products
3. Standardization and Irradiation Effects on Raw Materials and Finished Products
4. Summary

INTRODUCTION

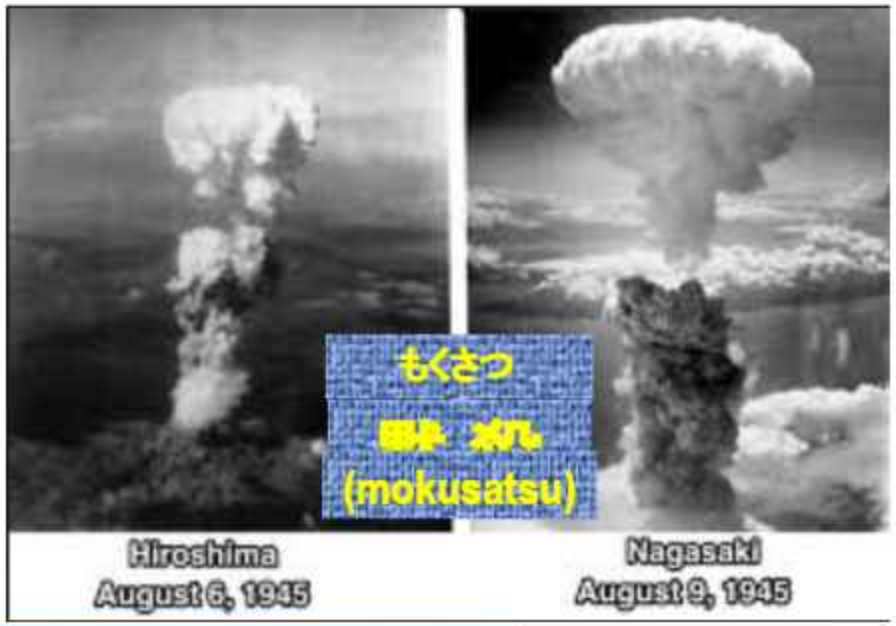
NUCLEAR & RADIATION

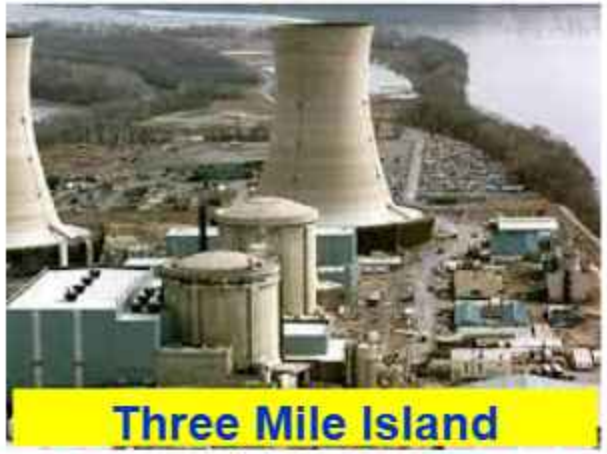
Is it necessary to know, to study, to understand, and to utilize the "nuclear" in our lives?

1. What are the NUCLEAR and RADIATION?
2. Is it dangerous?
3. Does it give the benefits ???

"NUCLEAR / ATOMIC NUCLEUS"

Atomic bombings of Hiroshima & Nagasaki





Three Mile Island (TMI-2)

28-03-79: Leakage of NPP in USA



26-4-86: CHERNOBYL Tragedy



Industrial Promotion Center of Hiroshima Prefecture



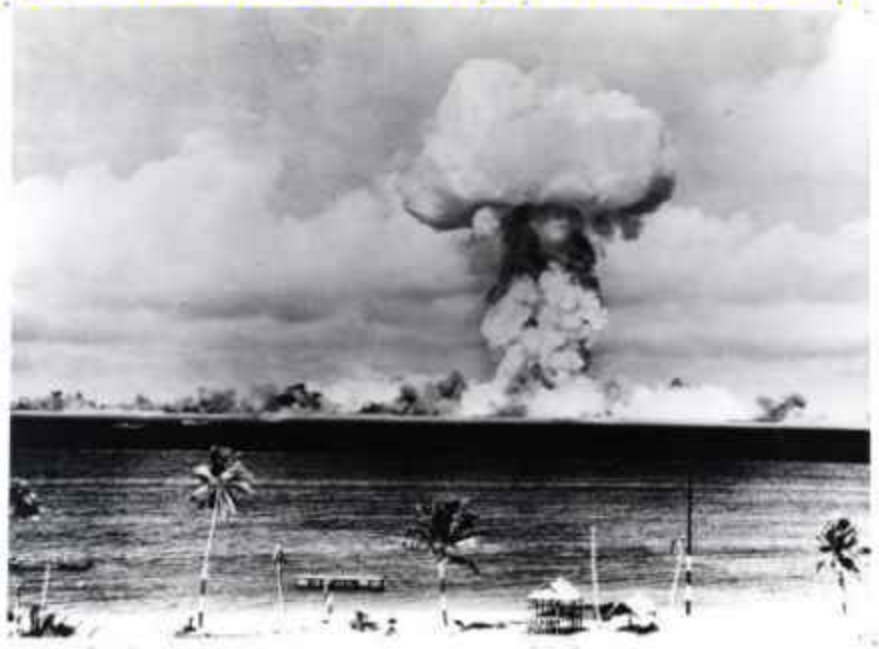
Hiroshima Peace Memorial Park (Genbaku Dome)



The effort of Japan to restore the global confidence after the "Fukushima nuclear accident"

ARE WE ONLY GOING TO REMEMBER THE NEGATIVE THINGS ???

The threat of atomic bombs to the Republic of Indonesia



The use of atomic bombs by the Allies in Hiroshima (August 6, 1945) and Nagasaki (August 9, 1945) triggered the superpowers to conduct nuclear weapons experiments after WW II in the Asia Pacific region.

To protect the sovereignty of the Republic of Indonesia

As a preventive effort, the Indonesian government formed a National Committee/ **PANITIA NEGARA** [Presidential Decree of the Republic of Indonesia No. 230 of 1954] which was tasked with tracking and assessing the possibility of the fall of remaining radioactive particles from weapons tests.



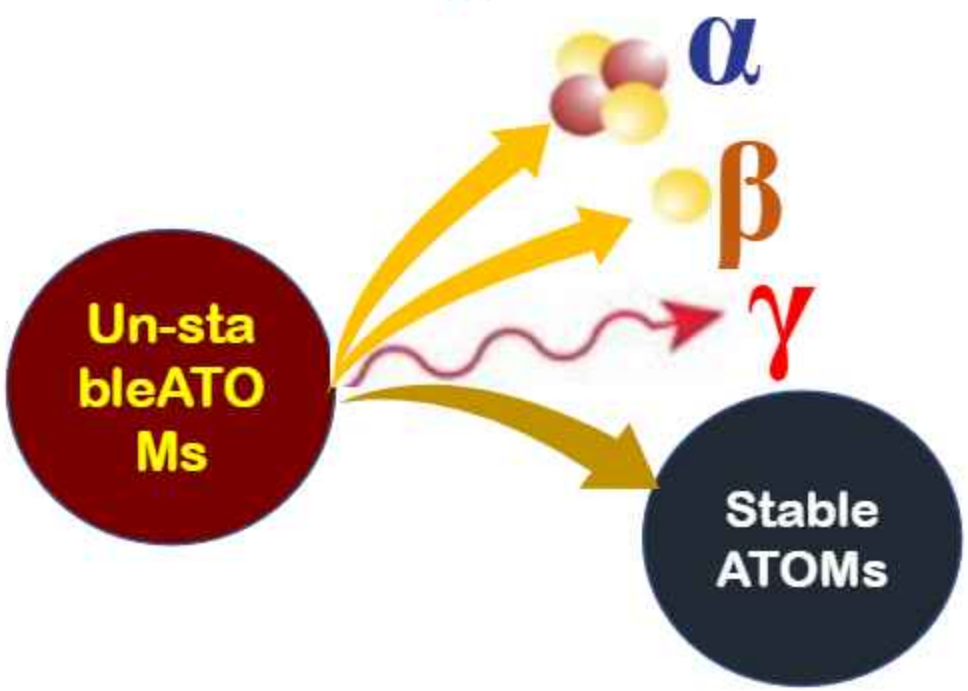
Nuclear for Peace

- **NUCLEAR MEDICINES**
- **RADIOLOGY**
- **RADIOTHERAPY**

wHat is radiation?

- ***Radiation***: emission and propagation of energy (in the form of waves or particles) through a space/ air and/or material medium
- Unstable atomic nucleus Radioisotopes emits radiation in an attempt to reach a more stable state [This process is called radioactive decays]

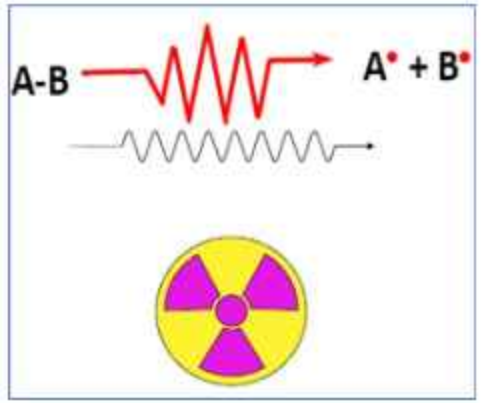
types of radiation



The characteristic of radiation

- Cannot be touched, smelled, or tasted;
- It can penetrate objects;
- Radiation can ionize materials and damage/alter DNA/living cells;
- It can detected (using DETECTOR)

RADIATION can be categorized into 2 main types: **ionizing radiation** and **non-ionizing radiation**, based on their ability to ionize atoms;



Ionizing radiation:

- **Definition**: radiation with sufficient energy to remove electrons from targets (atoms), creating ions;
- **Examples**: gamma rays, X-rays, alpha particles, beta particles, and neutrons;
- **Effects**: can damage cells and DNA, potentially leading to cancer or other health problems;
- **Sources**: radioactive materials, cosmic rays, medical imaging equipment (like X-ray machines), and certain industrial processes.

Non-ionizing radiation:

- **Definition**: radiation that does not have enough energy to remove electrons from atoms;
- **Examples**: radio-waves, microwaves, infrared radiation, visible light, and UV radiation;
- **Effects**: primarily causes atoms to vibrate or move, leading to heating effects. Some forms of non-ionizing radiation, like UV, can still cause damage (e.g., sunburn);
- **Sources**: sunlight, cell phones, microwave ovens, radio transmitters, and various other electronic devices.

The objectives of irradiation

(in foods, raw material of herbal medicines and finished products)

Tujuan utama iradiasi menggunakan radiasi pengion pada bahan pangan dan obat tradisional adalah:

1. **Sterilisasi**: menghilangkan atau mengurangi mikroorganisme (bakteri, jamur, virus) penyebab penyakit yang dapat mencemari bahan obat tradisional;
2. **Memperpanjang umur simpan**: memperlambat proses pembusukan dan kerusakan pada bahan pangan dan bahan obat (termasuk produk jadinya), sehingga produk dapat disimpan lebih lama;
3. **Pengendalian hama**: membasmi serangga yang dapat merusak atau mencemari bahan baku obat, terutama yang berasal dari tumbuhan;
4. **Meningkatkan kualitas produk**: Membantu menjaga kualitas fisik dan kimia bahan obat, serta mengurangi perubahan warna atau bau yang tidak diinginkan;
5. **Keamanan produk**: Mengurangi risiko infeksi atau keracunan akibat mikroorganisme patogen yang terdapat pada obat tradisional.

Note: Tantangan utama dalam mengatur iradiasi obat herbal adalah memastikan bahwa prosesnya aman dan efektif, serta tidak merusak khasiat obat herbal

Ionizing radiation sources used for sterilization and extending the shelf life of raw ingredients & finished product:

1. **Gamma (γ) ray**: it has a high penetrating power and can be used to sterilize large quantities of products.
2. **X-ray:** are similar to gamma rays, but have lower penetrating power.
3. **Electron beam (accelerator):** for surface-sterilization with the limited thickness.

Notes:

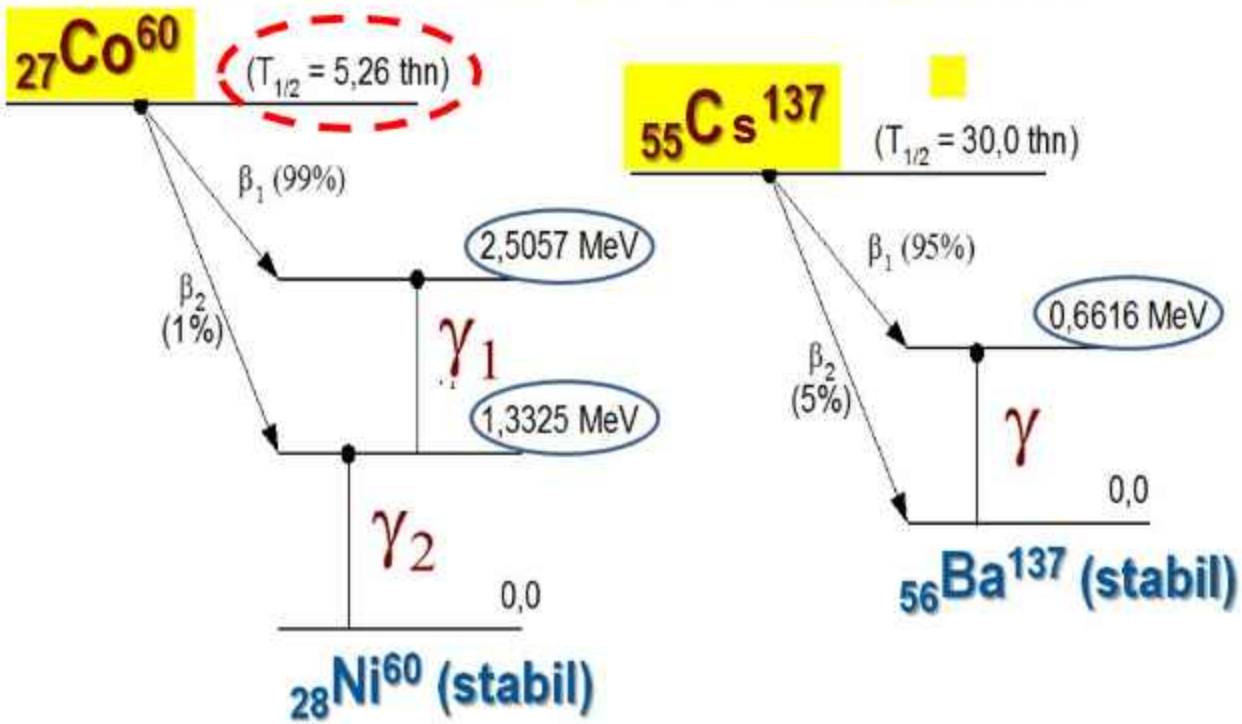
1) The irradiation dose used **must be precise and appropriate** for the type of the substances and the irradiation purposes;
2) The irradiation **doesn't cause the material to become radioactive** or there is no radioactive material left in the irradiated substances, making it safe for consumption;
3) **Any changes in the substances may occur after irradiation**, such as changes in texture or colour, but these changes are generally **not significant** and **can be minimized with the appropriate irradiation dosage**.

Sumber radiasi gamma dapat berasal dari Co-60 dan Cs-137

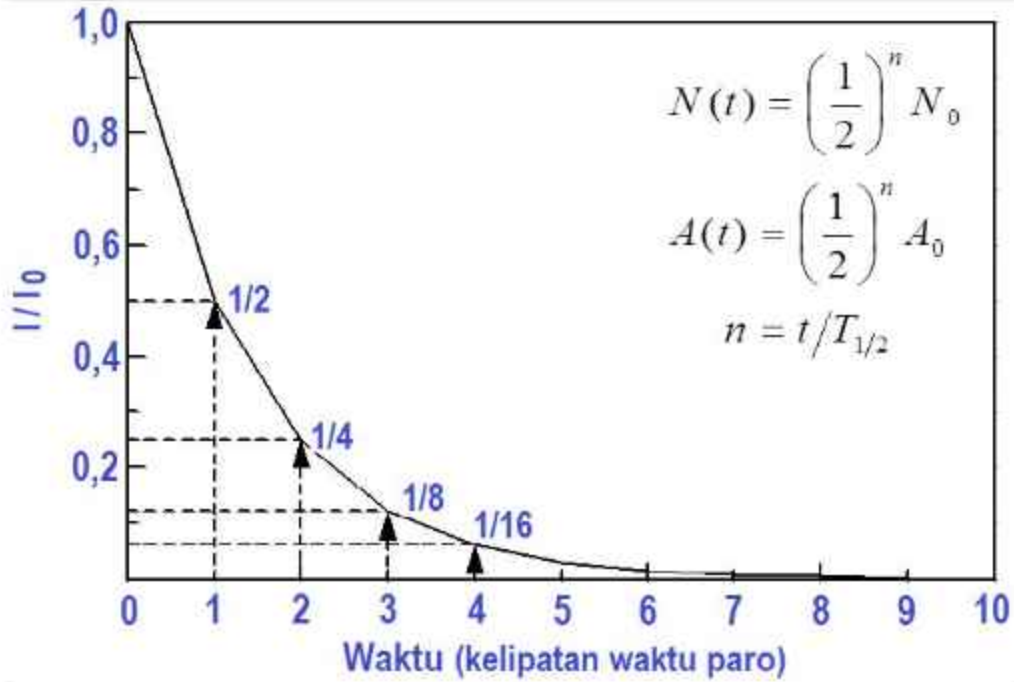
$$^{59}_{27}Co + {}^{1}_{0}n \rightarrow {}^{60}_{27}Co + \gamma\,(1{,}332 \text{ dan } 1{,}173 \text{ MeV})$$

$$^{235}U \xrightarrow{\text{fission}} {}^{137}Cs \xrightarrow{\beta} {}^{137}Ba + \gamma\,(0{,}66 \text{ MeV})$$

Skema Peluruhan Co-60 dan Cs-137



Kurva Peluruhan Zat Radioaktif



Waktu Paro : waktu yang diperlukan agar jumlah radionuklida berkurang menjadi separonya

Application of Radiation Technology on Raw Materials and Finished Products









DASAR HUKUM

1. Kep. Menkes RI No. HK 01.07/MENKES?187/2017: Formularium Ramuam OT;
2. Perka BPOM RI No. Hk.00.06.1.52.4011: Penetapan Batas Maksimum Cemaran Mikroba dan Kimia dalam Makanan;
3. Peraturan Menteri Kesehatan Republik Indonesia No. 826/MENKES/PER/XII/1987;
4. Permenkes RI No.701/Menkes/Per/VIII/2009: Tentang Pangan Iradiasi;
5. **Peraturan BPOM RI No. 32 Thn 2019: Persyaratan Keamanan dan Mutu Obat Tradisional;**
6. Berita Negara RI No. 393, 2011: Perka BPOM RI No. Hk.03.1.23.06.11.5629 Thn 2011: Persyaratan Teknis CPOTB;
7. Perka BPOM RI No 35 Thn 2013: Tata Cara Sertifikasi CPOTB;
8. **Peraturan Badan POM No. 3 Tahun 2018: Tentang Pangan Iradiasi;**
9. **Per. BPOM No. 18 Thn 2019: Cara Iradiasi Pangan Yang Baik;**
10. IAEA, 1992, *Irradiation of Spices, Hers, and Other Vegetable Seasonings: A Compilation of Technical Data for Its Authorization and Control.*

PERATURAN BPOM No.3 TAHUN 2018

No	Jenis Pangan	Tujuan Iradiasi	Dosis Maks
1	Umbi lapis dan umbi akar	Menghambat pertunasan	0,15 kGy
2	Sayur dan buah segar	a. Menunda pematangan b. Membasmi serangga c. Memperpanjang umur simpan d. Perlakuan karantina [a)]	1,0 kGy 1,0 kGy 2,5 kGy 1,0 kGy
3	Sayur olahan dan buah olahan termasuk pangan olahan semi basah	Memperpanjang umur simpan	7,0 kGy
4	Mangga	Memperpanjang umur simpan	0,75 kGy [1)]
5	Manggis	a. Membasmi serangga b. Perlakuan karantina	1,0 kGy 1,0 kGy
6	Serealia dan produk hasil penggilingannya, kekacangan, bebijihan penghasil minyak, polong- polong, buah kering	a. Membasmi serangga b. Mengurangi jumlah mikroba	1,0 kGy 5,0 kGy

a) Dosis serap minimum dpt disesuaikan, unt lalat buat 0,15 kGy

PERATURAN BPOM No.3 TAHUN 2018

No	Jenis Pangan	Tujuan Iradiasi	Dosis Maks
7	Ikan, pangan laut (*seafood* segar maupun beku)	a. Mengurangi jumlah mikroba patogen tertentu [b)] b. Memperpanjang umur simpan c. Mengontrol infeksi oleh parasit tertentu [b)]	5,0 kGy 3,0 kGy 2,0 kGy
8	Produk olahan ikan dan pangan laut	a. Mengurangi jumlah mikroba patogen tertentu [b)] b. Memperpanjang masa simpan	8,0 kGy 10,0 kGy
9	Daging dan unggas serta hasil olahannya (segar, beku)	a. Mengurangi jumlah mikroba patogen tertentu [b)] b. Memperpanjang umur simpan c. Megngontrol infeksi oleh parasit tententu [b)] d. Menghilangkan bakteri *Salmonella*	7,0 kGy 3,0 kGy 2,0 kGy 7,0 kGy
10	**Sayuran kering, bumbu, rempah kering (*dry herbs*), dan *herbs tea***	**a. Mengurangi jumlah mikroba patogen tertentu [b)]** **b. Membasmi serangga**	**10,0 kGy** **1,0 kGy**
11	Pangan berasal dari hewan yang dikeringkan	a. Membasmi serangga **b. Membasmi mikroba, kapang - khamir**	1,0 kGy **5,0 kGy**
12	Pangan olahan siap saji (misal: rendang, bandeng presto, pepes ikan, semur daging) [c)]	a. Sterilisasi dan membasmi mikroba patogen termasuk mikroba berspora,dan	60 kGy

b) Dosis minimum dpt diterapkan sesuai tujuan penakuan



Gamma Irradiator "MERAH PUTIH" belong to Indonesian Gov. established on 15 November 2017



Video-1: Irradiator facilities in Vinagamma, 2012

Herbal Temu Putih Untuk Obat Kanker





exp. date: 290818

exp. date: 16.02.2018

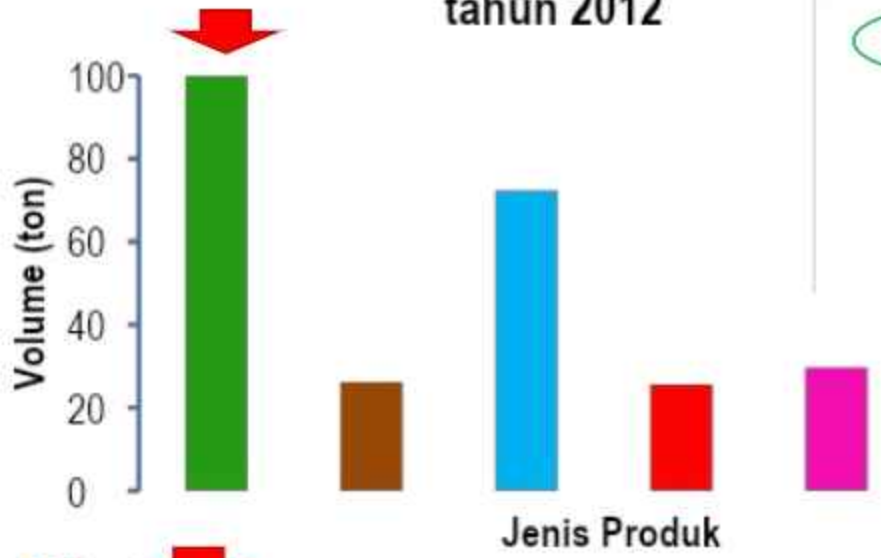
Herbal Keladi Tikus Untuk Obat Kanker

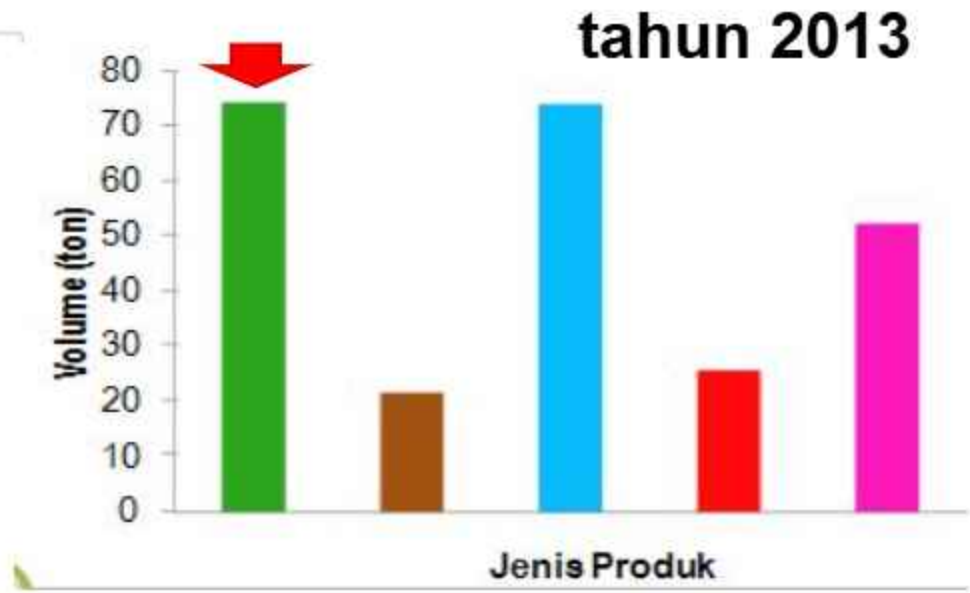




Foto diambil tahun 2015

Layanan Iradiasi BATAN (Pasar Jumat) 2012- 2015



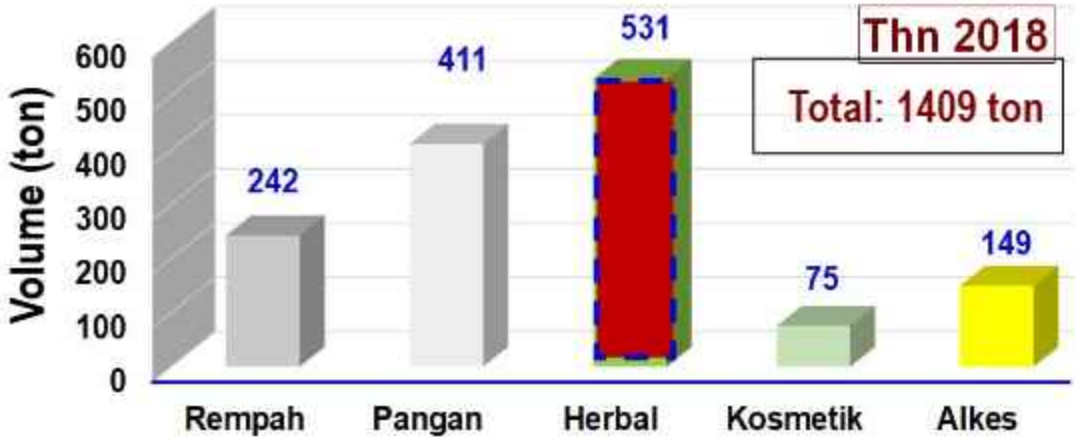


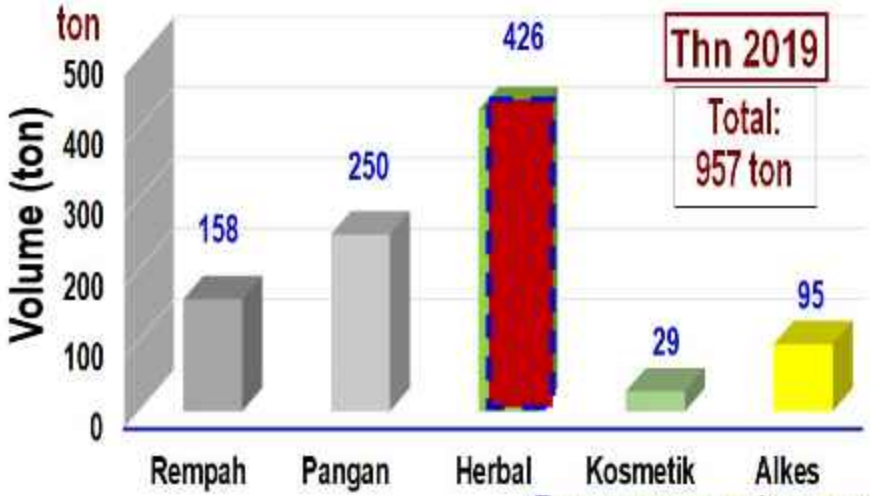


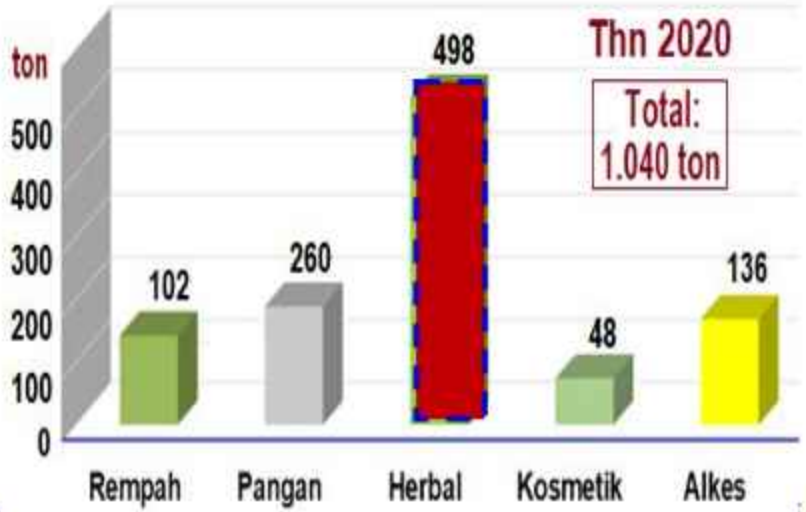


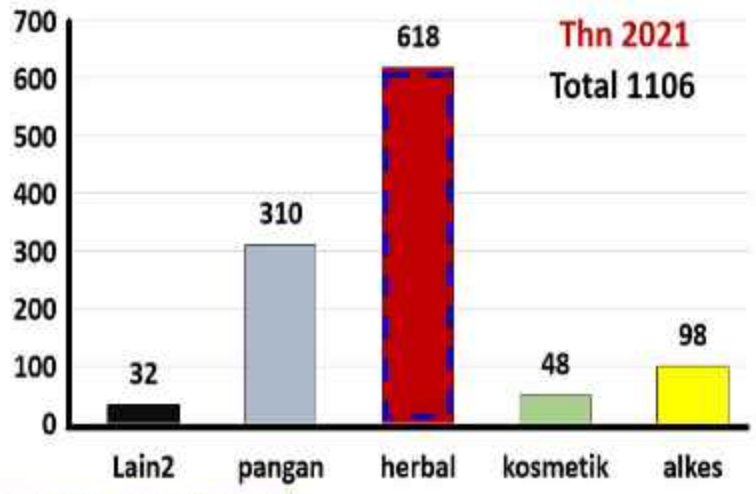
The Utilization of IRADIATOR GAMMA MERAH PUTIH 2017 – 2021







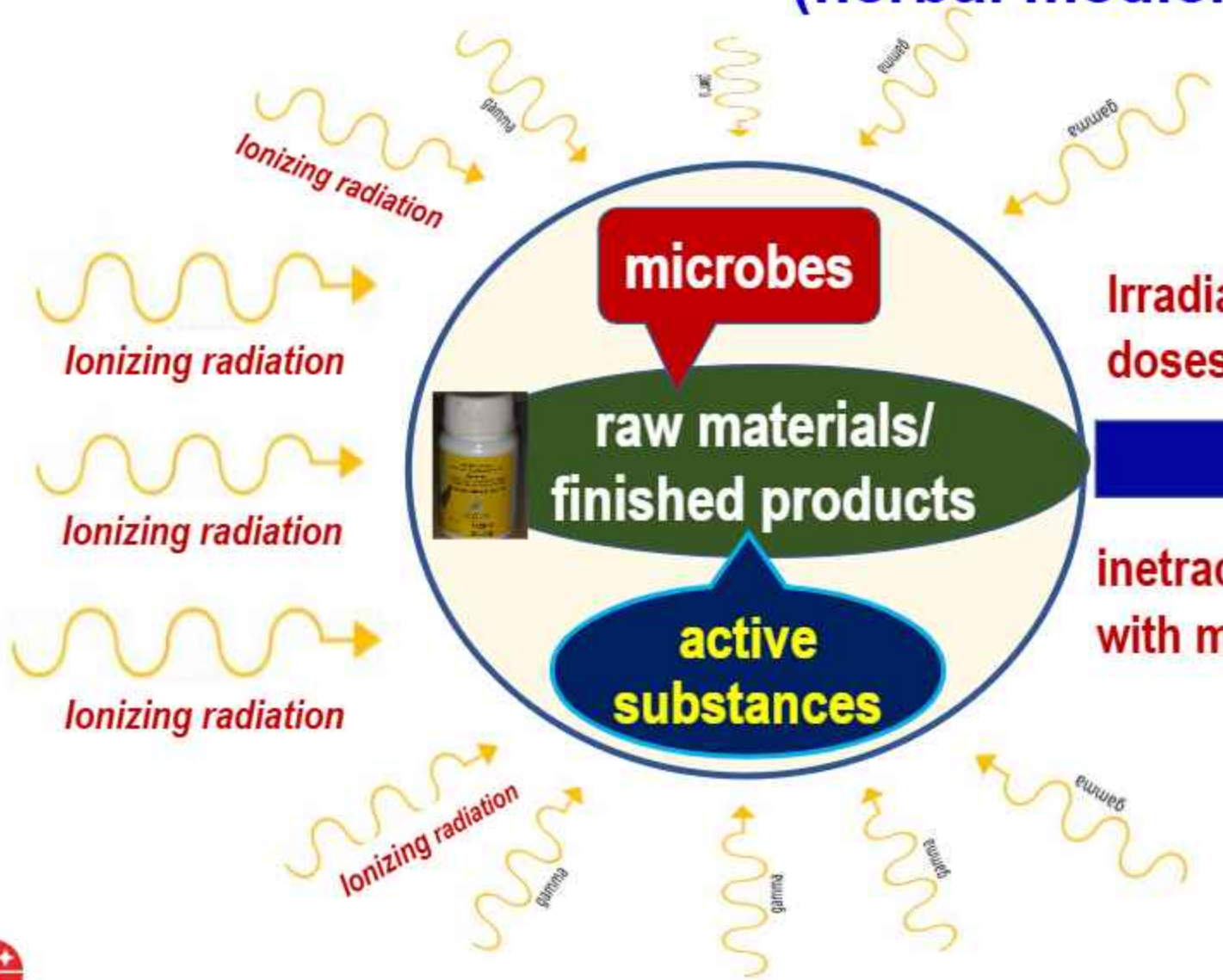




Penggunaan sinar gamma untuk dekontaminasi mikroba bahan awal OT dan Industri cukup tinggi;

Standardization and Irradiation Effects on Raw Materials and Finished Products

Interaction of gamma radiation with matters (herbal medicines)



Irradiation doses ?

inetraction with matters

- Contaminants ↓ decrease ↓ SAFE
- EFFICACY↓ does't significantly decrease
- Radiolytic produts ↓ SAFE

Radiation interaction (*γ -ray, X-ray, e⁻ beam)* with biological components

1. Direct effects

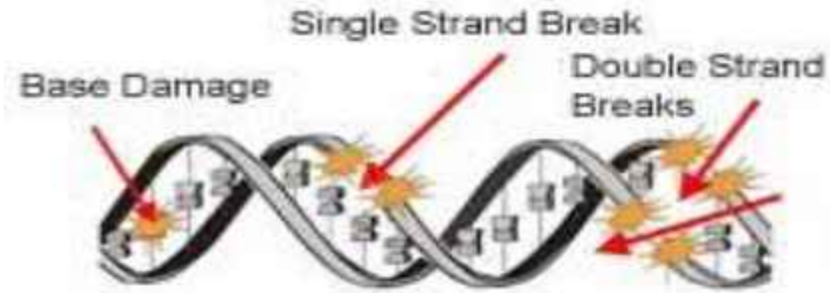


γ or e⁻

DNA of microbes

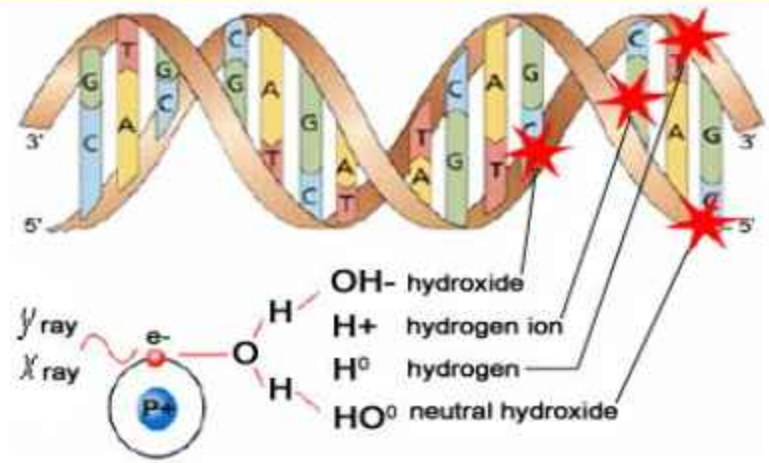
- Single strand break
- Double strand breaks
- Base damage

Microbes will be killed





2. Indirect effects (though radyolisis of water)



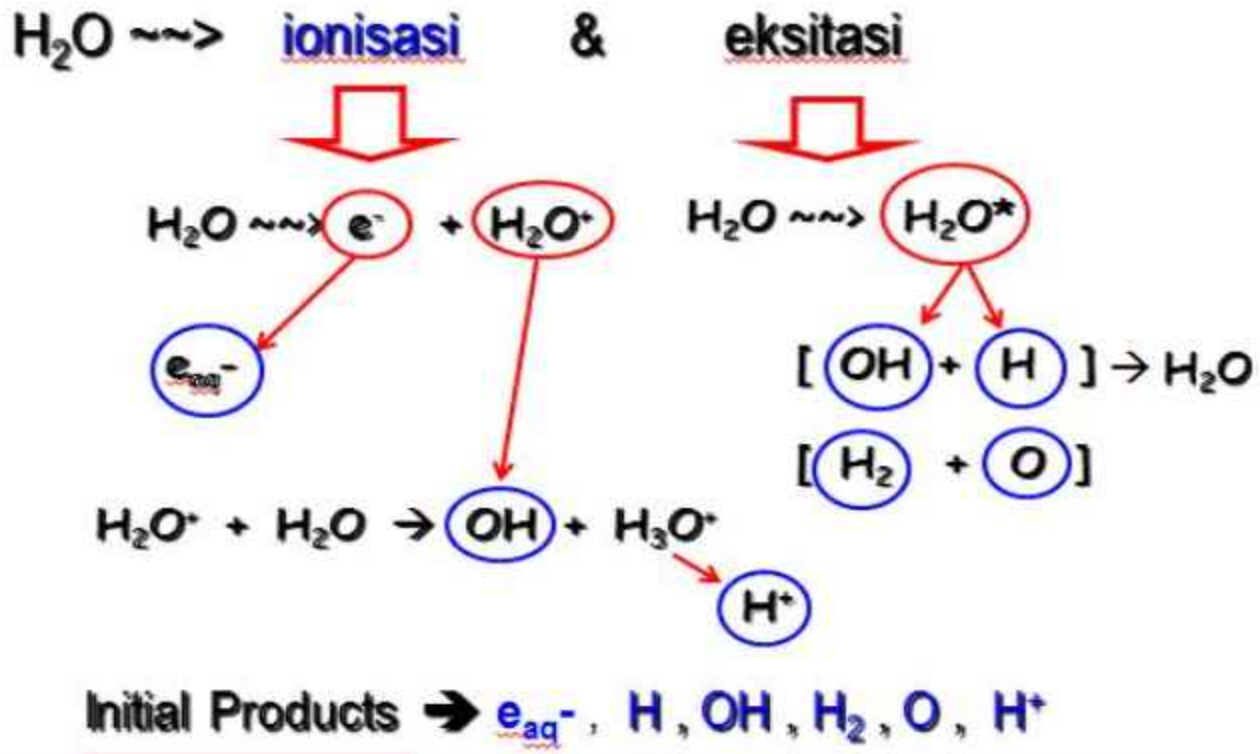
- Each microorganisms have different sensitivity to radiation.
- A resistance of microorganisms to radiation is determined by its D10 value.
- D10: The radiation dose required to kill 90% of a microorganism's population.

Radiasi pada Materi

Pada umumnya materi mengandung air efek langsung dan reaksi tidak langsung

Reaksi langsung: radiasi pengion ⟶ Komponen OBA/OT

Reaksi tidak langsung:



mengapa produk yang mengandung air > 10% tidak direkomendasikan untuk diradiasi pengion?

Radiation decontamination of herbs and spices

Chmielewski A.G and Migdal W., *Nunleonika*, 2005; 50(4): 179 - 184

Comparison of different physical and chemical methods of decontamination of herbal raw materials

Methods of decontamination	Efficiency of decontamination [%]
Ethylene oxide (1g/L; 6 h)	99.960
Methyl bromide (0.1g/L; 16 h)	96.830
Ionizing radiation (dose: 10 kGy)	99.988
Steam under pressure (121 °C, 15 min)	99.994

Radiation decontamination of herbs and spices

Chmielewski A.G and Migdal W., *Nukleonika*, 2005; 50(4): 179 - 184

Main substances in herbal raw materials	Methods of decontamination			
	Ethylene oxide	Methyl bromide	Ionizing radiation (dose 10 kGy)	Steam under pressure
Flavonoids	+	+		+
Polyphenylo-compounds				+
Tannins	–		–	+
Essential oils	+	–	+	–
Steroid saponins	+	+		
Anthra-compounds	+		–	+
Triterpene saponins	–		+	+
Iridoids	–		+	+
Phenolic glycosides	+		–	+
Coumarins		+	+	+
Cardic glycosides			+	
Oleanosides			+	+
Sulphur compounds			–	
Flavonoligands				+
Alkanoids				+
Plants mucus				–

+ Stable substances. – Unstable substances.

PRODUK RADIOLITIK*

Senyawa	Produk radiolitik/Efek	keterangan
Protein	ammonia, keto-acids, amide-like products and di-amino acids/ denaturasi, dissosiasi, *crosslinking*	Efek sama spt teknik lainya (pemanasan)
Karbohidrat/selulose	Gula (disakarida dan monosacharida)	Degradasi
Vitamin	Degradasi/berkurang aktivitas Bergantung dosis radiasi	Vit larut air (B, C) lbh sensitif drpd vitamin larut lemak (ADEK)
Tanin/polifenol	Stabil sd dosis 10 kGy	decreases in feed intake
Safonin (red Korean Ginseng)	Stabil thd radiasi sd dosis 25 kGy	Radioprotective agent, Anti inflamasi
alkaloid	Stabil sd dosis 10 kGy	Anti stres, anti kanker, anti inflamasi

***diperoleh dari beberapa, literatur**

Treatment of Irradiated Herbal Medicines

A. MICROBIOLOGICAL tests: DECREASE OF CONTAMINANTS [TAPC, TAYMC] SAFE

B. EFFICACY tests

 DOES NOT significantly DECREASED

C. ACCUTE TOXICITY tests*

1. **PHYSICOCHEMICAL property tests**
   a. TLC
   b. Densitometry
   c. HPLC
   d. GC-MS/LC-MS
   - Use the standard/ marker compounds
   - Appropriate system/condition
2. **CHEMICAL propertt tests**
   - Compound groups; example: polyphenol, flavonoid, terpenoid, alkaloid contents
3. **Biological activity tests as claimed**
   a. Antioxidant
   b. Antidiabetics (*in vitro, in vivo*)
   c. Antihypertension
   d. Antitumor (*in-vitro*)

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Radiation processing: An effective quality control tool for hygienization and extending shelf life of a herbal formulation, Amritamehari churnam

Suchandra Chatterjee [a,*], *Vivekanand Kumar* [a], *Swati Khole* [b], *Bhaskar Sanyal* [a], *T.S. Murali* [c], *Prasad S. Variyar* [a]

1. TLC densitometry; 2. HPLC analysis
3. Estimation of total phenolics content (TPC)
4. DPPH radical scavenging assay
5. Ferric reducing antioxidant power (FRAP) assay
6. Hydroxyl (OH) radical scavenging assay
7. Superoxide (SO) radical scavenging assay
8. Thiobarbituric acid reactive substances (TBARS) assay for lipid peroxidation activity
9. EPR/ESR spectroscopy

Table 4 – Compounds (mg/gm) estimated by densitometry and HPLC.

Storage (months)	Gallic acid				Ellagic acid				Three curcurminiods				Mangiferin			
	Densitometry		HPLC		Densitometry		HPLC		Densitometry		HPLC		Densitometry		HPLC	
	I	NI	I	NI	I	NI	I	NI	I	NI	I	NI	I	NI	I	NI
0	9.81 ± 1.47	10.12 ± 1.35	9.6 ± 0.17	9.71 ± 0.12	2.78 ± 0.17	2.81 ± 0.21	2.53 ± 0.11	2.46 ± 0.14	8.12 ± 0.22	8.19 ± 0.15	8.12 ± 0.22	8.19 ± 0.15	8.12 ± 0.22	8.19 ± 0.15	6.30 ± 0.11	6.31 ± 0.15
3	9.83 ± 1.51	9.98 ± 1.28	9.30 ± 0.27	9.38 ± 0.23	2.77 ± 0.19	2.73 ± 0.18	2.45 ± 0.07	2.46 ± 0.09	7.92 ± 0.18	8.11 ± 0.20	7.92 ± 0.18	8.11 ± 0.20	7.92 ± 0.18	8.11 ± 0.20	6.30 ± 0.11	6.35 ± 0.14
6	9.79 ± 1.39	10.09 ± 1.37	8.92 ± 0.18	8.91 ± 0.18	2.80 ± 0.22	2.76 ± 0.18	2.32 ± 0.13	2.37 ± 0.10	7.98 ± 0.24	8.01 ± 0.22	7.98 ± 0.24	8.01 ± 0.22	7.98 ± 0.24	8.01 ± 0.22	6.19 ± 0.11	6.22 ± 0.18
9	9.80 ± 1.43	9.94 ± 1.41		8.89 ± 0.14	2.72 ± 0.15	2.75 ± 0.16		2.21 ± 0.09	8.02 ± 0.26	7.95 ± 0.19	8.02 ± 0.26	7.95 ± 0.19	8.02 ± 0.26	7.95 ± 0.19		6.20 ± 0.08
12		10.03 ± 1.50		8.95 ± 0.13		2.72 ± 0.19		2.21 ± 0.03		8.10 ± 0.16		8.10 ± 0.16		8.10 ± 0.16		6.19 ± 0.13
15		9.92 ± 1.53		8.85 ± 0.06		2.78 ± 0.20		2.18 ± 0.10		7.99 ± 0.25		7.99 ± 0.25		7.99 ± 0.25		6.17 ± 0.14
18		9.89 ± 1.47		8.89 ± 0.12		2.74 ± 0.19		2.16 ± 0.14		8.04 ± 0.23		8.04 ± 0.23		8.04 ± 0.23		6.22 ± 0.09

- Radiation processing does not significantly affect the chemical composition, physical property, antioxidant activity and sensory quality while improving microbial quality of the herbal formulation of **Amritamehari churnam**.
- Hence the extent of changes, if any, depends on the nature of the herb and the conditions of post-harvest handling and storage radiation processing can thus be effectively used to improve shelf life and quality of herbal products.

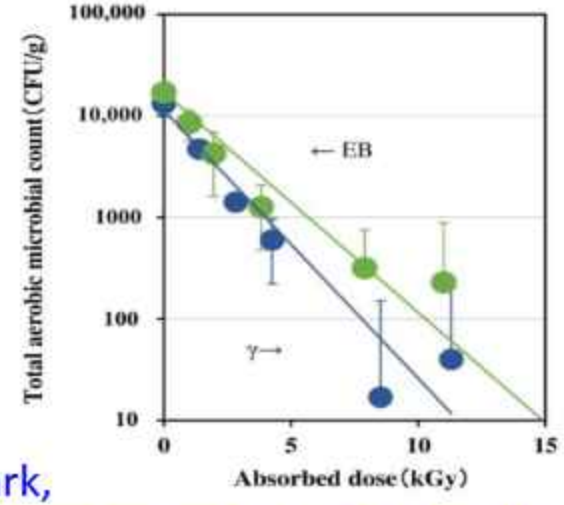
processes 2022, 10, 300. https://doi.org/10.3390/pr10020300 MDPI
https://www.mdpi.com/journal/processes

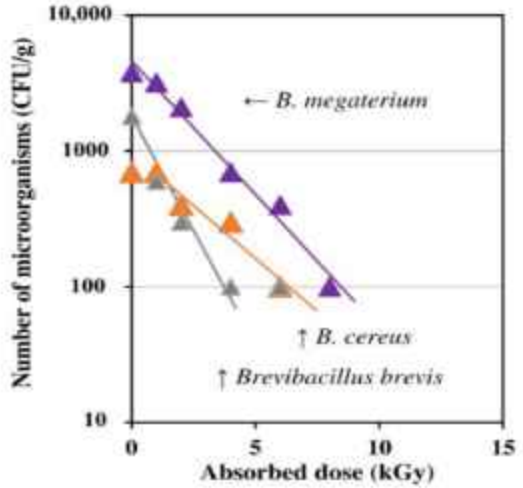
Article

Microbial Control in the Primary Packaging of Pills Using Ionizing Radiation and Its Effect on Characteristic Constituents for Quality Control in Irradiated Pills

Rumi Yamaoki *, Satoshi Uno and Shojiro Kimura

Pil Herbal





The components of the pills were four crude drugs (amount of ingredients, 80%): Swertia herb extract, powdered Phellodendron bark, powdered Cinnamon bark, powdered Glycyrrhiza (ratio of crude drug component, 1:2:2:1), medicinal carbon (amount of ingredients, 4%), and rice flour as inactive ingredients (amount of ingredients, 16%).

Table 3. Analysis of the indicator ingredients in the sample pills at varying irradiation doses.

Irradiation Dose (kGy)	Swertiamarin	Berberine	Cinnamic Acid (mg/g Pills)	Cinnamaldehyde	Glycyrrhizin
Control	9.13 ± 1.71 [a]	10.9 ± 0.19 [a]	0.17 ± 0.01 [a]	4.20 ± 0.04 [a]	6.61 ± 0.10 [a]
1	9.20 ± 1.41 [a]	10.9 ± 0.34 [a]	0.17 ± 0.01 [a]	4.26 ± 0.08 [a]	6.60 ± 0.20 [a]
6	9.13 ± 1.31 [a]	10.8 ± 0.08 [a]	0.19 ± 0.01 [a]	4.16 ± 0.16 [a]	6.59 ± 0.21 [a]
10	9.05 ± 1.16 [a]	10.6 ± 0.86 [a]	0.18 ± 0.01 [a]	4.26 ± 0.12 [a]	6.58 ± 0.16 [a]
20	9.04 ± 2.31 [a]	11.1 ± 0.63 [a]	0.19 ± 0.01 [a]	4.04 ± 0.05 [b]	6.65 ± 0.05 [a]
60	8.87 ± 1.82 [a]	11.0 ± 0.11 [a]	0.19 ± 0.01 [b]	4.10 ± 0.08 [a]	6.70 ± 0.01 [a]
100	8.71 ± 1.64 [a]	11.1 ± 0.07 [a]	0.18 ± 0.005 [a]	4.05 ± 0.10 [a]	6.65 ± 0.04 [a]

Note: same letters (a, b) are not significantly different from each other ($p = 0.05$).

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Gamma irradiation effect on physicochemical properties of *Guazuma ulmifolia* leaves and their antiproliferative activities against human cancer cell lines

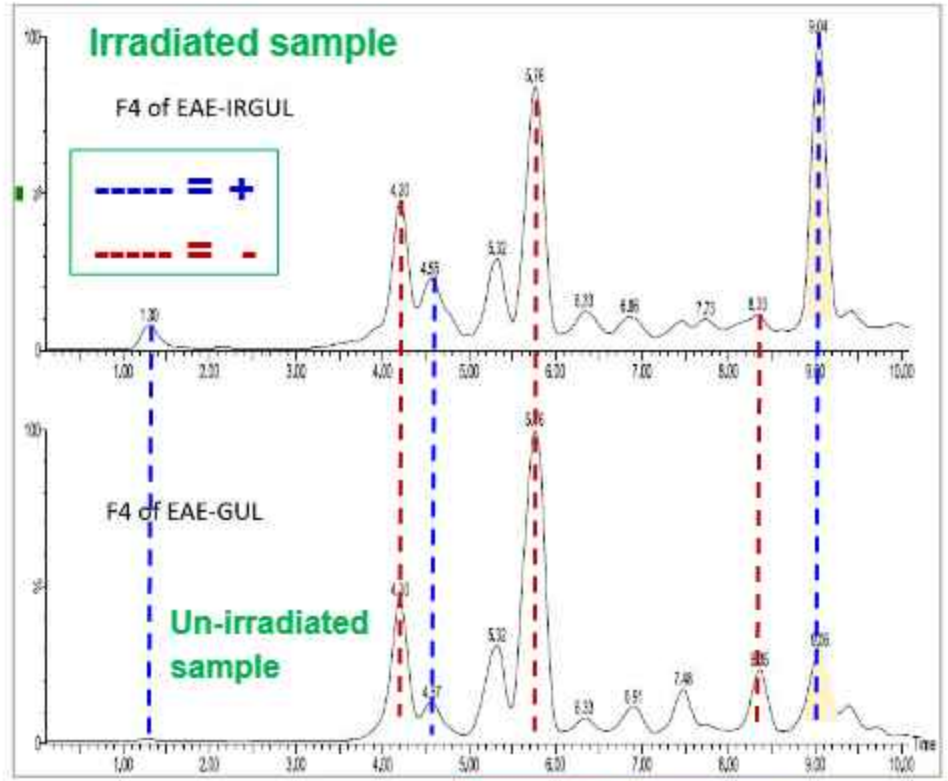
Hendig Winarno, Susanto Susanto, Ermin Katrin Winarno

Sample	EAE-GUL	EAE-IRGUL	The decrease
TPC (mg GAE/g)	10.76 ± 0.07	9.06 ± 0.18	1.70 (15.8%)
TFC (QE mg/g extract)	31.80 ± 0.43	30.24 ± 0.72	1.56 (4.9%)

Each value was the mean of duplicate.

EAE-GUL: Un-irradiated *Guazuma ulmifolia* leaves

EAE-IRGUL: Irradiated Guazuma ulmifolia leaves



HPLC chrom.

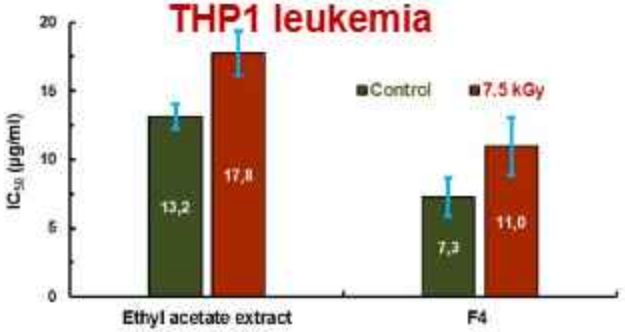


Fig. 1. IC_{50} values of EAE-GUL (control) and EAE-IRGUL (irradiated at 7.5 kGy) and its F4 against THP1 leukemia cells. [Each value was the mean of triplicate].

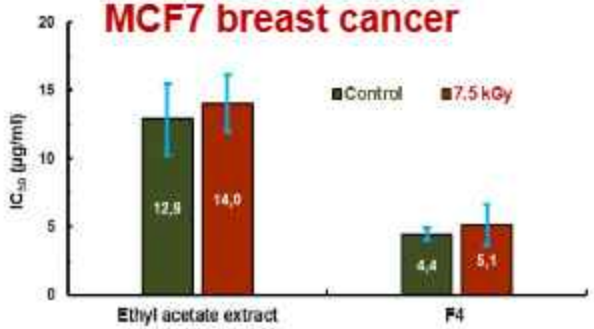


Fig. 2. IC_{50} values of EAE-GUL (control) and EAE-IRGUL (irradiated at 7.5 kGy) and its F4 against MCF7 breast cancer cells. [Each value was the mean of triplicate].

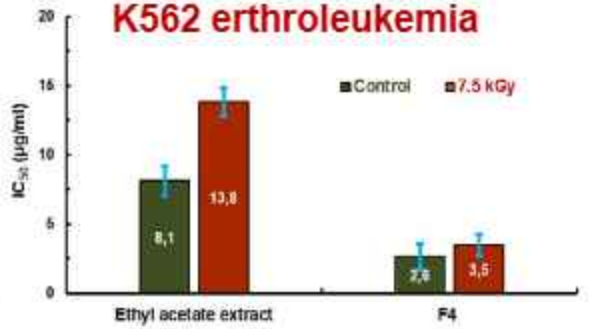


Fig. 3. IC_{50} values of EAE-GUL (control) and EAE-IRGUL (irradiated at 7.5 kGy) and its F4 against K562 erythroleukemia cells. [Each value was the mean of triplicate].

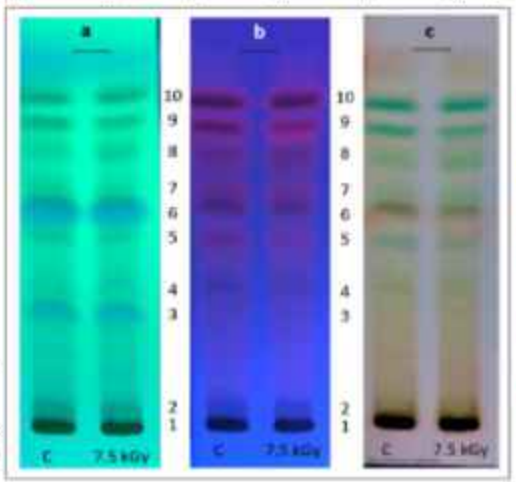


Fig. 4. TLC chromatogram of F4 of EAE-GUL (C) and F4 of EAE-IRGUL (7.5 kGy).

TLC Densittometry

10: - 16%

9: + 41%

8: - 41%

6: - 26%

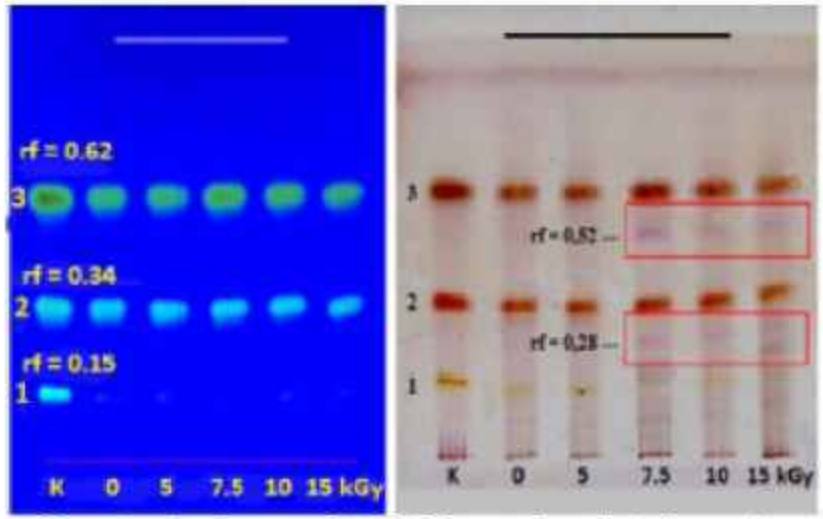
3: - 25%

TEMU LAWAK *(Curcuma xanthorrhiza)*

Atom Indonesia Vol. 45 No. 3 (2019) 159 - 164

Antiproliferative Activity of Extracts and Fractions from Irradiated *Curcuma zanthorrhiza* Rhizomes Against Mouse Leukemia and Human Cancer Cell Lines

E.K. Winarno*, H. Winarno and Susanto
Center for Isotopes and Radiation Application, National Nuclear Energy Agency,
Jl. Lebak Bulus Raya No. 49, Jakarta 12440, Indonesia



K = standard curcumin; 0 kGy = unirradiated sample.

(a) (b)

Fig. 2. Thin-layer chromatogram (TLC) of F3 from varying irradiation dose compared to the standard curcumin; (a) spots on the TLC plate under the UV lamp with λ 366 nm; (b) the TLC plate after spraying with reagent cerium sulfate and heating.

Mouse Leukemia L1210 cell lines

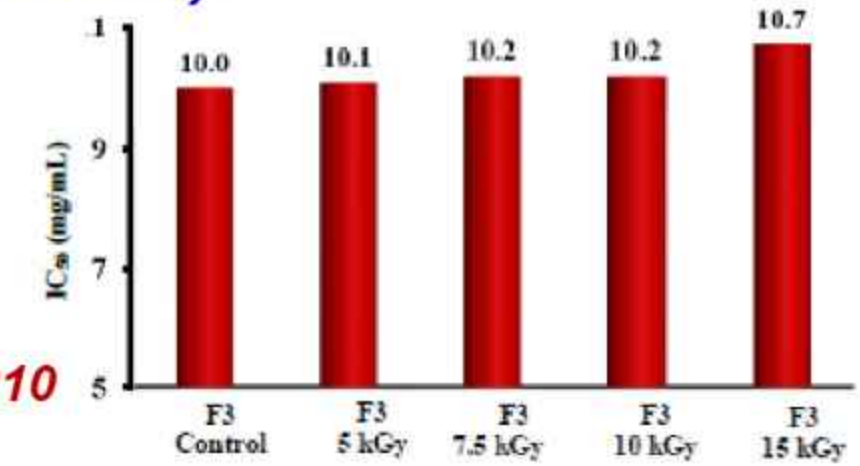


Fig. 3. Cytotoxicity against mouse leukemia L1210 cells of F3 from ethyl acetate extract of irradiated samples of each varying

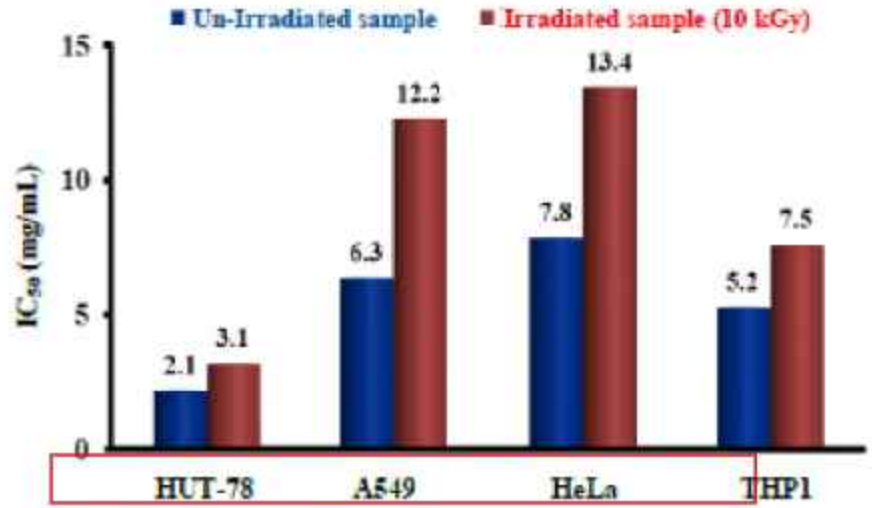


Fig. 4. IC_{50} value of F3 from ethyl acetate extract of unirradiated and irradiated samples at 10 kGy against human cancer cell lines (HUT78, A549, HeLa, THP1).

Human Cancer cell lines

- 0 kGy (kontrol)
- 10 kGy

goji-berry

Radiation Physics and Chemistry 179 (2021) 109144

Contents lists available at ScienceDirect

Radiation Physics and Chemistry

journal homepage: www.elsevier.com/locate/radphyschem

Effects of electron beam irradiation on the bioactive components of goji-berry

Flavio Thihara Rodrigues[a], Amanda C. Ramos Koike[b], Pamela Galo da Silva[b], Bianca Guimarães Negrão[b], Severino Matias de Alencar[c], Jorge Mancini Filho[d], Anna Lucia C.H. Villavicencio[b,*]

- Irradiated and non-irradiated samples did not present a significant difference in antioxidant activity in the DPPH assay.
- On the other hand, this work showed that EB irradiation improved the total antioxidant activity of the samples in ORAC (oxygen radical absorbance capacity assay), as well as a total flavonoid and total phenolics assays.

- From the standpoint of the functional properties, irradiation treatment significantly **increase the presence of its phytochemicals** after ionizing radiation processing in goji-berry.
- That is the evidence that EB irradiation is a clean technology and a safe process with which is possible not only to maintain but also **enhance the nutritional goji-berry quality**.

Influence of Radiation on the Content of Biologically Active Substances in Herbal Raw Materials Pharmacological Activity of Herbal Drugs after Microbiological Decontamination by Irradiation

W. MIGDAL, H. B. OWCZARCZYK
Institute of Nuclear Chemistry and Technology, Warsaw, Poland

- Decontamination by irradiation is one of most effective method for decreasing of number of microorganisms in herbal raw materials.
- The content of biologically active substances in many raw herbal materials did not change in a significant degree after irradiation.
- The therapeutically properties herbal drugs are identical before and after their irradiation at the dose 10 kGy.

Influence of Irradiation on The Content of Mainly Active Substances in Herbal Raw Materials Before (A) and After Microbiological Decontamination (B)

Herbal raw materials	Active substances	Content of substance A	Content of active substances B	Decrease of content %
Hyperrici herba	flavonoids	1,05	1,06	0
	hypericin	0,04	0.04	6.7
Thymi herba	oils	1,40	1,36	2.9
	thymol	98,80	94,80	4.4
Urticae folium	flavonoids	0,70	0,69	1.4
Tiliae inflorescentia	flavonoids	0.50	0,51	0
Frangulae cortex	antraquinone	3,65	3,70	0
Glycyrrhizae radix	glycyrrhizoic acid	1,21	1,11	8.3

Irradiation dose: 10 kGy

Example: Investigation of compound group in **sambiloto extract**

No	compound groups	Irradiation doses		
		0 kGy (un-irradiated)	5 kGy	10 kGy
1	Alkaloid	++++	++++	++++
2	Saponin	++	++	++
3	Tanin	++++	++++	++++
4	Fenolic	-	-	-
5	Flavonoid	++++	++++	++++
6	Triterpenoid	++	+++	++++
7	Steroid	++	+	-
8	Glycoside	+	++	++++

Note: - = not detected, + = positif lemah, ++ = positif, +++ = positif kuat, ++++= positif kuat sekali

- **WHO**, International Atomic Energy Agency (**IAEA**), and Joint Expert Committee on Food Irradiation (**JECFI**) which has been **published by WHO in 1999** concluded that the irradiation dose up to 10 kGy of any food commodity "**presents no toxicological hazard**", however, it **may affect the active compounds** in irradiated medicinal plants.

1) Thongphasuk, P., Thongphasuk, J., 2012. Effects of irradiation on active components of medicinal plants: A review. Rangsit J. Arts Sci. 2(1), 57-71. https://doi.org/10.14456/rjas.2012.7.

- Ionizing radiation can **cause chemical changes** of the molecules. The initial molecules can **change into new molecules**, caused the changes in **the physical**, **chemical**, and ultimately **biological properties** of the material.

1) Wojnárovits, L., 2011. Radiation Chemistry: In Handbook of Nuclear Chemistry, Vértes, A. et al (eds), second ed., Springer, Boston, MA. 1263–1331. https://doi.org/10.1007/978-1-4419-0720-2_23.

- It was reported that irradiation **did not cause significant changes in the physical properties** and the **content of bioactive compounds of herbal products.**

1) Alijaniha, F. et al. 2021. Effect of gamma irradiation on cytotoxicity, phenolics content and acute toxicity of *Cuscuta chinensis* L. extract. Radiat. Phys. Chem. 185 (2021) 109508. https://doi.org/10.1016/j.radphyschem.2021.109508
2) Choi, J.I. et al. 2012. Effect of radiation on disinfection and mechanical properties of Korean traditional paper, Hanji. Radiat. Phys. Chem. 81 (8), 1051–1054.
3) Koseki, P.M. et al., 2002. Effects of irradiation in medicinal and eatable herbs. Radiat. Phys. Chem. 63 (3–6), 681–684. https://doi.org/10.1016/S0969-806X(01)00658-2.

ARE IRRADIATED PRODUCTS SAFE-1* ?

Paeoniae radix (traditional herbal medicine from South Korea) was irradiated at a **dose of 10 kGy**. The aqueous extract of Paeoniae radix was then tested for genotoxicity using the following methods:

(a) Ames test in *Salmonella typhimurium*; and
(b) micronucleus test in cultured Chinese hamster ovary (CHO) cells.

RESULTS:

- The irradiated extract **of Paeoniae radix** was **neither mutagenic nor cytogenic**;
- The HPLC chromatogram of irradiated Paeoniae radix was **NOT SIGNIFICANTLY DIFFERENT** from that of the non-irradiated extract;
- The irradiated Paeoniae radix (at 10 kGy) was **toxically safe** and **chemically stable**.

ARE IRRADIATED PRODUCTS SAFE-2 ?

- Acute toxicity test of ethanolic extracts from **irradiated temu lawak (*C. xanthorizza*)** at **5 and 10 kGy** on Swiss Webster mice up to a dose of 7500 mg/kg body weight showed **no significant difference** compared to un-irradiated samples. [SAFE]
- Acute toxicity test of ethanolic extracts from **irradiated *sambiloto herb*** (*A. paniculata*) at **7.5 kGy** on Swiss Webster mice up to a dose above 5000 mg/kg body weight **showed no significant difference** compared to un-irradiated samples. [SAFE]
- Acute toxicity test of ethyl acetate extracts from **irradiated *jati belanda*** (*G. ulmifolia*) at **7.5 kGy** on DDY mice up to a dose above 5000 mg/kg body weight showed **no significant difference** compared to un-irradiated samples. [SAFE]

1. H. Winarno. Safety evaluation of the ethyl acetate extract on irradiated tea parasite: Acute toxicity study on mice. *J. Sains dan Teknologi Nuklir* 12 (2), (2011) 85-94.
2. Ermin Katrin, Susanto dan H. Winarno. Toksisitas akut ekstrak etanol temulawak (*Curcuma xanthorrizha* Roxb.) iradiasi yang mempunyai aktivitas antikanker. *J. Ilmiah Aplikasi Isotop dan Radiasi* 7 (1), (2011) 41-52.
3. Ermin Katrin, Susanto dan H. Winarno. Keamanan Sambiloto (A. paniculata Ness) yang diiradiasi gamma berdasarkan aspek toksisitas akutnya terhadap mencit Swiss webster, *J. Sains dan Teknologi Nuklir*, Vol. 15 (2), (2014) 1003-118
4. E.K. Winarno, Andayani, Susanto, H. Winarno. [Pengaruh iradiasi gamma pada toksisitas akut oral ekstrak etanol jahe merah (Zingiber officinale), *Jurnal Ilmiah Aplikasi Isotop dan Radiasi*, 10 (1), (2014) 55-70.
5. H. Winarno, E.K. Winarno, Susanto. Oral acute toxicity study on ethanolic extracts of un-irradiated- and irradiated Guazuma ulmifolia leaves in DDY mice.AIP Conference Proceedings 2391, 050006 (2022); Published Online: 24 March 202

SUMMARY

- Ionizing radiation is **an alternative method** for **reducing microbial contamination** in a matters and extending its shelf life.
- The irradiation dose used **depends on the initial contamination level**, **the ingredient composition, and the irradiation conditions**.
- The selection of the appropriate dose (as low as possible) is necessary to reduce the contamination without compromising its claimed efficacy.
- Irradiating the raw materials / herbal medicines / finished products **at high doses above the recommended dose limits can damage the efficacy of the raw materials**.
- The combination of irradiation treatment and the implementation of **Good Manufacturing Practices** (GMP) can produce the high-quality of herbal medicines.
- BRIN continues to improve the (nuclear) technology that can be utilized by the public in various sectors.

PT. PHYTOCHEMINDO REKSA

“Benchmarking Quality Assurance/ Quality Control In GMP Manufacturing”

JAKARTA, 19 AGUSTUS 2025



THE HISTORY

PT. PHYTOCHEMINDO REKSA

Drs. Wim Kalona, an pharmacist, entrepreneur, founder IKATAN APOTEKER INDONESIA (IAI) and several pharmaceutical companies in Indonesia.

Prof. DR. Oei Ban Liang, a distinguished biotechnologist & organic chemistry from ITB and Biotechnology pioneer in Indonesia.



FOUNDERS OF PHYTOCHEMINDO

NATURAL EXTRACT



Healthcare

- Powder Extract
- Liquid Extract
- Volatile oil



Cosmetic & Personal Care

- Oils
- Glycolic extract
- Natural Scrub



Food & Beverage

- Powder
- Liquid Extract
- Granule extract



Veterinary

- Powder Extract
- Liquid Extract

TOLL MANUFACTURING



Bottle



Blister



Pouch



Strip



Tea Bag



PHYTOCHEMINDO REKSA - KLAPANUNGGAL

Building Space : 2,880m2

Sertifikasi : BPOM, FSSC22000, Halal, Kosher, K3

Fasilitas :

- Natural Ingredients Extraction
- R&D Food, OT/SK, Analytical Development
- Manufacturing facility process rooms
- QA& QC Laboratorium
- WWTP (Waste Water Treament Process)
- Canteen
- Prayer Room (Musholla)

Natural Active Ingredients

CUR X-ZOL®

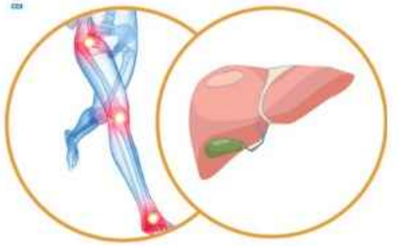
GABOOSTPRO ®

PLUMERIA OBTUSE GE

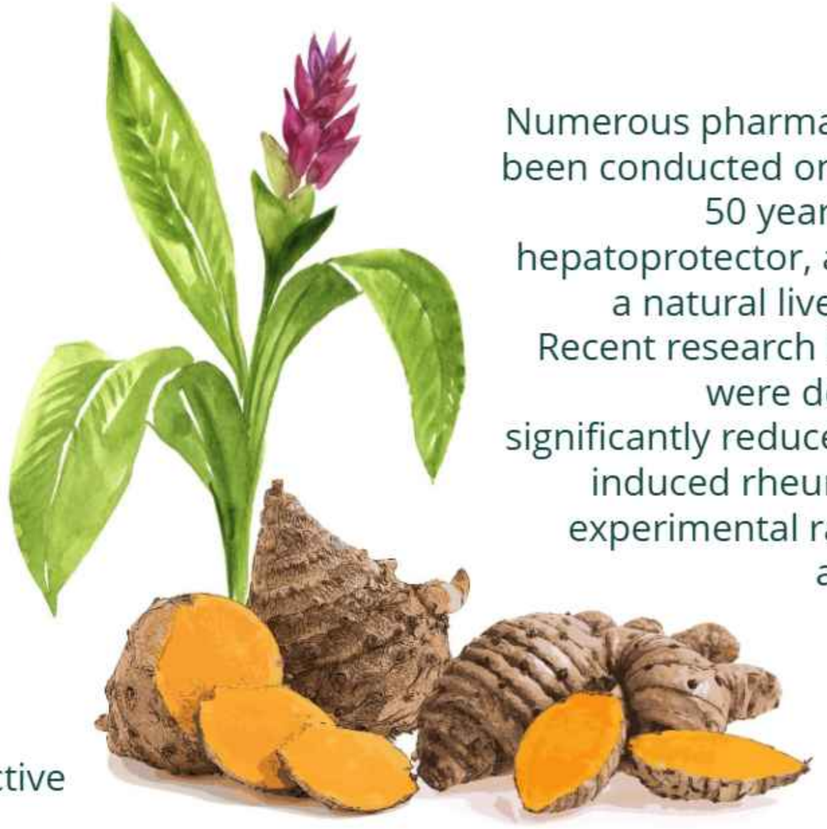


CUR X-ZOL®

Curcuma xanthorrhiza Extract / Java Turmeric, Temulawak



Belonging to the Zingiberaceae family, Curcuma xanthorrhiza is indigenous to Java, Indonesia. The large rhizome of the plant is commonly used as a key ingredient in traditional Indonesian medicine to treat liver or gallbladder disorders, diarrhoea, digestive problems, and rheumatism. Curcuma xanthorrhiza is considered a national icon and often referred to as “Indonesia Ginseng”.



Numerous pharmacological and clinical studies have been conducted on Curcuma xanthorrhiza in the last 50 years. Curcuma xanthorrhiza acts as a hepatoprotector, accelerates bile flow, which acts as a natural liver cleanser and lowers cholesterol. Recent research by Indian and Indonesian scientist were demonstrated that the ***CUR X-ZOL®*** significantly reduce the Complete Freund’s Adjuvant-induced rheumatoid arthritis progression in the experimental rats due to its potential antioxidant and health-promoting properties.1



Phytochemindo began its research on Curcuma xanthorrhiza in 1978 andsuccessfully isolated the active ingredients, curcuminoid and Curcuma xanthorrhiza oil. Curcuminoid contain curcumin and desmethoxycurcumin. Curcuma xanthorrhiza oil contains xanthorrhizol and ar/β Curcumin. Phytochemindo has developed a proprietary branded ***Curcuma xanthorrhiza extract: CUR X -ZOL®.***

Patrick A Kalona, Uma Sundaresan, Chellappandian M, Ariharasivakumar. 2024. Curcuma xanthorrhiza Rhizome Extract Attenuates the Complete Freund’s Adjuvant-induced Rheumatoid Arthritis in Rats. Journal Name: Journal of Pharmacology and Pharmacotherapeutics: India.

GABOOSTPRO®

Channa Striata (Ikan Gabus)

Channa striata has proven medical benefits due to the high protein content of snakehead fish. It has been traditionally used to enhance wound healing after surgical operations, reduces post-operative pain and helps to fulfil protein needs or supplementation for breastfeeding, child growth, and general health.





Channa striata (striped snakehead) habitats is widely distributed across Indonesia:

1. South Sumatera Province
2. West Java Province
3. South Kalimantan Province

POSSIBLE MECHANISMS:

Protein Source: Channa striata provides essential amino acids necessary for collagen synthesis, a key component of new tissue formation.

Anti-inflammatory Effects: Some studies suggest potential anti-inflammatory properties of certain compounds in the fish, which can help reduce inflammation around the wound and promote healing.

FEATURES:

Meets the Standar Nasional Indonesia (Indonesian National Standard) for Channa striata extract.

Odourless with no fishy smell and may be applied on a wide range of formulation in capsules uncoated tablets, powder drink, and syrup.

Is halal certified.

Manufactured in a GMP certified production facility, with in-house laboratories to assure that the product quality meets the relevant regulations.

Manufactured in a facility whose management system is certified as being in conformity with ISO 22000 for food safety.

PLUMERIA OBTUSE GE

WINNER ICI 2025

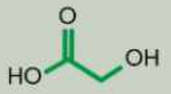




For the Balinese people, frangipani flowers are not just ornamental plants, but also have deep meaning in everyday life, such as in traditional ceremonies and daily worship. This flower is often found in house yards, temples and other important places. The pure white colour represents purity and sincerity, making it highly valued in religious contexts and everyday life.

In addition to being the capital of Bali Province, Denpasar is also known as a center for producing frangipani flowers. The fallen flowers are collected and then dried to become raw materials for making cosmetics, incense and aromatherapy. In a week, around 3-5 tons of dried flowers can be produced.





One of the bioactive compounds in frangipani flowers is glycolic acid.



Glicolic acid benefits in beauty care:


Skin brightening


Tighten the skin


Soften the skin


Treat acne & scar



Small studies of 5% application in cosmetics*
- it doesn't sting
- no acne appears
- Odour less
- skin feels brighter

**Compare with papain + lactic acid formulation in 7 days of used*

TABLE SUMMARY









Extract Production Flow Process

Quality parameters for:

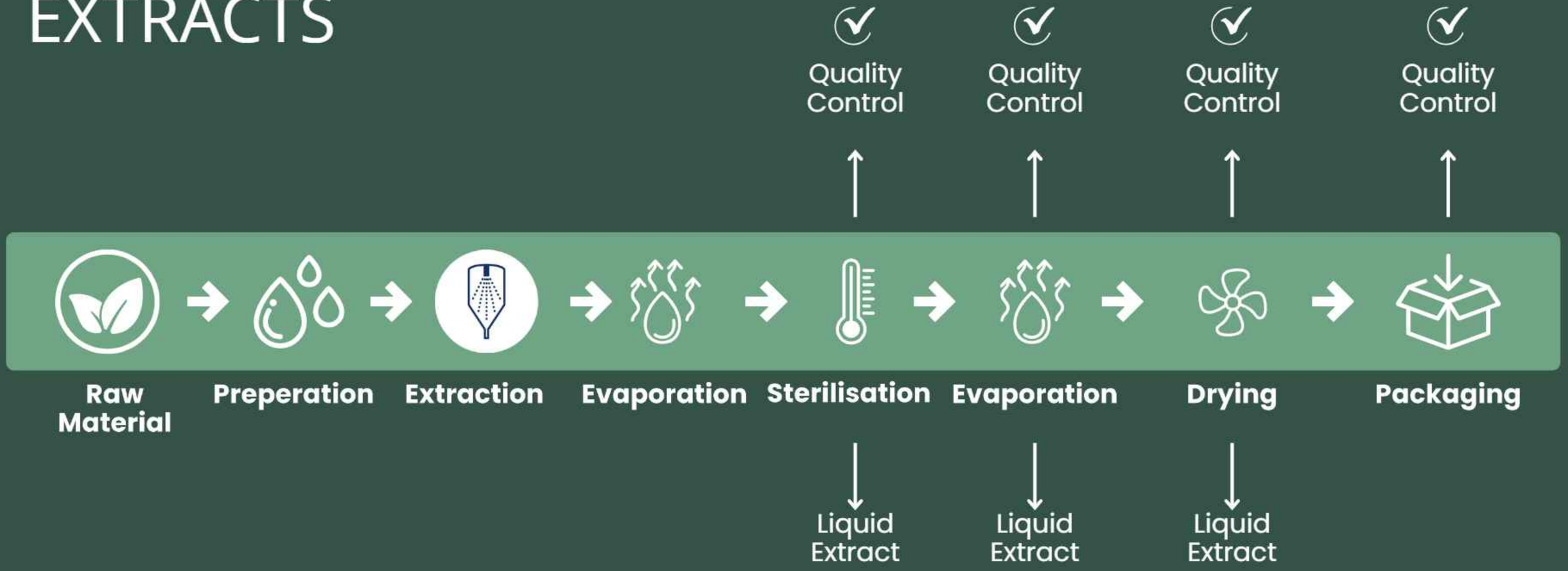
- Raw Materials
- Plant Based Extracts

Handling

- Raw Materials
- Plant Extracts

Distribution of Plant Extracts

FLOWCHART FOR PLANT EXTRACTS



CONTROL POINTS FOR PLANT EXTRACT PROCESS



Plant Extraction Temperature

The size of the raw material is relevant to the size of the contact with the solvent is being used.



Methods of Extraction

The method of extractions with depend on the type of raw materials, types of raw materials, solvents being used and the optimal process being used.



Type of Solvents

The method of extractions with depend on the type of raw materials, types of raw materials, solvents being used and the optimal process being used.

CONTROL POINT PROCESS OF EXTRACT PRODUCTION



Amount of Solvents

The amount of solvent depends on the particle size of the simplisia raw material and the extraction method used.



Temperature Process

The process temperature highly depends on the characteristics of the active compound and the optimal boiling point of the solvent used.



Conditions of Process

The process temperature highly depends on the characteristics of the active compound and the optimal boiling point of the solvent used.

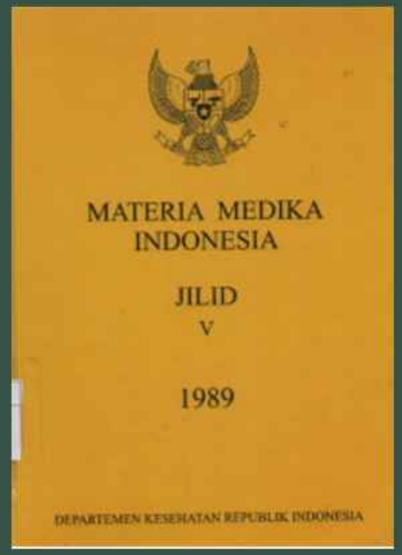
QUALITY CONTROL PARAMETERS FOR RAW MATERIALS

1.References Available



Editions:

- ⟶ 2008
- ⟶ 2010
- ⟶ 2013
- ⟶ 2017
- ⟶ **2022**



Editions :

- ⟶ 1977
- ⟶ 1978
- ⟶ 1979
- ⟶ 1980
- ⟶ 1989
- ⟶ 1995

Internal Specifications



QUALITY CONTROL PARAMETERS FOR RAW MATERIALS

2. Type of parameters

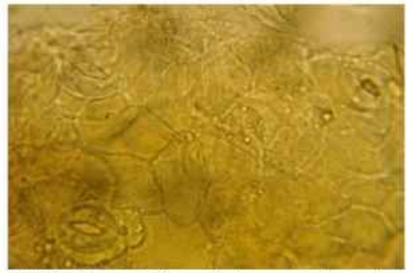
Identity of Raw Material

Macroscopic materials



Simplisia daun binahong

Microscopic Descriptions



1. Epidermis bawah dengan stomata



2. Mesofil daun dengan kristal kalsium oksalat bentuk roset



3. Epidermis atas



4. Berkas pengangkut dengan penebalan tipe spiral

QUALITY CONTROL PARAMETERS
RAW MATERIALS

2. Type of parameters

Physical Parameters

Loss on drying <111 > Less than 10%

Total Ash<81> Less than 16,3%

Acid-insoluble ash <82> Less than 1,9%

Water Soluable extract<91> Less than 13,5%

Ethanol-soluble extract < 92>



QUALITY CONTROL PARAMETERS RAW MATERIALS
Plant Extracts

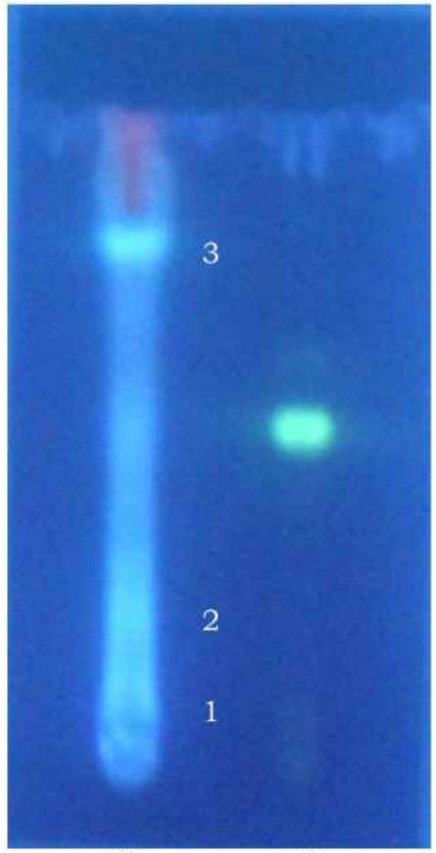
Residual Solvents

Qualitative

The examination is only for the presence of the active compound

Quantitative

Examination of the amount of active compound contained



Keterangan:
S: Simplisia daun binahong
P: Pembanding rutin
R_f pembanding rutin 0,50
R_x 1. 0,14
R_x 2. 0,36
R_x 3. 1,60

QUALITY CONTROL PARAMETERS RAW MATERIALS
Plant Extracts

1.Reference



Edisi:

⟶ 2008
⟶ 2010
⟶ 2013
⟶ 2017
⟶ 2022

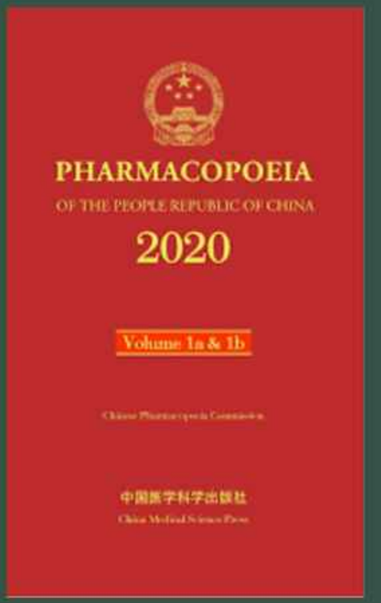


Edisi:

⟶ 1977
⟶ 1978
⟶ 1979
⟶ 1980
⟶ 1989
⟶ 1995

Internal Specifications





PERATURAN BADAN PENGAWAS OBAT DAN MAKANAN NOMOR 29 TAHUN 2023 TENTANG PERSYARATAN KEAMANAN DAN MUTU OBAT BAHAN ALAM

QUALITY CONTROL PARAMETERS RAW MATERIALS

Plant Extracts

Organoleptic

Physical

- Water content
- Type of Extract– Liquid Extract
- Total Solid -- Ekstrak Kental
- Bulk Density – Dry Extract

Chemical

- Qualititative
- Quantitative

QUALITY CONTROL PARAMETERS RAW MATERIALS
Plant Extracts

2.Type of Parameters

Microbiology

E. Microbial contamination

•Total Plate Count (TPC)	:not more than 105 koloni/g
•Yeast and Mold Count (YMC)	:not more than 103 koloni/g
•Escherichia coli	: not more than 10 AM/g *
•Other Enterobacteriaceae	: not more than 103 AM/g*
•Clostridia	: negative/g
•Salmonella	: negative/g
•Shigella	: negative/g

For liquid medicine, the unit is calculated per mL.

f. Total aflatoxins (aflatoxin B1, B2, G1, and G2)

The total aflatoxin content (aflatoxin B1, B2, G1, and G2) must not exceed 20 mg/kg, with the condition that aflatoxin B1 must not exceed 5 µg/kg.
Let me know if you'd like this phrased for a formal report or regulatory document—I can help tailor it to your needs.

Heavy metals

g. Heavy metal contamination

• Lead (Pb)	:not more than 10 mg/kg or mg/L or ppm
• Cadmium (Cd)	:not more than 0,3 mg/kg or mg/L or ppm
• Arsenic (As)	:not more than 5 mg/kg or mg/L or ppm
• Mercury (Hg)	:not more than 0,5 mg/kg or mg/L or ppm



QUALITY CONTROL PARAMETERS RAW MATERIALS
Plant Extracts

2.Type of Parameters

Residual Solvents

h. **Residual limit of extraction solvents other than water**

- Etanol : 1 % or 10.000 ppm
- n- Heksana : 0,029 % or 290 ppm
- Etil asetat : 0,5 % or 5.000 ppm
- Metanol : 0,3% or 3.000 ppm

The use of solvents other than those mentioned above must be accompanied by an assessment of safety and benefits



QUALITY CONTROL PARAMETERS RAW MATERIALS
Plant Extracts

1. Raw Material Specifications – includes :

- ☑ Material Name
- ☑ Material Code
- ☑ Plant Part
- ☑ Plant Origin
- ☑ Storage Condition
- ☑ Storage Duration
- ☑ Examination Reference
- ☑ Examination Parameter
- ☑ Parameter Category
- ☑ Metods of Analysis
- ☑ Picture of Material

2. Raw Material Specifications – contains:

- ☑ Extract Name
- ☑ Extract Description
- ☑ Extract Producer
- ☑ Storage Condition
- ☑ Storage Duration
- ☑ Examination Reference
- ☑ Examination Parameter
- ☑ Parameter Category
- ☑ Metods of Analysis
- ☑ Reference for Analysis Results
  Extract (Spectro, Chromotogram)

QUALITY CONTROL PARAMETERS RAW MATERIALS
Plant Extracts

3. Certificate of Analysis – contains:

Results of raw material and extract product testing compared to specifications.

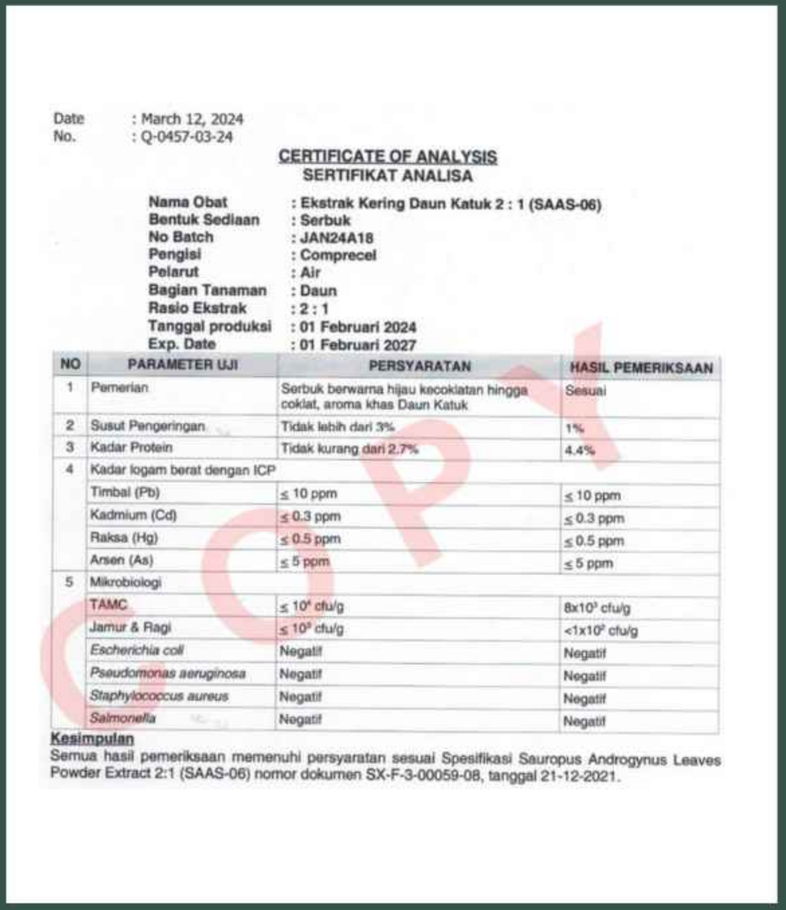


Customer Account	200206
Customer PO No.	B1983/72F3/1123/L1
Net Weight Shipped	25.0 Kgs
Manufacturing Date	January 05, 2024
Best Used Before	January 03, 2026

CERTIFICATE OF ANALYSIS

MORINDA POWDER EXTRACT	
Material Code	**10000109**
Customer Product Code	**-**
Batch No.	**0000107980**

	Specification	Test Results	Unit
Appearance	Powder	Pass	
Color	Pale brown	Pass	
Odor	Characteristic of *Morinda citrifolia*	Pass	
Taste	Slightly acid	Pass	
Moisture Content	NMT 8.0	4.5	%
Solubility	Soluble in water	Pass	
Microbiological Data			
Total Plate Count	NMT 10,000	<10	cfu/g
Yeast and Mold	NMT 100	<10	cfu/g
Coliforms	None detected	None detected	cfu/g
E. Coli	None detected	None detected	cfu/g
Salmonella	None detected	None detected	/25g



Date : March 12, 2024
No. : Q-0457-03-24

CERTIFICATE OF ANALYSIS
SERTIFIKAT ANALISA

Nama Obat : Ekstrak Kering Daun Katuk 2 : 1 (SAAS-06)
Bentuk Sediaan : Serbuk
No Batch : JAN24A18
Pengisi : Comprecel
Pelarut : Air
Bagian Tanaman : Daun
Rasio Ekstrak : 2 : 1
Tanggal produksi : 01 Februari 2024
Exp. Date : 01 Februari 2027

NO	PARAMETER UJI	PERSYARATAN	HASIL PEMERIKSAAN
1	Pemerian	Serbuk berwarna hijau kecoklatan hingga coklat, aroma khas Daun Katuk	Sesuai
2	Susut Pengeringan	Tidak lebih dari 3%	1%
3	Kadar Protein	Tidak kurang dari 2.7%	4.4%
4	Kadar logam berat dengan ICP		
	Timbal (Pb)	≤ 10 ppm	≤ 10 ppm
	Kadmium (Cd)	≤ 0.3 ppm	≤ 0.3 ppm
	Raksa (Hg)	≤ 0.5 ppm	≤ 0.5 ppm
	Arsen (As)	≤ 5 ppm	≤ 5 ppm
5	Mikrobiologi		
	TAMC	≤ 10^4 cfu/g	$8x10^3$ cfu/g
	Jamur & Ragi	≤ 10^3 cfu/g	$<1x10^2$ cfu/g
	Escherichia coli	Negatif	Negatif
	Pseudomonas aeruginosa	Negatif	Negatif
	Staphylococcus aureus	Negatif	Negatif
	Salmonella	Negatif	Negatif

Kesimpulan
Semua hasil pemeriksaan memenuhi persyaratan sesuai Spesifikasi Sauropus Androgynus Leaves Powder Extract 2:1 (SAAS-06) nomor dokumen SX-F-3-00059-08, tanggal 21-12-2021.

RAW MATERIAL HANDLING



INCOMING RAW MATERIALS

Raw materials are received in clean condition at the Raw Material Warehouse. After receipt, the raw material status is set to quarantine for sampling by the QC Department.



RAW MATERIAL STORAGE

Raw material storage is based on specified storage conditions (temperature & humidity) and shelf life as stated in the specifications. The most important aspect is the address system that is implemented.



RAW MATERIAL QUALITY INSPECTION

After sampling, the raw material is inspected according to applicable specifications. The inspection result can be either APPROVED or REJECTED. If APPROVED, it can be used immediately; if REJECTED, it follows the HULS mechanism.



REPROSESSING RAW MATERIALS

Raw material preprocessing may be carried out if additional treatment is needed before use in production, such as drying, size reduction, or soaking with specific liquids.

EXTRACT PRODUCT INSPECTION



EXTRACT PRODUCT INSPECTION

Inspection of extract products is based on applicable specifications. The inspection results serve as the basis for product approval. If the product is APPROVED, it can be sent to the warehouse; if REJECTED, it may be reprocessed or destroyed.



STORAGE OF EXTRACT PRODUCTS

Storage of finished extract products is based on conditions (packaging, temperature, and humidity) as well as the storage duration stated in the specifications. The storage system must also provide a clear address identification.
Let me know if you'd like help formatting this into a warehouse management SOP or guideline!



DISTRIBUTION OF EXTRACT PRODUCTS

Extract dispatch from the warehouse is based on the FEFO (First Expired First Out) principle. Shipment must be carried out under conditions that match the storage requirements.\

PLANT EXTRACT DISTRIBUTION

Main points

1. Distribution Conditions

Must comply with storage requirements and be monitored periodically as observed.

2. Distribution Arm

Must undergo transportation vendor audit and ensure truck conditions are appropriate.

3. Delivery Duration

Must be based on stability study data during transportation



Keypoints of Presentation and Benchmarking

Selection of IEBA extract suppliers must be certified with CPOTB, ensuring accountability for their quality assurance.

One form of document that guarantees extract quality is the CoA (Certificate of Analysis). Therefore, the accuracy of the data source and its traceability must be ensured.

Quality assurance of the extract begins from the selection of raw materials through to the distribution of the extract product.

Thank You





SCAN ME

PT. PHYTOCHEMINDO REKSA

For others information products,
please visit our website
www.phytochemindo.com

PENGGUNAAN TEKNOLOGI NANO SEBAGAI FITOTERAPI DAN STANDARISASINYA

Prof.Dr.Apt.Heni Rachmawati, M.Si

School of Pharmacy – Bandung Institute of Technology

Capacity Building and Workshop on Quality Standardization of Extracts and Quality Control Assessment in Traditional and Herbal Medicine Products
BPOM – Jakarta, 19-20 Agustus 2025

Definisi Fitoterapi dalam Pengobatan Tradisional

Pengertian Umum

Fitoterapi berasal dari bahasa Yunani:

- *Phyto* = tumbuhan
- *Therapeia* = pengobatan

Dengan demikian, **fitoterapi adalah pengobatan penyakit atau pemeliharaan kesehatan menggunakan bahan aktif yang berasal dari tumbuhan**, baik dalam bentuk **simplisia**, **ekstrak**, maupun **formulasi produk jadi**.

Fitoterapi merupakan bagian dari **pengobatan tradisional yang berbasis ilmiah**, berbeda dengan penggunaan tumbuhan secara empiris atau magis. Fitoterapi memanfaatkan senyawa bioaktif tanaman yang telah diketahui efek biologisnya, dengan pendekatan **farmakologi modern** dan **evidence-based**.



Ciri Khas Fitoterapi

Aspek	Penjelasan
Asal Bahan	Tumbuhan obat: akar, daun, bunga, kulit batang, buah, getah
Bentuk Sediaan	Simplisia kering, teh herbal, tincture, kapsul ekstrak kering, sirup, salep
Pendekatan	Ilmiah: melalui studi fitokimia, farmakologi, toksikologi
Tujuan	Mengobati penyakit, meningkatkan kesehatan, mencegah kekambuhan
Berbasis Bukti	Didukung oleh uji praklinik, uji klinik, atau studi observasional
Berbeda dari	•Jamu (berbasis empirik, belum tentu terstandar) • Homeopati (prinsip pengenceran ekstrim) •Aromaterapi (berbasis minyak atsiri, tidak selalu sistemik)

Fitoterapi dalam Konteks Pengobatan Tradisional

Dalam sistem pengobatan tradisional (Indonesia, Tiongkok, Ayurveda, dsb), fitoterapi sering menjadi bagian integral. Namun, fitoterapi modern menekankan pada:



Kuantifikasi dan standarisasi kandungan zat aktif



Kepastian dosis dan mutu



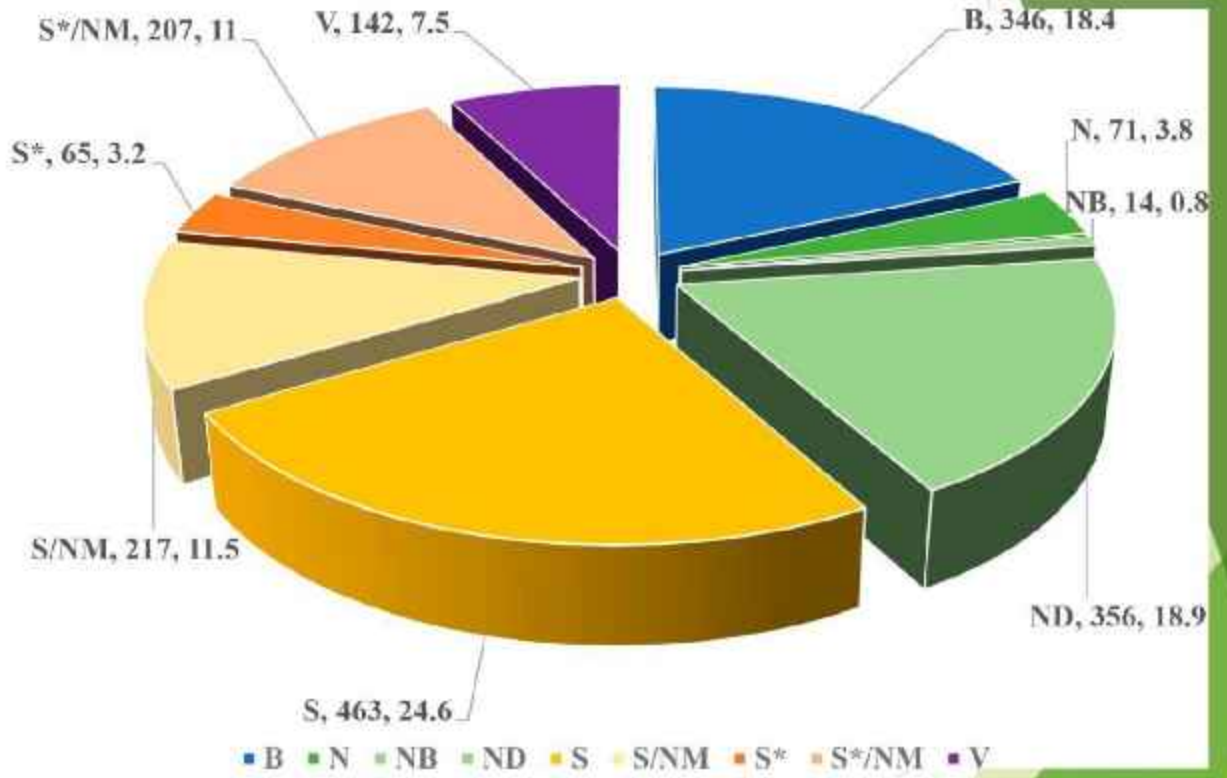
Uji efikasi dan keamanan



Integrasi ke dalam pelayanan kesehatan modern (misalnya, sebagai complementary medicine)

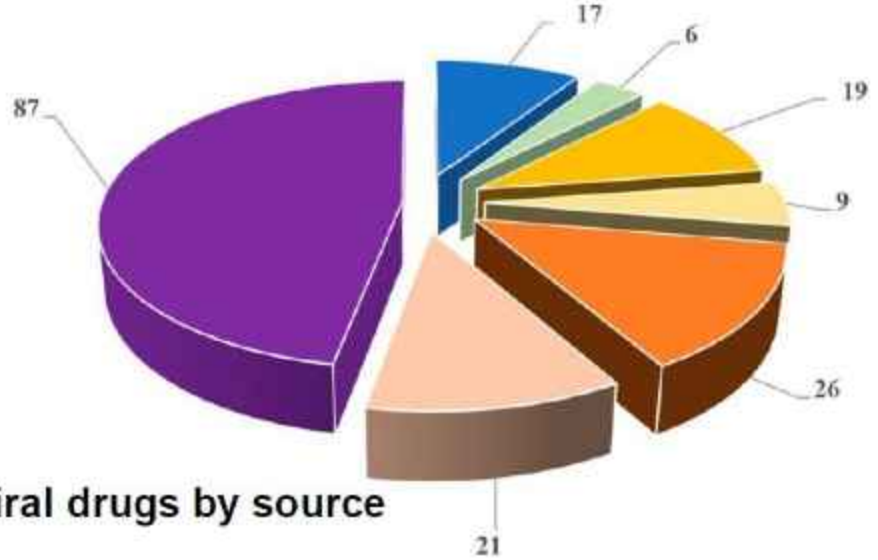
THE ROLE OF NATURAL PRODUCTS IN MEDICINE DURING THE LAST FORTY YEARS

code	brief definition
B	biological macromolecule
N	unaltered natural product
NB	botanical drug (defined mixture)
ND	natural product derivative
S	synthetic drug
S*	synthetic drug (NP pharmacophore)
V	vaccine
/NM	mimic of natural product

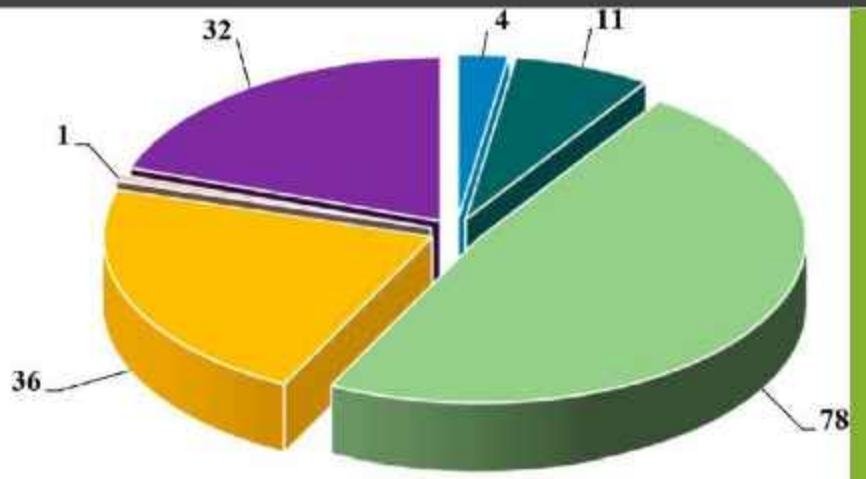


All new approved drugs 01JAN81 to 30SEP19; *n* = 1881.

Newman DJ, Cragg GM. Natural Products as Sources of New Drugs over the Nearly Four Decades from 01/1981 to 09/2019. J Nat Prod. 2020 Mar 27;83(3):770-803. doi: 10.1021/acs.jnatprod.9b01285. Epub 2020 Mar 12.



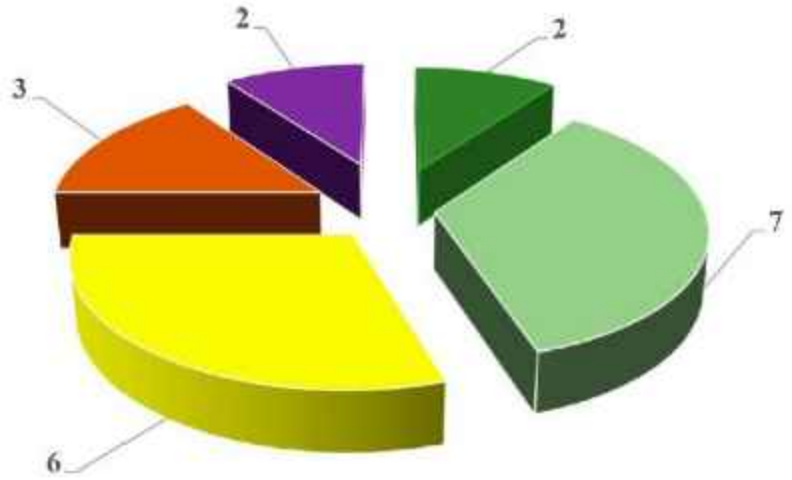
Antiviral drugs by source



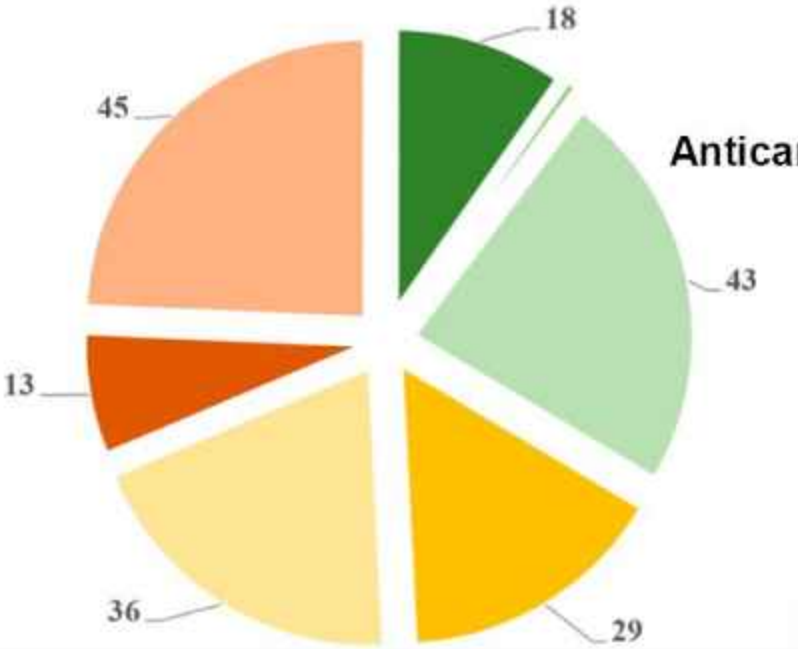
Antibacterial drugs by source

B N ND S S*/NM V

B ND S S/NM S* S*/NM V



Antiparasitic drugs by source



Anticancer drugs by source

NATURAL PRODUCTS: about 326,000 molecules

http://bioinformatics.charite.de/supernatural

http://dnp.chemnetbase.com/faces/chemical/ChemicalSearch.xhtml

WHY THERE IS AN INCREASING INTEREST IN NATURAL PRODUCTS?

-unique structures and unique mechanisms of action



NATURAL PRODUCTS: about 326,000 molecules

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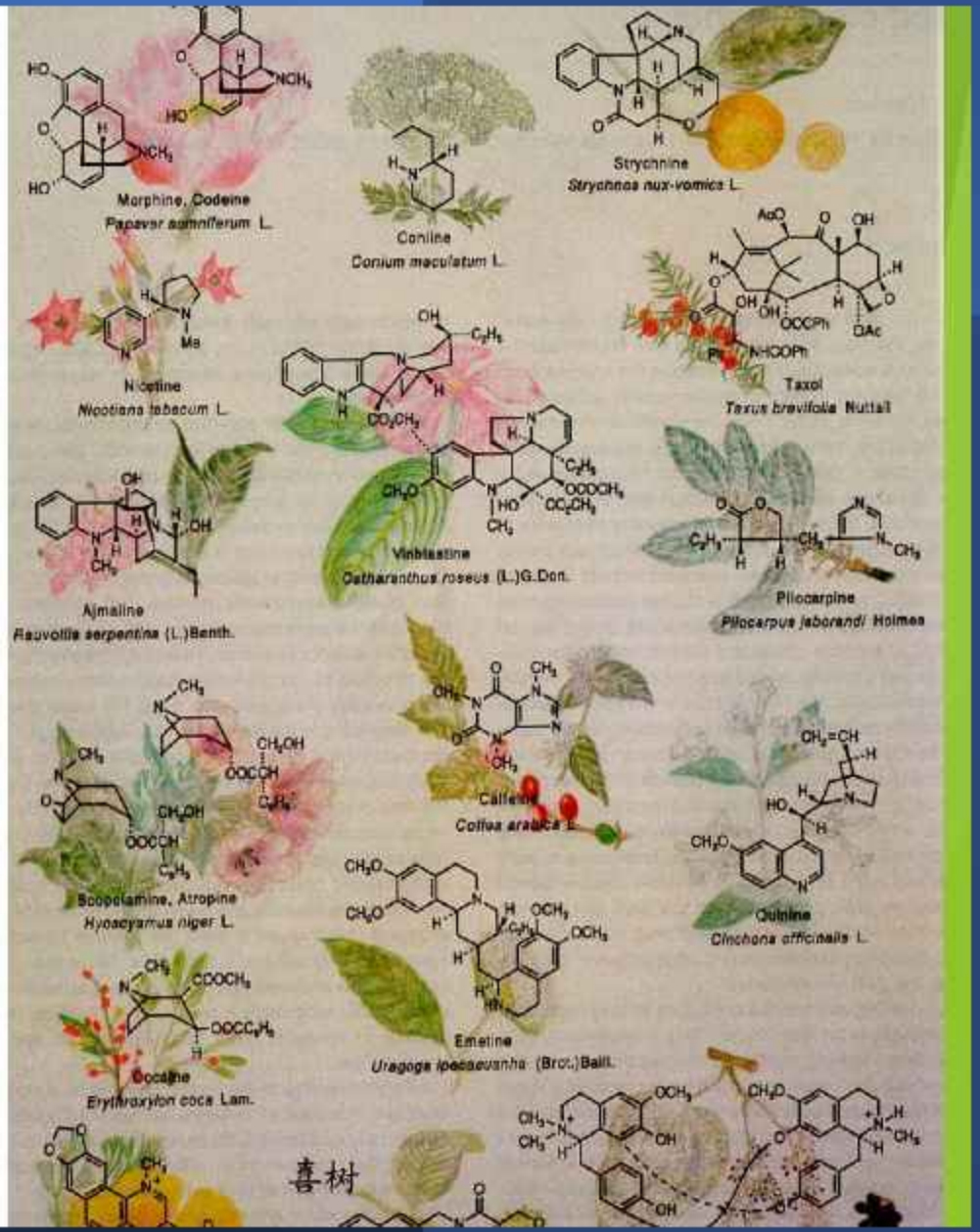

NATURAL PRODUCTS: about 326,000 molecules

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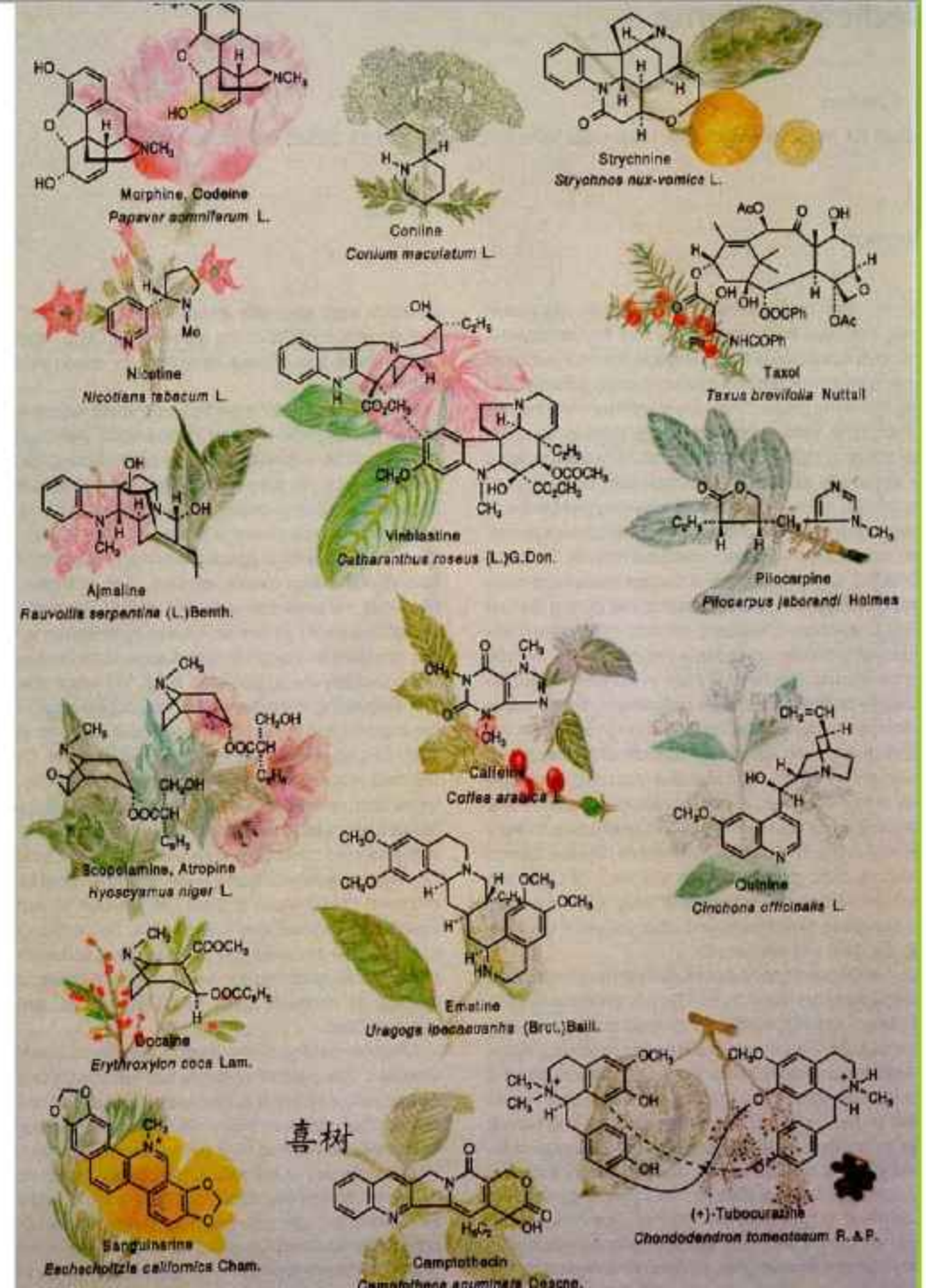
WHY THERE IS AN INCREASING INTEREST IN NATURAL PRODUCTS?

-unique structures and unique mechanisms of action

-beneficial health effects

-efficacious drugs

-safe and no side-effects associated

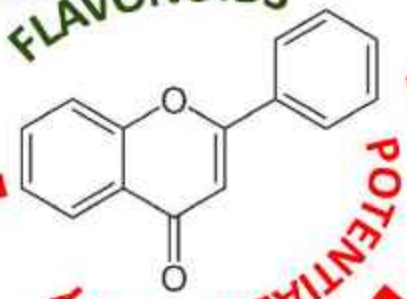


BIOCHEMICAL MECHANISMS

- ↑AMPK phosphorylation
- ↑PGC-1α expression
- ↓TLR4 expression
- ↓NF-κB activation
- ↑PKA activation
- ↓ERK1/2 phosphorylation
- ↓P38MAPK phosphorylation
- ↓MAPKs phosphorylation
- ↑PPAR-α expression
- ↑PPAR-γ expression
- ↑IRS2 expression and signalling
- ↑L-type calcium channels
- ↓SREBP-1c level
- ↓TNF-α level
- ↓tyrosine kinase



FLAVONOIDS



POTENTIAL ACTIVITY

SKELETAL MUSCLE/ CELLS
- ↑glucose uptake and oxidation
- ↑glucose tolerance and insulin sensitivity
- ↑mitochondrial biogenesis
- ↑adiponectin receptor 1 level
- ↓TG accumulation

MIOCARDIAL, RENAL TISSUE AND IMMUNE SYSTEM
- ↓pro-inflammatory citokines
- ↓inflammatory cell infiltra
- ↓apoptosis



BRAIN
- ↑nitric oxide levels
- ↓glucose transporters
- ↓ROS production
- ↓Beta secretase-1
- ↓acetylcholine
- ↑cholinesterases
- ↑ microglial activation
- ↓dopamine levels
- ↑ monoamino oxidase

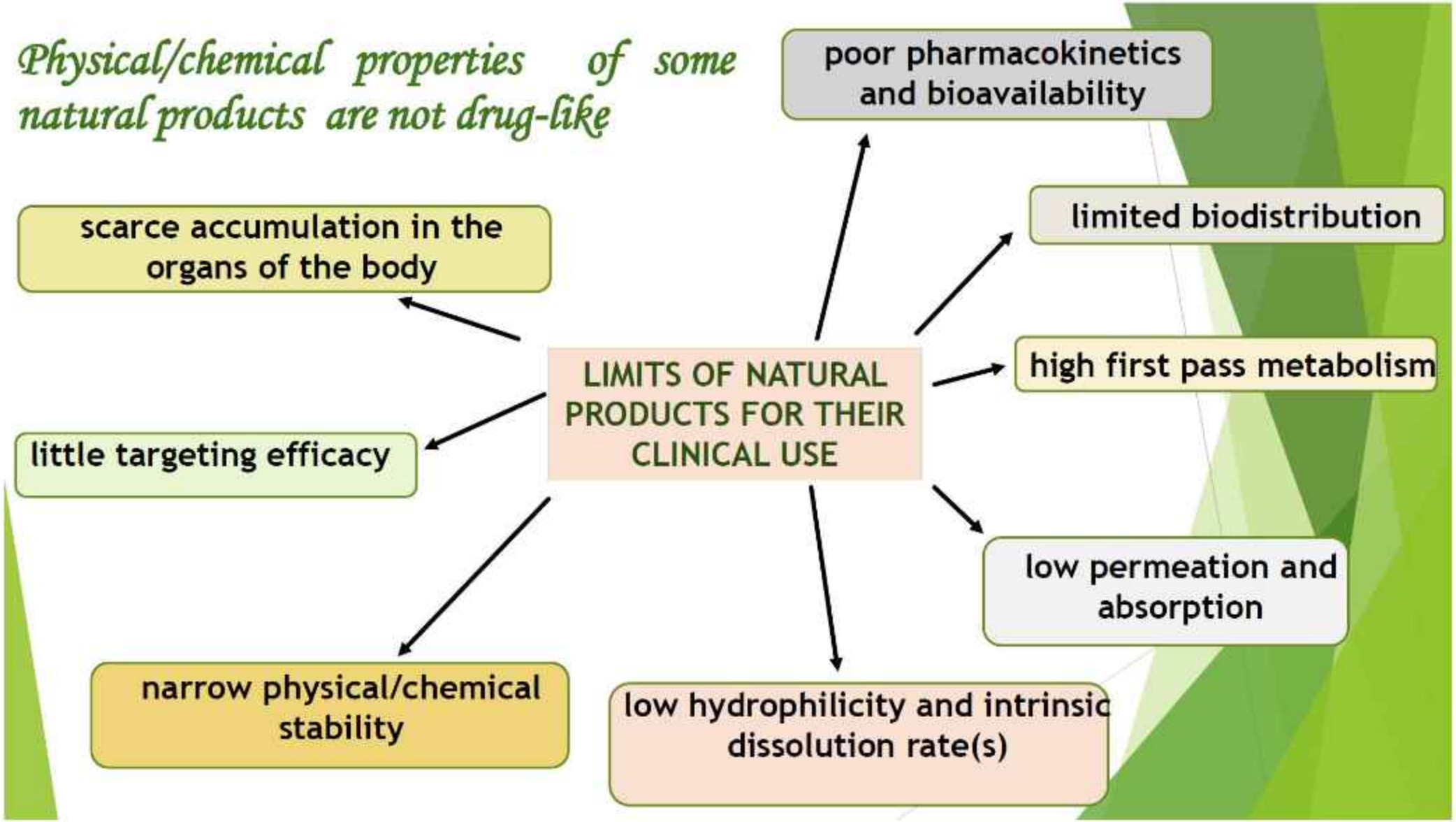


VASCULAR SMOOTH MUSCLE AND ENDOTHELIAL CELLS
- ↑eNOS activation
- ↑nitric oxide levels
- ↑vasodilatation
- ↓blood pressure
- ↓ROS production

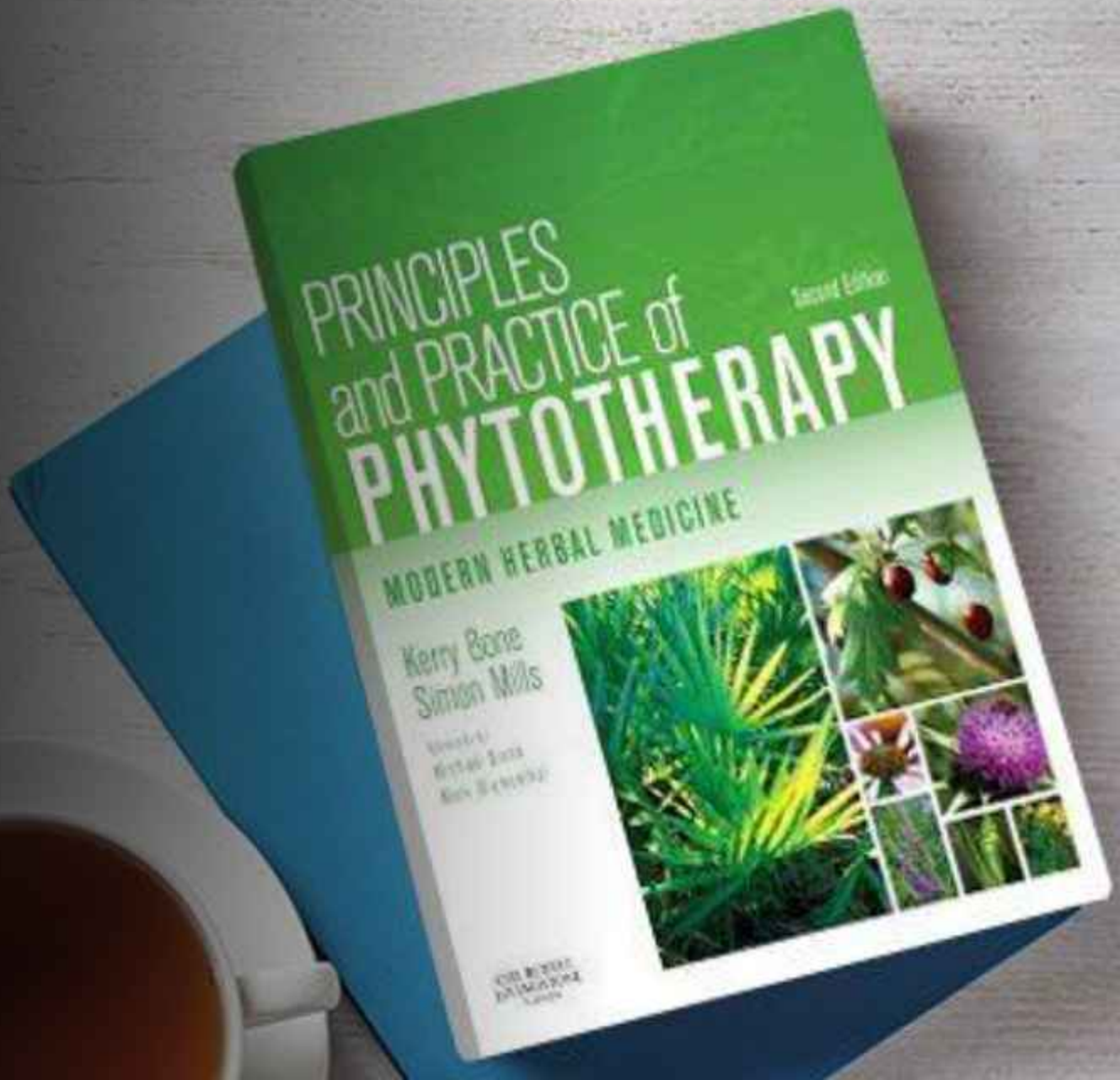
LIVER AND PANCREAS
- ↑β-cell survival and function
- ↑adiponectin receptor 1 and 2
- ↑fatty acid oxidation
- ↓lipogenesis
- ↓hepatic steatosis

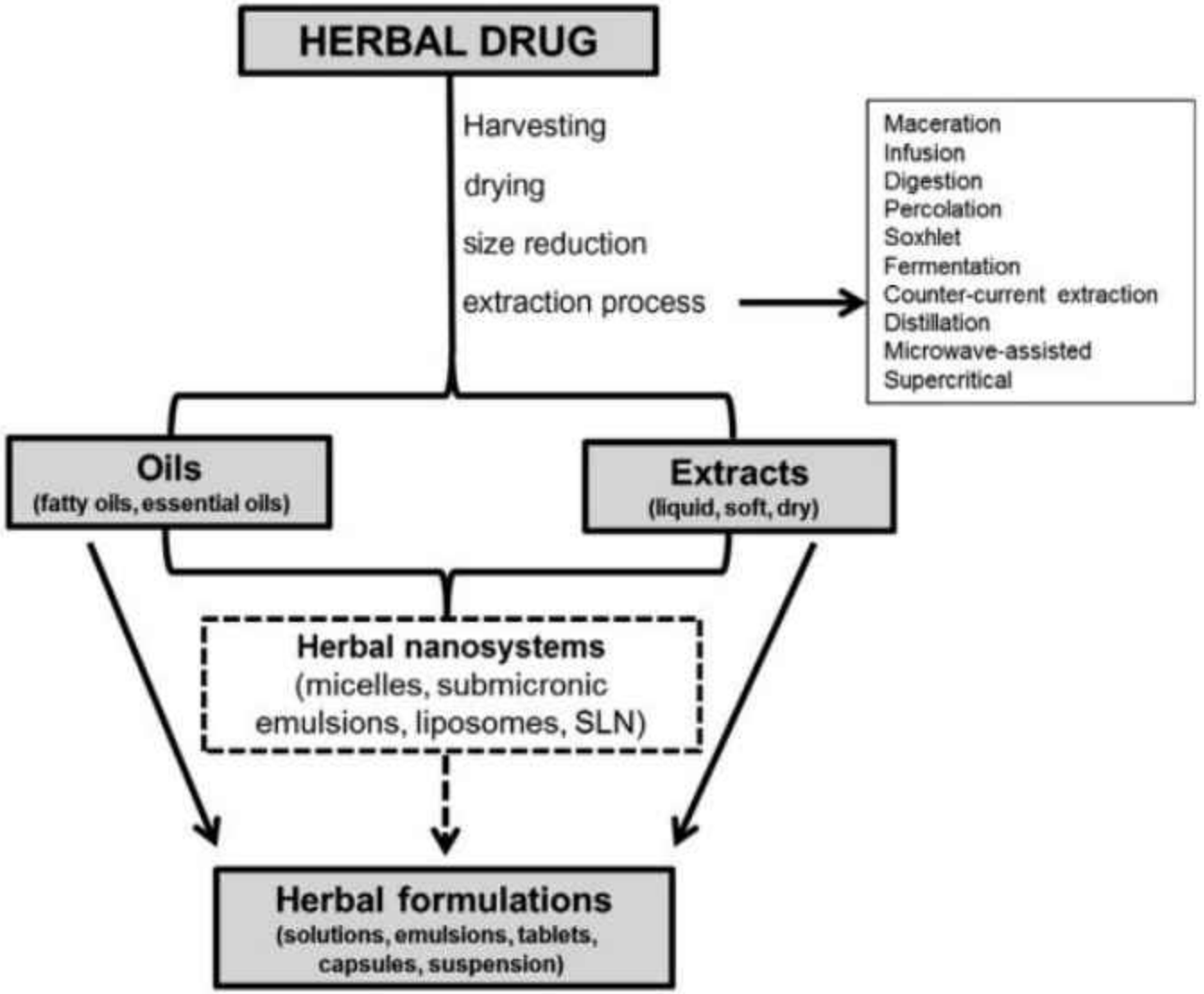
ADIPOSE TISSUE
- ↑insulin-stimulated glucose uptake
- ↑adiponectin
- ↑GLUT4 gene expression
- ↑energy expenditure
- ↓inflammation
- ↑thermogenic gene expression in brown adipose tissue

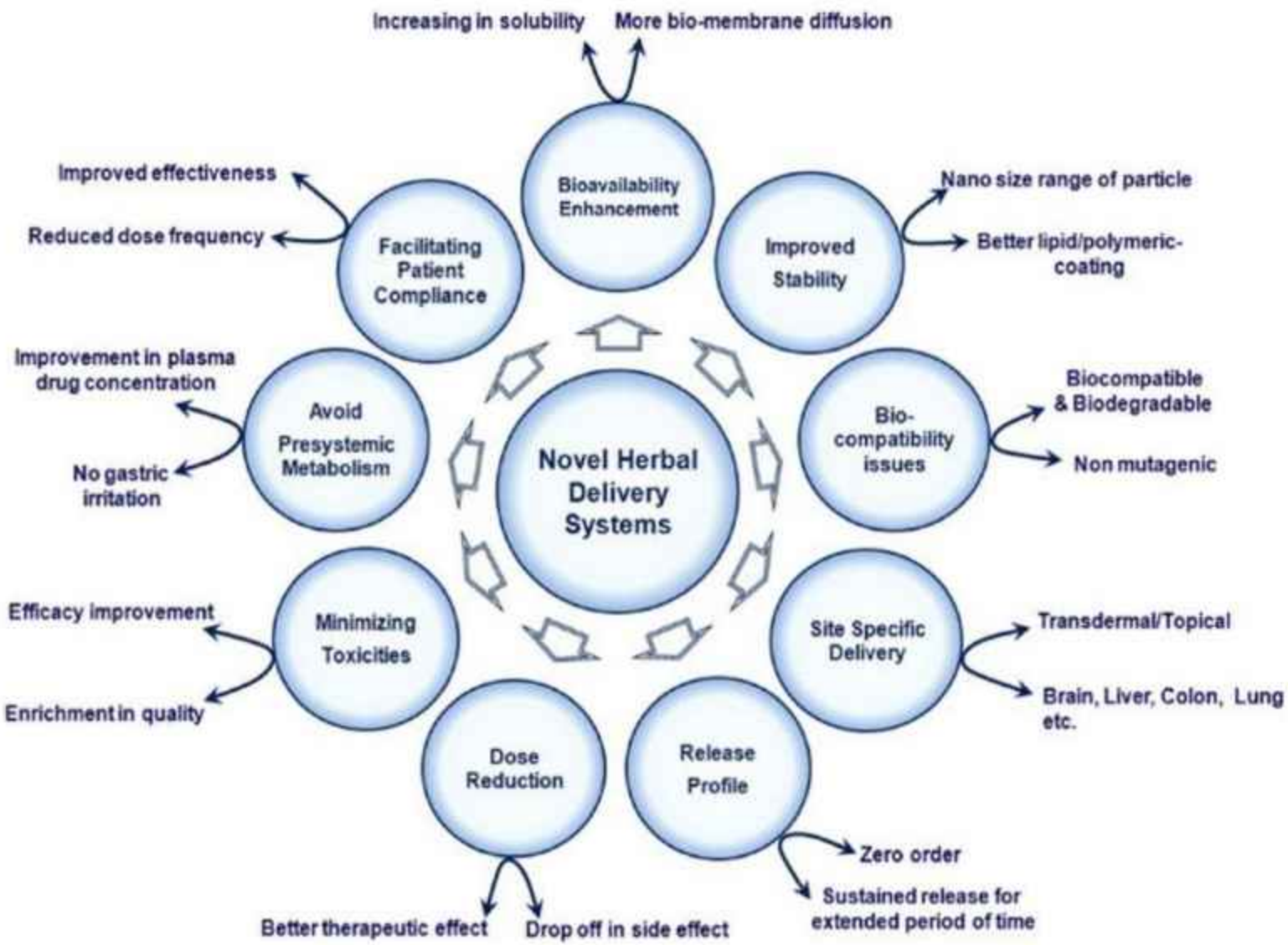
Physical/chemical properties of some natural products are not drug-like

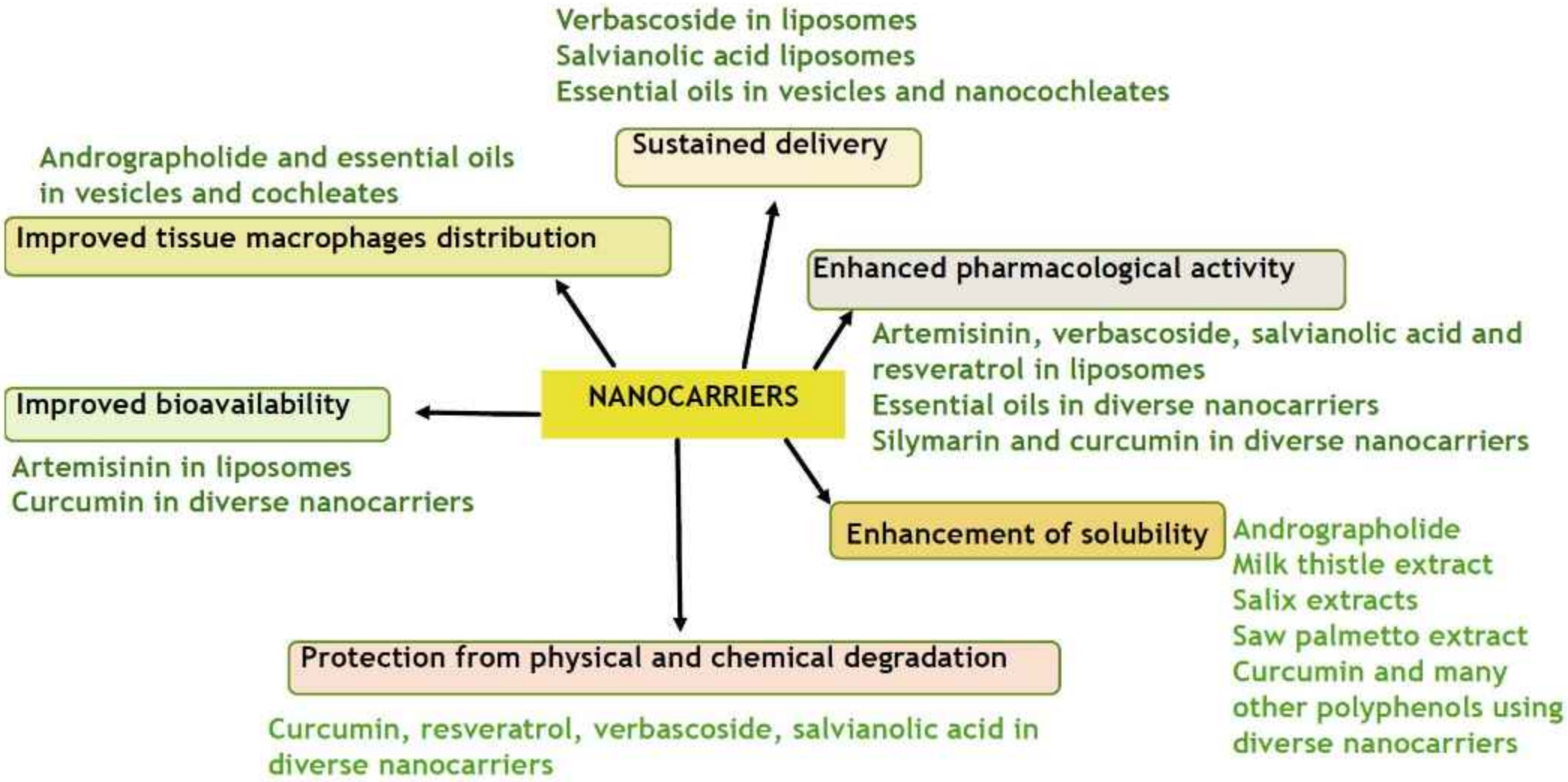


DASAR-DASAR NANOTEKNOLOGI DALAM FITOTERAPI




HERBAL DRUG
Harvesting
drying
size reduction
extraction process
Maceration
Infusion
Digestion
Percolation
Soxhlet
Fermentation
Counter-current extraction
Distillation
Microwave-assisted
Supercritical
Oils
(fatty oils, essential oils)
Extracts
(liquid, soft, dry)
Herbal nanosystems
(micelles, submicronic emulsions, liposomes, SLN)
Herbal formulations
(solutions, emulsions, tablets, capsules, suspension)


Novel Herbal Delivery Systems
Bioavailability Enhancement
Increasing in solubility
More bio-membrane diffusion
Improved Stability
Nano size range of particle
Better lipid/polymeric-coating
Bio-compatibility issues
Biocompatible & Biodegradable
Non mutagenic
Site Specific Delivery
Transdermal/Topical
Brain, Liver, Colon, Lung etc.
Release Profile
Zero order
Sustained release for extended period of time
Dose Reduction
Better therapeutic effect
Drop off in side effect
Minimizing Toxicities
Efficacy improvement
Enrichment in quality
Avoid Presystemic Metabolism
Improvement in plasma drug concentration
No gastric irritation
Facilitating Patient Compliance
Improved effectiveness
Reduced dose frequency


Verbascoside in liposomes
Salvianolic acid liposomes
Essential oils in vesicles and nanocochleates
Sustained delivery
Andrographolide and essential oils in vesicles and cochleates
Improved tissue macrophages distribution
Enhanced pharmacological activity
Artemisinin, verbascoside, salvianolic acid and resveratrol in liposomes
Essential oils in diverse nanocarriers
Silymarin and curcumin in diverse nanocarriers
NANOCARRIERS
Improved bioavailability
Artemisinin in liposomes
Curcumin in diverse nanocarriers
Enhancement of solubility
Andrographolide
Milk thistle extract
Salix extracts
Saw palmetto extract
Curcumin and many other polyphenols using diverse nanocarriers
Protection from physical and chemical degradation
Curcumin, resveratrol, verbascoside, salvianolic acid in diverse nanocarriers

NANOCARRIERS

- To optimize biopharmaceutical properties
- To obtain passive or active targeting
- To decrease doses and side effects
- To reach therapeutic levels over extended times

Bilia, et al. Essential oils loaded in nanosystems: a developing strategy for a successful therapeutic approach. Evid Based Complement Alternat Med. 2014;2014:651593. doi: 10.1155/2014/651593.

Bilia,et al. Flavonoids loaded in nanocarriers: an opportunity to increase oral bioavailability and bioefficacy. Food and Nutrition Sciences, 2014, 5:13, Article ID:47717,16 pages

Bilia, et al. Improving on Nature: The Role of Nanomedicine in the Development of Clinical Natural Drugs. Planta Med. 2017 Mar;83(5):366-381.

Bilia, et al. Plants Extracts Loaded in Nanocarriers: An Emergent Formulating Approach. Nat Prod Commun, 2018, 13 (9): 1157-1160.

Bilia, et al. Nanocarriers: A Successful Tool to Increase Solubility, Stability and Optimise Bioefficacy of Natural Constituents Curr Med Chem. 2019;26(24):4631-4656.

Casamonti, et al. Andrographolide Loaded in Micro- and Nano-Formulations: Improved Bioavailability, Target-Tissue Distribution, and Efficacy of the "King of Bitters". Engineering, February 2019, 5: 69-75.

Efferth, et al. Expanding the Therapeutic Spectrum of Artemisinin: Activity Against Infectious Diseases Beyond Malaria and

JENIS-JENIS SISTEM NANO UNTUK FITOTERAPI

- Sistem nano dalam fitoterapi dirancang untuk mengatasi berbagai keterbatasan senyawa herbal terutama yang bersifat lipofilik, tidak stabil, atau memiliki bioavailabilitas rendah.
- Sistem nano membantu meningkatkan efektivitas, stabilitas, dan penyerapan zat aktif.

Kategori	Pendekatan Top-Down	Pendekatan Bottom-Up
Definisi	Memecah material besar menjadi struktur nano menggunakan gaya mekanik atau fisik	Membangun struktur nano dari molekul atau ion melalui proses kimia/fisika
Prinsip	Reduksi ukuran partikel	Self-assembly atau presipitasi molekul
Tujuan dalam Fitofarmaka	Meningkatkan kelarutan dan bioavailabilitas senyawa aktif tanaman yang poorly soluble	Meningkatkan stabilitas dan efektivitas pengantaran senyawa aktif

Nanomaterial dari Pendekatan Top-Down

Jenis Nanomaterial	Deskripsi	Metode Produksi	Contoh Aplikasi
Nanokristal	Kristal murni senyawa aktif ukuran <1000 nm	Wet milling, high-pressure homogenization	Nanokristal resveratrol dari kulit anggur
Micronized particles	Partikel herbal dengan ukuran mikro ke nano	Jet milling, ultrasonikasi	Serbuk nano daun sirsak
Nanoherbal suspension	Suspensi kasar senyawa herbal dengan ukuran partikel diperkecil	Cryo-grinding, ball milling	Suspensi nano curcumin untuk inflamasi

METODE TOP-DOWN DALAM NANOTEKNOLOGI FITOFARMAKA

Prinsip Umum

•Metode **top-down** berfokus pada **reduksi ukuran** partikel dari material besar (bulk) menjadi skala nano (<1000 nm) melalui **gaya mekanik, fisika, atau tekanan tinggi**.

•Metode ini **tidak mengubah struktur kimia** senyawa aktif secara signifikan, melainkan **memperkecil ukuran** untuk meningkatkan:

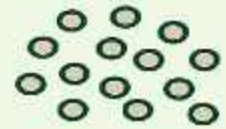
- ✔ Luas permukaan
- ✔ Kelarutan (solubility)
- ✔ Laju disolusi
- ✔ Bioavailabilitas

Skema Strategis Metode Top-Down dalam Fitofarmaka Kelarutan Rendah

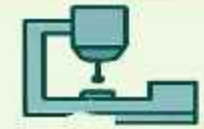
(Integrasi teknologi + kontrol proses + stabilisasi)



Bahan Herbal Kasar



Ukuran Mikro/Kasar



Milling (Wet/Dry) High Pressure / Beads



Nanokristal Fitofarmaka

- Ukuran < 1 µm
- Permukaan luas → kelarutan ↑
- Tanpa pelarut organik
- Kemurnian dan aktivitas tetap terjaga



Kontrol Proses dan Stabillsasi

- Tablet, kapsul, suspensi, gel
- Pemilihan surfaktan/penstabil sesual jenis senyawa aktif
- Optimasi suhu, tenagan, dan waktu milling
- Monitoring ukuran partikel & distribusi dengan DLS/SEM



Formulasi Produk Akhir Fitofarmaka

- Tablet, kapsul, suspensi, gel
- Bioavailabilitas meningkat sinifikan
- Kompatibel untuk scaling up industrstri

Metode-Submetode Utama Top-Down

Metode	Deskripsi	Alat/Proses	Contoh Fitofarmaka
1. High Pressure Homogenization (HPH)	Cairan bertekanan tinggi (100–1500 bar) dipaksa melalui celah sempit → menciptakan gaya geser dan tumbukan	High-pressure homogenizer	Nanoresveratrol dari kulit anggur
2. Wet Milling / Media Milling	Partikel besar digerus menggunakan bead milling di media cair	Bead mill atau ball mill	Nanokristal silymarin, curcumin
3. Ultrasonikasi (Ultrasound-assisted milling)	Gelombang ultrasonik menghasilkan kavitasi yang memecah agregat partikel	Probe sonicator	Nanoekstrak jahe, daun sirsak
4. Jet Milling / Air Jet Pulverization	Partikel dihantam oleh aliran udara berkecepatan tinggi → ukuran menyusut	Jet mill chamber	Micronized ekstrak sambiloto
5. Cryo-milling	Penggilingan pada suhu sangat rendah (misalnya dengan nitrogen cair) untuk bahan sensitif panas	Cryo grinder	Ekstrak flavonoid, antioksidan polifenol
6. Nanogrinding (Superfine grinding)	Penggunaan penggiling ultra-halus untuk menghasilkan ukuran <1 µm	Superfine grinder	Ekstrak kayu manis, ginseng

Parameter Penting dalam Top-Down

Parameter	Penjelasan
Ukuran partikel akhir	Biasanya 100–1000 nm; ditentukan dengan DLS, SEM
Polydispersity Index (PDI)	Ukuran sebaran partikel; ideal <0.3
Zeta Potential	Stabilitas elektrostatik; ideal > ±30 mV
Yield dan recovery	Efisiensi proses; minimal kehilangan senyawa aktif
Suhu proses	Perlu dijaga agar senyawa aktif tidak terdegradasi

Keunggulan Metode Top-Down

Aspek	Keterangan
Praktis untuk senyawa yang sulit larut	Cocok untuk fitofarmaka lipofilik seperti kurkumin, resveratrol
Tidak membutuhkan pelarut kimia kompleks	Ramah lingkungan jika proses basah
Cocok untuk produksi skala besar	Digunakan oleh banyak industri farmasi

Keterbatasan

Tantangan	Mitigasi
Konsumsi energi tinggi	Gunakan metode efisien seperti wet milling dengan kontrol suhu
Potensi degradasi senyawa	Aplikasikan cryo-milling untuk senyawa termolabil
Agregasi partikel	Tambahkan surfaktan atau stabilizer alami (misalnya lesitin, arabic gum)
Kontaminasi dari media grinding	Gunakan media grinding food grade dan lakukan validasi kebersihan

Keunggulan VS Keterbatasan

Aspek	Top-Down	Bottom-Up
Skalabilitas	Umumnya cocok untuk produksi massal	Lebih cocok untuk penelitian atau skala kecil
Presisi kontrol ukuran dan morfologi	Terbatas	Lebih tinggi
Stabilitas kimia	Tergantung metode	Umumnya stabil karena enkapsulasi
Biokompatibilitas	Bergantung bahan asal	Bisa disesuaikan dengan material alami (biopolimer, lipid)
Energi dan biaya	Relatif tinggi (butuh alat besar)	Efisien bila metode sederhana
Contoh bahan	Resveratrol, silymarin, flavonoid, tanin	Kurkumin, propolis, andrographolide, minyak atsiri

Nanomaterial dari Pendekatan Bottom-Up

Jenis Nanomaterial	Deskripsi	Metode Produksi	Contoh Aplikasi
Nanoemulsi	Dispersi minyak-air stabil dalam skala nano	Spontaneous emulsification, low-energy method	Nanoemulsi minyak zaitun-ekstrak jahe
Nanopartikel polimerik	Polimer biodegradable membungkus senyawa aktif	Ionic gelation, solvent evaporation	Nanopartikel kitosan-ekstrak sambiloto
Liposom	Vesikel fosfolipid yang mengenkapsulasi senyawa herbal	Thin film hydration, ethanol injection	Liposom ekstrak pegagan untuk antiaging
Solid Lipid Nanoparticles (SLN)	Matriks lipid padat mengandung senyawa aktif	High shear homogenization + cooling	SLN ekstrak kunyit
Nanogels	Hidrogel ukuran nano yang menyimpan senyawa aktif	Emulsification, cross-linking	Nanogel propolis topikal
Carbon dots berbasis herbal	Titik karbon berukuran nano dari sumber herbal	Pyrolysis, hydrothermal synthesis	Carbon dots dari kurkumin untuk antioksidan

Metode Bottom-Up dalam Pengembangan Nanomaterial Fitofarmaka

PRINSIP UMUM

- Metode **bottom-up** membangun nanomaterial **dari unit molekul, ion, atau atom** ke struktur nano melalui **reaksi kimia, presipitasi, atau self-assembly**.

Cocok untuk:

- Senyawa aktif herbal yang **rentan rusak oleh tekanan atau gesekan**
- Produk berbasis **nanocarrier** (nanoemulsi, liposom, SLN, nanogel, dll)
- **Kontrol struktur**, ukuran, dan permukaan lebih presisi dibanding top-down

Teknik Utama Metode Bottom-Up

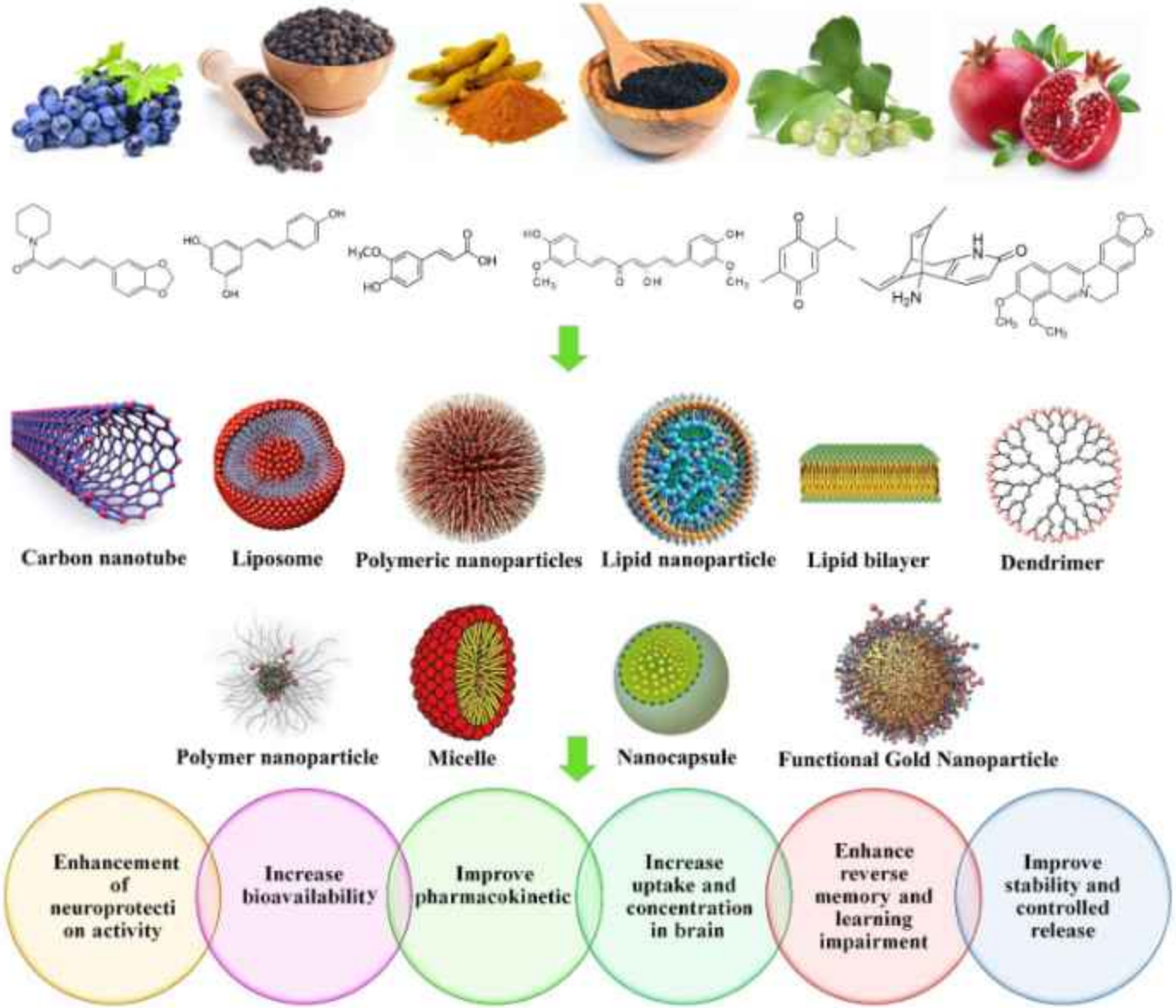
Metode	Deskripsi	Contoh Aplikasi Fitofarmaka
1. Spontaneous Emulsification / Nanoemulsi	Campuran fase minyak, surfaktan, dan air → terbentuk secara spontan ukuran droplet < 200 nm	Nanoemulsi minyak atsiri jahe atau serai
2. Ionic Gelation (Nanopartikel Polimerik)	Polimer kationik (mis. kitosan) berikatan dengan senyawa anionik (mis. TPP) → pembentukan nanopartikel	Nanopartikel kitosan-ekstrak sambiloto
3. Solvent Evaporation	Senyawa aktif dan polimer dilarutkan dalam pelarut organik → emulsifikasi → penguapan pelarut → terbentuk nanopartikel	Kurkumin-PLGA nanopartikel
4. Thin-Film Hydration (Liposom)	Fosfolipid dilarutkan → dibuat lapisan tipis → dihidrasi dengan air mengandung senyawa aktif → terbentuk vesikel	Liposom ekstrak pegagan atau propolis
5. Hot/Cold Homogenization (SLN)	Senyawa aktif dilarutkan dalam lipid cair → emulsifikasi dalam air → pendinginan → SLN terbentuk	Solid lipid nanoparticles minyak kelapa + ekstrak kayu manis
6. Green Synthesis of Carbon Dots / Nanogels	Bahan herbal (mis. kurkumin, daun pepaya) dipanaskan/diolah secara kimia → terbentuk titik karbon	Carbon dots dari kunyit untuk antioksidan
7. Coacervation (Nanokapsul)	Proses pemisahan fase kolidal dari larutan polimerik → terbentuk kapsul nano	Nanokapsul flavonoid, tanin dari daun teh atau jati belanda

Karakteristik Produk Nano Bottom-Up

Parameter	Deskripsi
Ukuran Partikel	Dapat dikontrol 10–500 nm tergantung metode dan bahan
Distribusi Ukuran (PDI)	Ideal <0.3 untuk distribusi seragam
Morfologi	Bulat, kapsular, vesikular tergantung sistem (diamati via SEM/TEM)
Zeta Potential	Stabilitas elektrostatik; ideal > ±30 mV
Kapasitas Enkapsulasi	Efisiensi pemuatan senyawa aktif; dipengaruhi oleh afinitas kimia
Pelepasan Terkontrol	Bisa diatur berdasarkan komposisi matriks dan tipe carrier

Keunggulan Metode Bottom-Up

Aspek	Manfaat
Presisi ukuran dan struktur	Cocok untuk produk dengan target pelepasan dan target organ
Tidak butuh gaya mekanik tinggi	Aman untuk senyawa herbal sensitif
Bisa dikombinasikan dengan biopolimer alami	Biodegradable dan biokompatibel (mis. kitosan, gelatin, arabic gum)
Fleksibel untuk berbagai bentuk sediaan	Oral, topikal, transdermal, nasal, mukoadhesif


Carbon nanotube
Liposome
Polymeric nanoparticles
Lipid nanoparticle
Lipid bilayer
Dendrimer
Polymer nanoparticle
Micelle
Nanocapsule
Functional Gold Nanoparticle
Enhancement of neuroprotecti on activity
Increase bioavailability
Improve pharmacokinetic
Increase uptake and concentration in brain
Enhance reverse memory and learning impairment
Improve stability and controlled release

International Journal of Pharmaceutics

journal homepage: www.elsevier.com/locate/ijpharm

Improving solubility and chemical stability of natural compounds for medicinal use by incorporation into liposomes

Maria Coimbra[a], Benedetta Isacchi[b], Louis van Bloois[a], Javier Sastre Torano[c], Aldo Ket[a], Xiaojie Wu[a], Femke Broere[d], Josbert M. Metselaar[a], Cristianne J.F. Rijcken[a], Gert Storm[a], Rita Bilia[b], Raymond M. Schiffelers[a,*]

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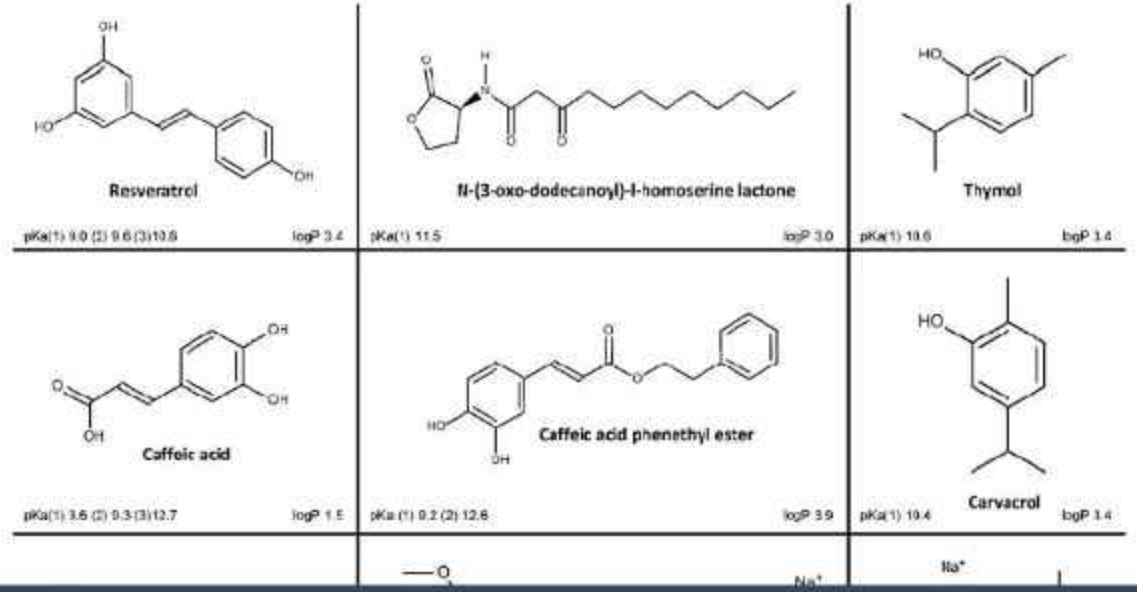
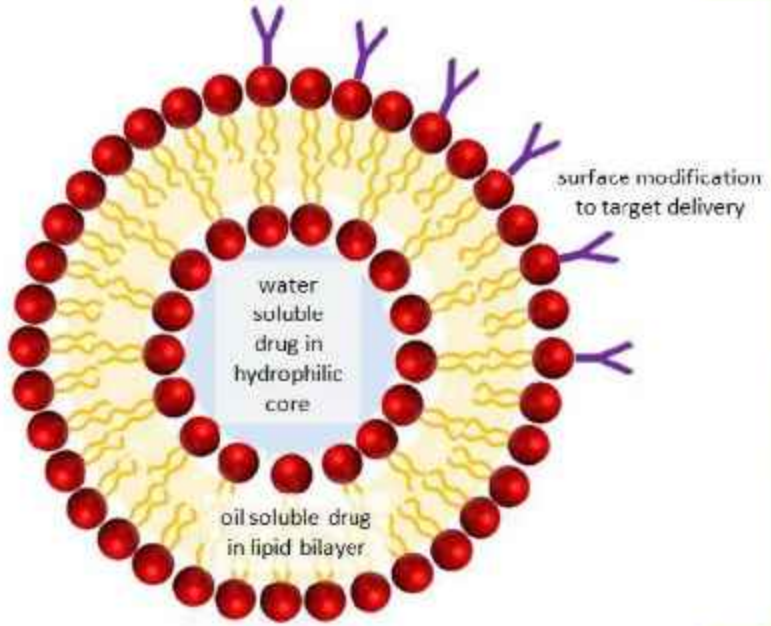
[b] Department of Pharmaceutical Sciences, University of Florence, via U. Schiff 6, 50019 Sesto Fiorentino, (FI), Italy
[c] Biomedical Analysis, Utrecht Institute for Pharmaceutical Sciences, Dept. of Pharmaceutical Sciences, Faculty of Science, Utrecht University, Utrecht, The Netherlands
[d] Division of Immunology, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands



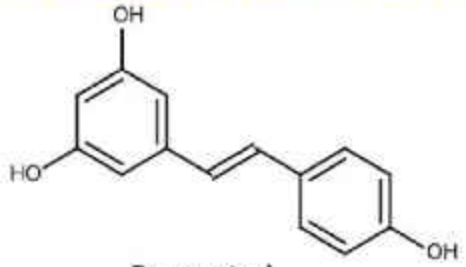
LIPOSOMES



CONCLUSIONS

Taken together, these results show that many poorly soluble natural compounds can be incorporated into liposomes. Compounds that are in the bilayer tend to be extracted in the presence of albumin, limiting the function of the liposome to that of a solubilizing excipient, simply allowing drug delivery. So far, the in vivo

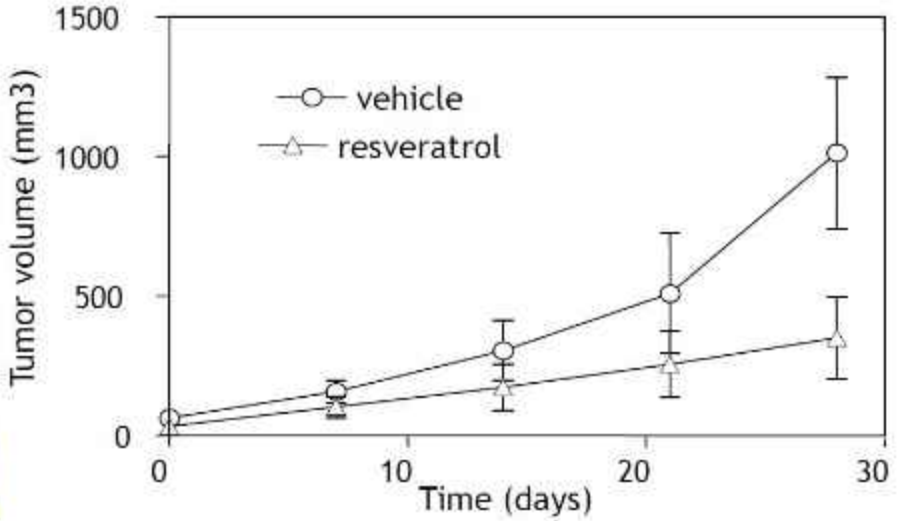
RESVERATROL encapsulated in long circulating liposomes (LCL)



Resveratrol

Resveratrol exhibits a strong antioxidant activity and inhibition of hydro peroxidase, protein kinase C, Bcl-2 phosphorylation, Akt, focal adhesion kinase, NF-B, and matrix metalloprotease-9 (Kraft et al., 2009).

When tumours reached 50–100 mm^3, mice were included in the study, consisting of 6 mice per treatment group. At this time, mice received 5mg/kg liposomal resveratrol or equivalent dose of empty liposomes intravenously via the tail vein. Injections were repeated each 3 days





vehicle

resveratrol-loaded LCL

RESULTS: Liposomes

-protect trans-cis isomerization
-protect under UV light exposure
-change bioavailability giving an effective antitumor response

European Journal of Pharmaceutical Sciences 44 (2011) 552–558

Contents lists available at SciVerse ScienceDirect

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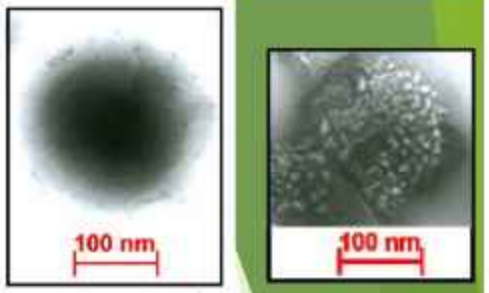
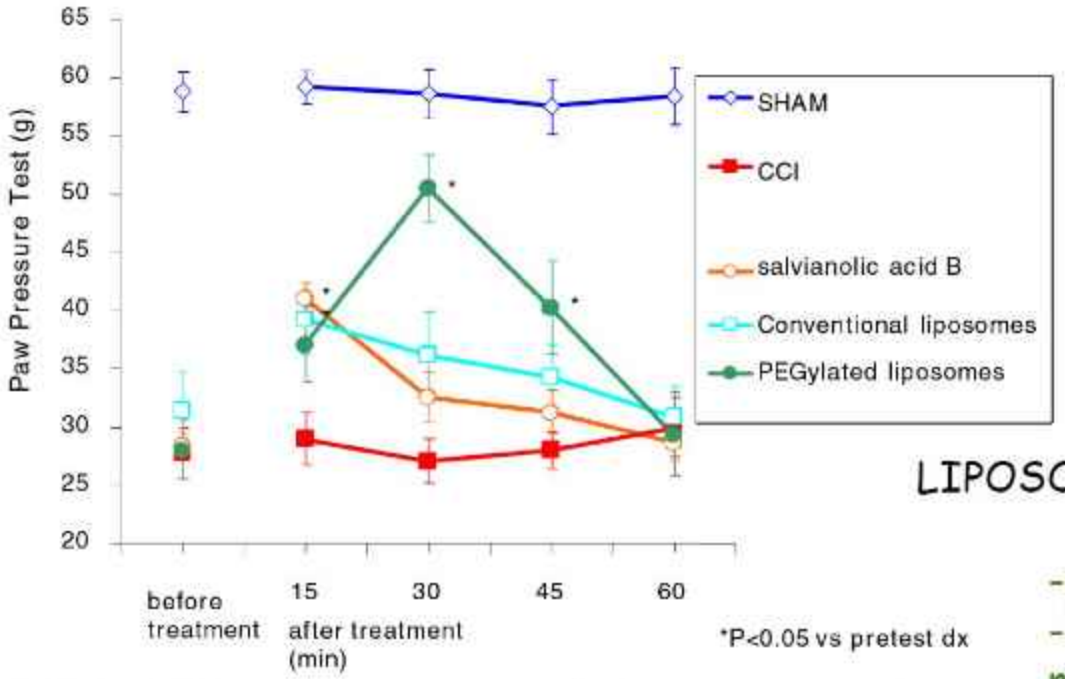
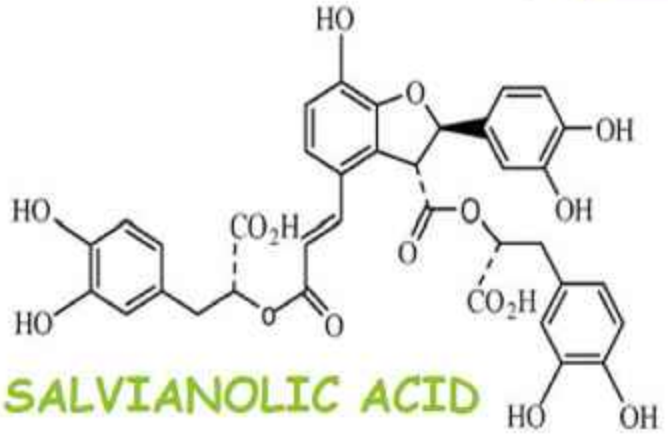




SalB-loaded liposomes intraperitoneal administration in a chronic constriction injury of the sciatic nerve (CCI) in the rat paw-pressure test.



SALVIANOLIC ACID

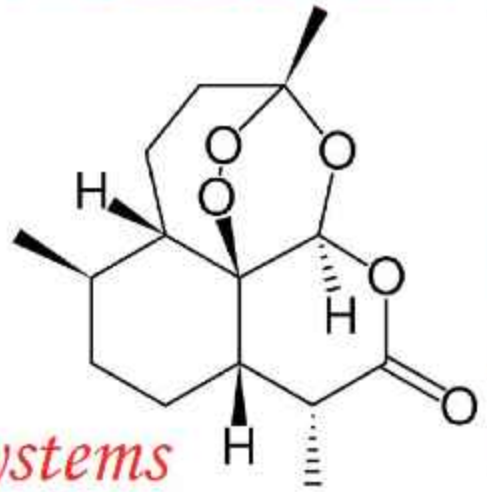
LIPOSOMES

-protect from hydrolisis
-improve bioavailability giving a more effective antihyperalgesic activity

Limiting factors

- low solubility
- quickly metabolized in vivo
- initial burst effect and high peak concentration
- not stable
- short-duration effect

ARTEMISININ



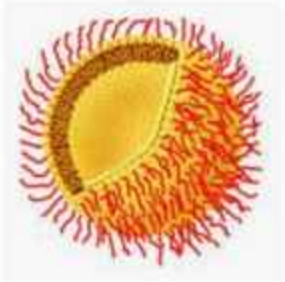


Drug delivery systems

Passive targeting:

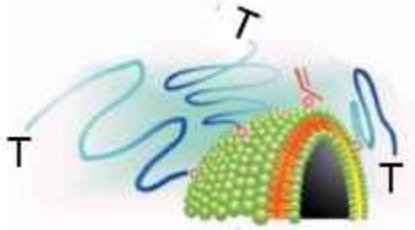
conventional and stealth liposomes





Active targeting:

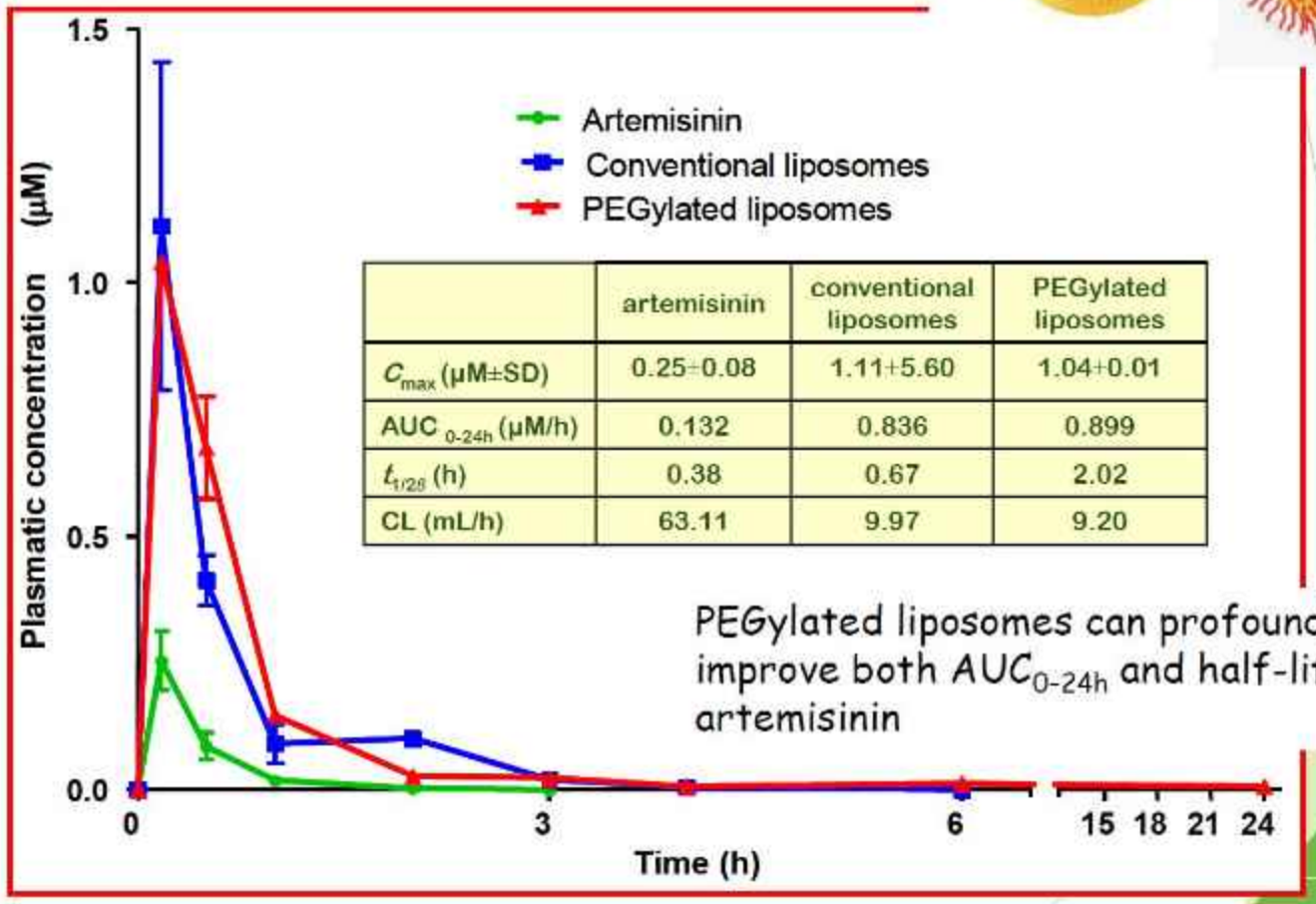
Transferrin conjugated liposomes



Pharmacokinetic profiles in mice





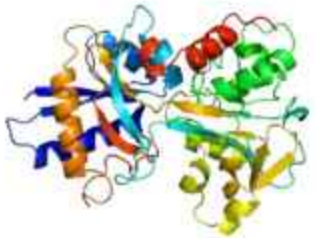


	artemisinin	conventional liposomes	PEGylated liposomes
C_{max} (μM±SD)	0.25±0.08	1.11±5.60	1.04±0.01
AUC $_{0\text{-}24h}$ (μM/h)	0.132	0.836	0.899
$t_{1/2\beta}$ (h)	0.38	0.67	2.02
CL (mL/h)	63.11	9.97	9.20

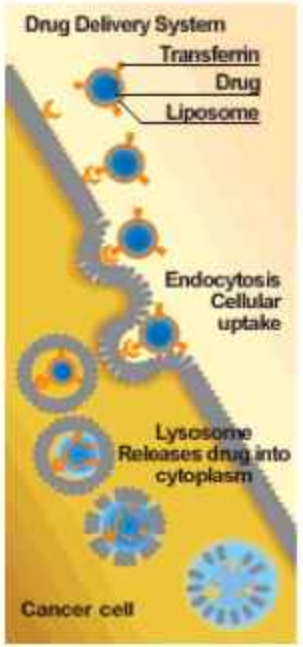
PEGylated liposomes can profoundly improve both $AUC_{0\text{-}24h}$ and half-life of artemisinin

Isacchi et al., J. Lipos. Res. (2011) 20: 1-8.

TRANSFERRIN CONJUGATED LIPOSOMES FOR ARTEMISININ DELIVERY

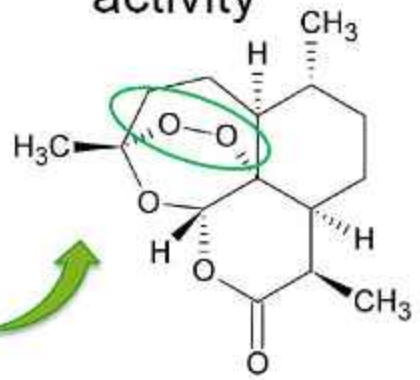


Enhanced selectivity





Enhanced activity



- Transferrin is a medium size protein with two domains where iron binds to a cavity in each domain. The level of transferrin receptor expression varies depending on cell types.

- Most cancer cells express a high concentration of transferrin receptors on cell surface and have a high amount of Fe(III) ion uptake into cells. Because cancer cells have higher iron influx rates compared to the corresponding normal cells, cancer cells are more susceptible to the cytotoxic effect of artemisinin.

Tantangan Metode Bottom-Up

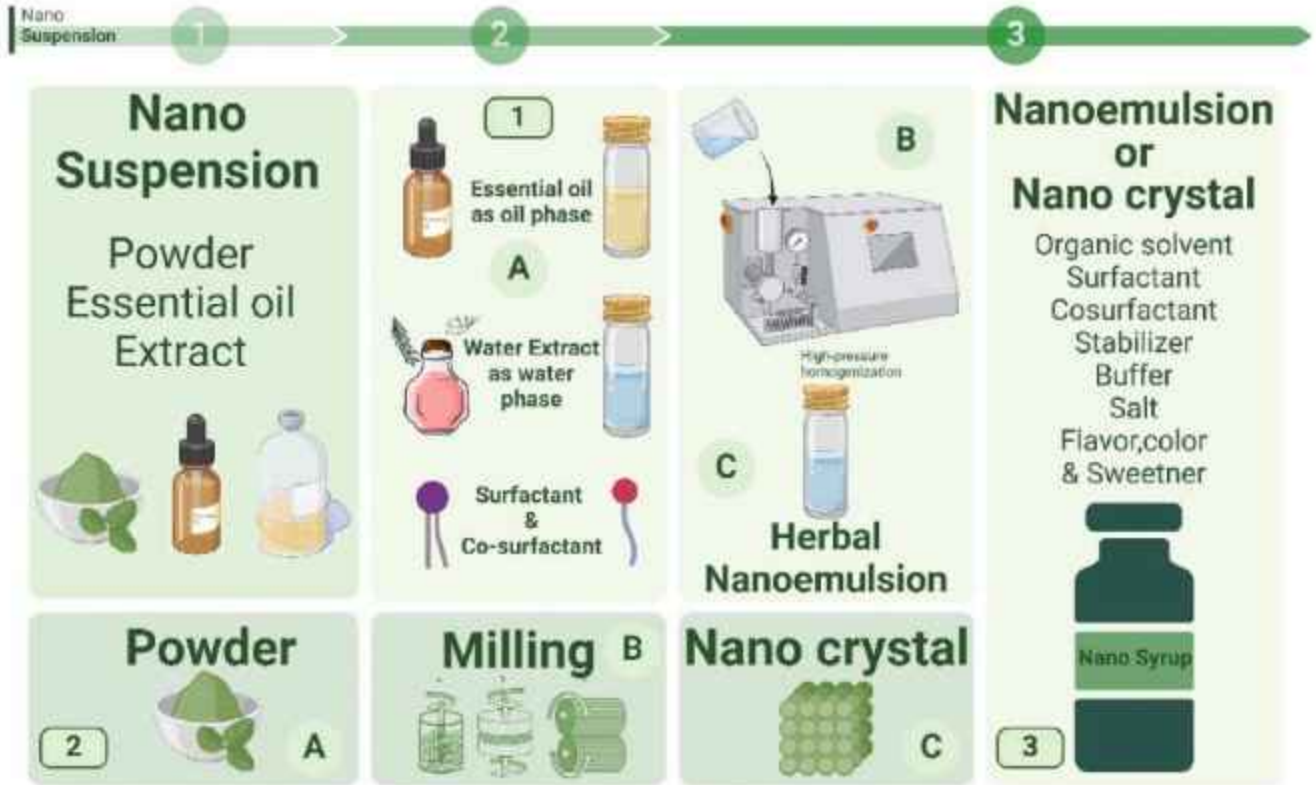
Kendala	Solusi/Mitigasi
Stabilitas emulsi atau nanopartikel	Gunakan kombinasi surfaktan alami dan optimasi pH
Potensi residu pelarut organik	Gunakan pelarut food-grade atau metode bebas pelarut
Reproduksibilitas batch	Diperlukan kontrol proses yang ketat (QbD, DoE)
Karakterisasi kompleks	Perlu perangkat DLS, FTIR, HPLC, UV-Vis, TEM/SEM
Regulasi belum sepenuhnya baku	Perlu rujukan WHO, BPOM, ICH untuk nanosediaan herbal

Catatan Kontekstual Fitofarmaka

Pendekatan top-down ideal untuk zat aktif herbal tunggal yang memiliki kristal padat dan sulit larut.

Pendekatan bottom-up cocok untuk pengembangan sistem penghantaran cerdas (smart delivery system) yang juga memperhitungkan lokasi aksi (misalnya topikal, mukosal, gastrointestinal).

STANDARISASI PRODUK NANO FITOFARMAKA



Standarisasi produk nano fitofarmaka:

- aspek bahan baku,
- proses formulasi,
- produk akhir,
- metode analisis,
- kerangka regulasi yang relevan.

Standarisasi penting untuk menjamin nanosediaan berbasis herbal memenuhi persyaratan **mutu, keamanan, efikasi**, dan dapat **didaftarkan secara resmi** sesuai regulasi nasional maupun global.

1. Tujuan Standarisasi

- Memastikan **konsistensi mutu antar batch**
- Menjamin **stabilitas dan bioaktivitas senyawa aktif**
- Menilai **keamanan dan toksisitas nanosistem**
- Mendukung **klaim khasiat dan efikasi klinis**
- Memenuhi **persyaratan pendaftaran** (BPOM, WHO, ASEAN, ICH)

2. Ruang Lingkup Standarisasi

Tahapan	Elemen Standar	Keterangan
Bahan Baku	Ekstrak terstandar	Profil senyawa aktif, kadar marker, residu pelarut, cemaran
	Bahan pembawa (carrier)	Kualitas pharma grade, biodegradable, non-toksik
Proses Formulasi	Parameter proses kritis	Ukuran partikel, kecepatan homogenisasi, suhu, pH
Produk Akhir	Parameter mutu fisikokimia	Ukuran partikel, PDI, zeta potential
	Efisiensi enkapsulasi & profil pelepasan	Reproduksibilitas dan efektivitas pelepasan zat aktif
	Stabilitas	Stabilitas selama penyimpanan 6–12 bulan (ICH Q1A)
Label dan Klaim	Identitas, dosis, indikasi, bentuk sediaan	Harus berdasarkan data uji valid dan tidak menyesatkan
Keamanan	Uji toksisitas atau iritasi	In vitro dan/atau in vivo sesuai guideline WHO/BPOM
Efikasi	Uji bioaktivitas (mis. antioksidan, antiradang)	Minimum: uji in vitro; idealnya: uji klinik terbatas

3. Parameter dan Metode Standarisasi

Aspek	Parameter Kunci	Metode Uji	Kriteria/Standar
Ukuran Partikel	D90, rata-rata diameter	PSA, DLS, TEM, SEM	< 500 nm (tergantung sistem)
PDI (Polydispersity Index)	Homogenitas ukuran	DLS	< 0.3 (ideal)
Zeta Potential	Stabilitas fisik	ELS	> ±30 mV (ideal)
Efisiensi Enkapsulasi (EE%)	Bioavailabilitas	Centrifugasi + HPLC/UV	≥ 70%
Profil pelepasan	Kinetika pelepasan zat aktif	Disolusi,Franz cell, Dialysis bag	Tergantung rute & tujuan formulasi
Stabilitas Accelerated	Perubahan ukuran, EE, pH, morfologi	Uji suhu 40°C/75% RH selama 6 bulan	Tidak ada perubahan signifikan
Profil Fitokimia	Marker compound, profil HPLC fingerprint	HPLC, TLC-densitometri	Konsisten antar batch
Cemaran	Mikroba, logam berat, pestisida	Standar BPOM/SNI	Sesuai regulasi
Toksisitas	Sitotoksik, hemolitik, iritasi	In vitro (MTT), In vivo (oral/topikal)	Tidak toksik pada dosis uji

4. Dokumentasi Standar dan QC (Quality Control)

Dokumen Teknis	Isi Wajib
Spesifikasi bahan baku & nanoformulasi	Komposisi, sumber, kualitas, supplier
Batch record	Parameter proses, waktu, suhu, hasil
COA (Certificate of Analysis)	Ukuran partikel, EE, pH, PDI, mikrobiologi
Protokol stability	Waktu, suhu, pengambilan sampel
Data uji keamanan & efikasi	Hasil laboratorium dan/atau klinik
Label dan leaflet produk	Informasi penggunaan, dosis, peringatan

INFORMASI PENTING UNTUK REGULATOR TERKAIT NANO FITOFARMAKA

Kategori	Informasi Kunci	Keterangan
Definisi dan Ruang Lingkup	Nano fitofarmaka adalah sediaan berbasis bahan alam (fitoterapi/fitofarmaka) yang menggunakan sistem penghantaran berukuran nano (<1000 nm) untuk meningkatkan efikasi, stabilitas, atau bioavailabilitas.	Meliputi: nanoemulsi, liposom, nanopartikel polimerik, SLN, nanogels, nanokapsul
Perbedaan dari fitofarmaka konvensional	Karakteristik fisik dan biologis berubah signifikan → memerlukan evaluasi khusus	Misalnya: peningkatan absorpsi → potensi toksisitas lebih tinggi
Parameter Mutu Khusus	Ukuran partikel, PDI, zeta potential, efisiensi enkapsulasi, profil pelepasan, stabilitas nano	Belum tercakup dalam sistem penilaian mutu obat herbal konvensional
Kebutuhan Karakterisasi Tambahan	Wajib: SEM/TEM/DLS, FTIR, DSC, uji in vitro release, stabilitas akselerasi	Harus diintegrasikan dalam format evaluasi registrasi
Validasi Marker Komponen	Penetapan senyawa aktif utama tetap diperlukan	Untuk menjamin konsistensi fitokimia dan klaim khasiat
Evaluasi Keamanan Khusus	Partikel nano berpotensi menembus sawar biologis (kulit, mukosa, sel) → risiko toksisitas sistemik	Perlu uji sitotoksisitas, iritasi, hemolisis, dan/atau in vivo
Label dan Klaim Produk	Harus mencantumkan teknologi nano bila berpengaruh signifikan terhadap cara kerja produk	Dilarang mencantumkan klaim berlebihan atau tidak terbukti
Pedoman Standar Rujukan	WHO, ICH (Q6A, Q8–Q12), ASEAN HERBALS, ISO 10993-22, US FDA nanotech guidance	Belum ada pedoman nasional yang komprehensif untuk nano-herbal
Pemantauan Produksi (CPOTB)	Produksi nanosediaan perlu sistem kontrol proses ketat (kontrol suhu, kecepatan homogenisasi, pH)	Perlu revisi atau lampiran tambahan dalam CPOTB untuk nanosediaan
Stabilitas Produk Nano	Stabilitas partikel dan senyawa aktif → harus diuji di berbagai kondisi (25°C/60%, 40°C/75%)	Wajib minimal 6 bulan data stabilitas awal
Dokumentasi Registrasi Tambahan	Desain formulasi, metode pembuatan, parameter kritis proses, hasil karakterisasi, uji keamanan, dan efikasi	Harus tersedia sebelum pemberian izin edar

Contoh Regulasi Negara Lain tentang Standarisasi Nanomaterial

Negara/Organisasi	Regulasi/Pedoman	Isi Pokok & Relevansi untuk Nano Fitofarmaka
Amerika Serikat (FDA)	**Guidance for Industry: FDA-Regulated Product Involves the Application of Nanotechnology** (2022) https://www.fda.gov/science-research/nanotechnology-programs-fda/nanotechnology-guidance-documents	Definisi produk nano: ukuran 1–1000 nm. Produk herbal berbasis nano wajib evaluasi tambahan jika ada perubahan sifat farmakokinetik. Merekomendasikan uji toksisitas khusus dan karakterisasi lengkap (size, morphology, surface)
Uni Eropa (EMA)	**Nanotechnology-based Medicinal Products for Human Use (2025)**	Menekankan perlunya uji **keamanan preklinis khusus**, termasuk bioakumulasi dan biodistribusi. Herbal nanosystem diperlakukan selaras seperti produk sintetik berbasis nano
India (Ministry of AYUSH)	**Guidelines for Evaluation of Nanopharmaceuticals in AYUSH** (Draft, 2021)	Menetapkan klasifikasi nano-ayurvedic berdasarkan sistem pengantar (liposom, nanoemulsi, SLN, dll). Memuat parameter wajib: ukuran, PDI, zeta potential, EE, profil pelepasan, toksisitas in vitro dan in vivo.
WHO	**WHO Guidelines for the Assessment of Herbal Medicines** (TRS 863, TRS 1010)	Belum spesifik mengatur sediaan nano, tetapi mendukung penilaian tambahan jika ada perubahan cara kerja atau bioavailabilitas. Rekomendasi penggunaan parameter farmasetika dan toksikologi modern pada produk inovatif
ASEAN	**ASEAN Guidelines on Quality, Safety, and Efficacy of Traditional Medicines and Health Supplements (AHPA)**	Belum mengatur sediaan nano secara spesifik. Namun menyarankan pengujian tambahan untuk formulasi non-konvensional

Penjaminan Mutu Produk Jadi Hasil Nanoteknologi

- Pengendalian bahan baku: identitas, kemurnian, dan keseragaman
- Validasi proses produksi: memastikan konsistensi skala laboratorium hingga industri
- Uji stabilitas: fisik, kimia, dan bioaktivitas zat aktif
- Karakterisasi nanomaterial: ukuran partikel, distribusi, morfologi, dan muatan permukaan
- Pengujian keamanan dan toksisitas nanosistem
- Kepatuhan terhadap regulasi nasional dan internasional (BPOM, ISO, ICH)
- Dokumentasi dan pelacakan batch untuk keperluan audit dan recall

CLOSING

PERAN NANOTEKNOLOGI



Mengatasi keterbatasan herbal (lipofilik, tidak stabil, bioavailabilitas rendah) → mingkatkan efektivitas, stabilitas, penyerapan

PENJAMINAN MUTU



Kontrol bahan baku, validasi proses, uji stabilitas & toksisitas, karakterisasi nano kepatuhan regulasi (BPOM, ISO, ICH) dokumentasi batch

STANDARISASI

Meliputi bahan baku, proses, produk akhir, analisis, regulasi → menjamin mutu, keamanan, efikaci pendaftaran resmi



IPB University
Bogor Indonesia

SEAFAST Center and
Department of
Food Science and Technology

IPB University
Bogor Indonesia

BADAN POM

Capacity Building and Workshop on Quality Standardization of Extracts and Quality Control Assessment in Traditional and Herbal Medicine Products

World Health Organization
Indonesia

Standarisasi Produk Fermentasi Sebagai Obat Tradisional

Prof. Lilis Nuraida, MSc., PhD.

20 Agustus 2025

Outline

- Definisi Fermentasi
- Tujuan penggunaan fermentasi
- Produk fermentasi, probiotik dan postbiotik
- Mikroorganisme penting pada proses fermentasi
- Fermentasi Herbal
- Manfaat kesehatan herbal terfermentasi dan potensinya sebagai OBA atau obat tradisional
- Penjaminan mutu produk herbal fermentasi





Sejarah Fermentasi

Era Fermentasi Misterius





- 300 SM: fermentasi serealia dan sayuran di Cina
- 200 SM: fermentasi teh di Cina

Fermentasi sejak jaman Neolitik (7000-6600 SM) terutama untuk fermentasi minuman dan keju.
1500 SM: fermentasi untuk mengembangkan roti

1680	• Antonie van Leeuwenhoek mengamati khamir di bawah mikroskop
Abad 19	• Louis Pasteur menemukan bahwa khamir berperan penting pada pembuatan minuman beralkohol.









Fermentasi herbal sebagai obat tradisional berkembang bersama dengan pangan fermentasi

Fermentasi

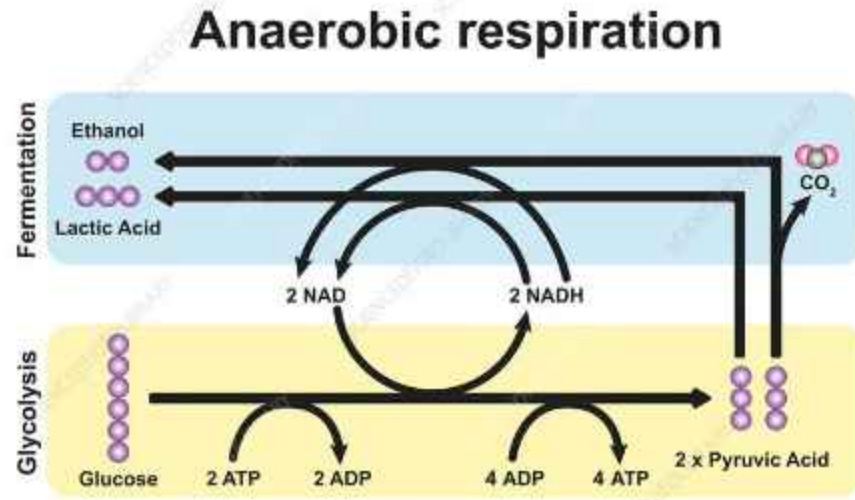
- Kata Fermentasi dari Bahasa Latin: fervere, mendidihkan
  - Menggambarkan aksi khamir terhadap sari buah dan barley yang sudah berkecambah
  - Penampakan seperti mendidih karena adanya metabolisme anaerobik dari gula yang ada pada sari buah atau ekstrak kecambah barley

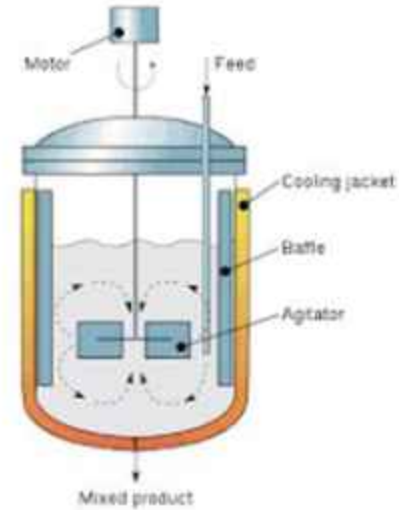




Definisi Fermentasi

- Saat ini terdapat dua pengertian fermentasi:
  - Biokimia: terkait dengan proses menghasilkan energi dari senyawa organik pada kondisi anaerobik (donor dan akseptor elektron senyawa organik).
  - Industri mikrobiologi: menggambarkan proses produksi suatu produk dengan menggunakan kultur mikroorganisme



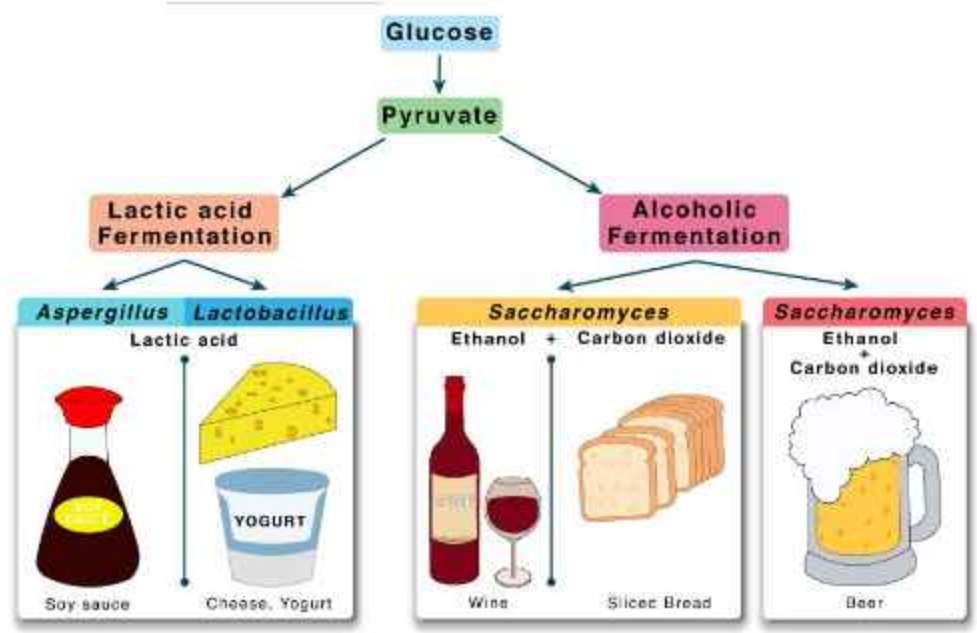


Teknologi Fermentasi

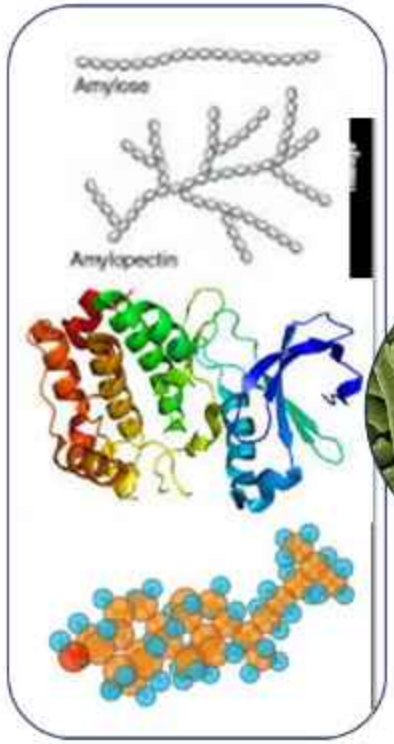
Lilis Nuraida, 20 Agustus 2025

Fermentasi dalam industri mikrobiologi

- Fermentasi adalah transformasi senyawa organik menjadi senyawa yang lebih sederhana dengan aksi enzim yang diproduksi selama pertumbuhan mikroorganisme yang diinginkan seperti kapang, khamir atau bakteri
  - Produksi pangan fermentasi
  - Produksi senyawa-senyawa yang digunakan di industri: pangan dan non-pangan



Tujuan Fermentasi



Susbtrate organik



Pangan dan pakan fermentasi



Senyawa bioaktif



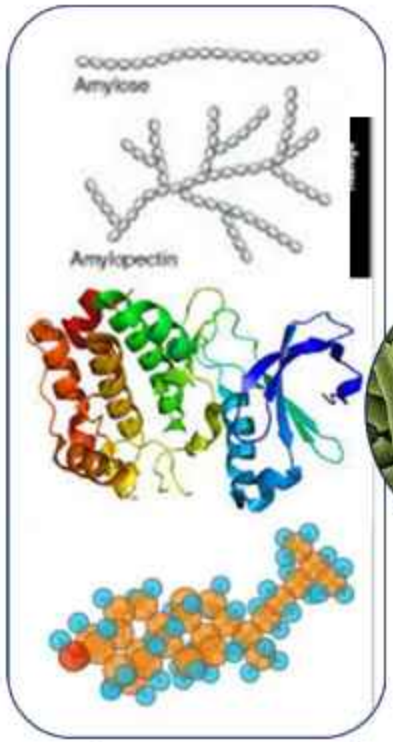
Manfaat Kesehatan, Nutraceutical, Obat

Senyawa bernilai

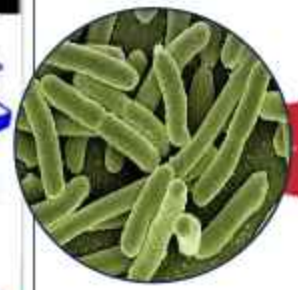
Enzim, Asam organik, alcohol/bioethanol, aseton, bakteriosin dll



Apa yang yang dilakukan mikroorganisme selama fermentasi?



Susbtrate organik



Alcohol, asam organic, Polisakarida, gula alcohol, aseton, asam lemak, asetoin dan senyawa organic ainnya

Gula

Protein

Lemak

Asam lemak

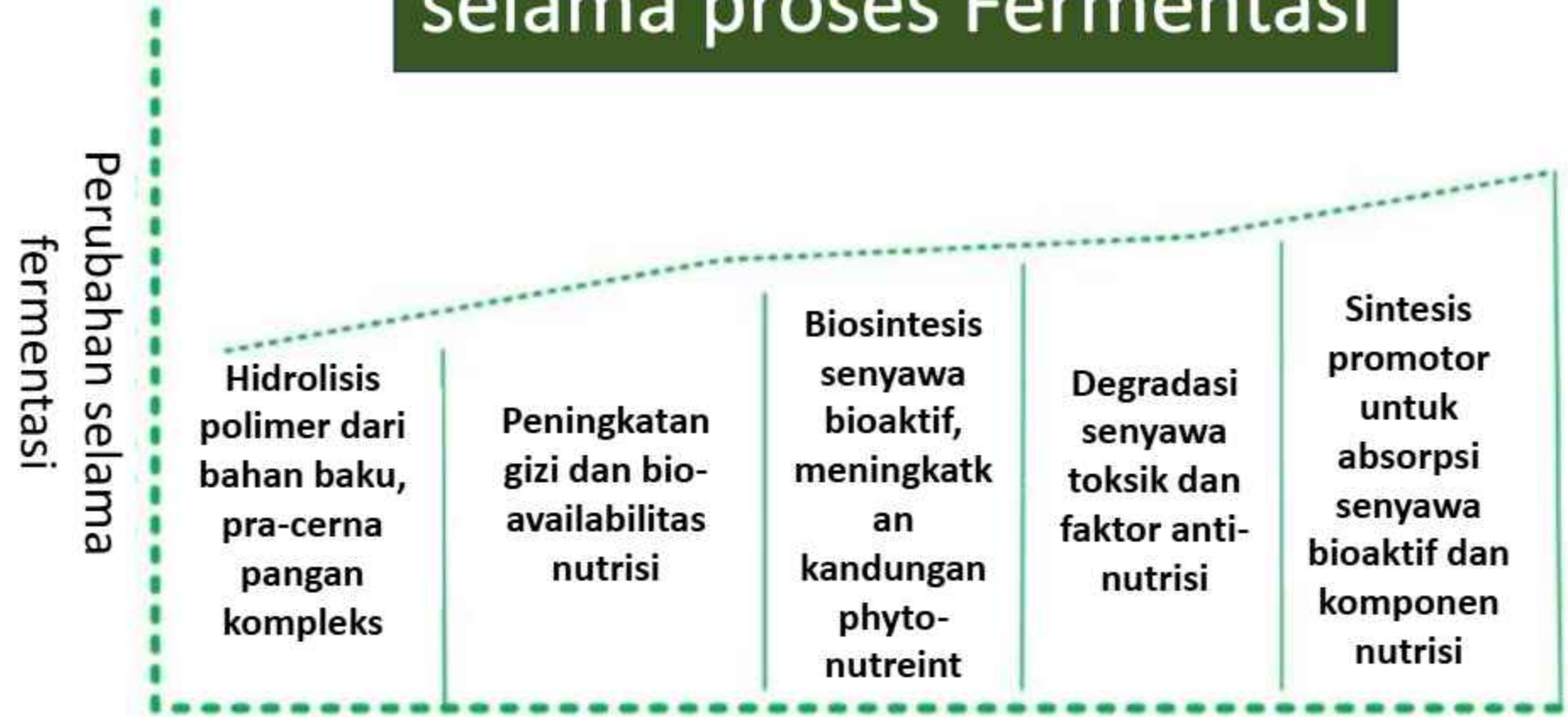
Peptida, asam amino

Energi dan komponen sel

Biomassa

Metabolit sekunder: Antibiotik, toksin, pigmen, enzim, faktor pertumbuhan, GABA, bakteriosin (antimikroba). Memiliki aktivitas biologis: anti-infective, anti-inflammation and anti-cancer, dll

Perubahan senyawa selama proses Fermentasi



- Produk fermentasi dapat berperan sebagai pembawa probiotik

Perkembangan Teknologi Fermentasi





Fermentasi spontan: Tidak ditambahkan mikroorganisme, tergantung pada mikroorganisme yang ada pada bahan



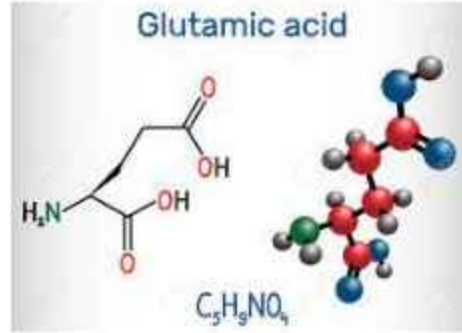
Fermentasi Spontan

Kultur starter untuk memperbaiki konsistensi produk

Penambahan kultur starter:
-Back sloping
-Kultur starter

Kultur starter GMO

"mikroorganisme super" yang memproduksi senyawa yang diinginkan dalam jumlah banyak



Sampai saat ini fermentasi spontan masih digunakan

Fermentasi spontan

- Tidak ditambahkan mikroorganisme, mengandalkan mikroorganisme yang ada pada bahan baku
- Fermentasi mudah
- Pertumbuhan mikroorganisme dikendalikan dengan pengaturan kondisi seperti **penambahan garam, penutupan (kondisi anaerobic), pengaturan suhu.**
- Kelemahan
  - Produk seringkali tidak konsisten
  - Kualitas tidak bisa dijamin
  - Sering terjadi kegagalan
  - Sering terkontaminasi mikroorganisme penyebab penyakit (pathogen)



Kultur starter

Kultur starter adalah sediaan mikroorgansime hidup yang ditujukan untuk memulai proses fermentasi, memproduksi perubahan spesifik pada komposisi kimia dan karakteristik sensori substrate untuk memperoleh produk yang homogen

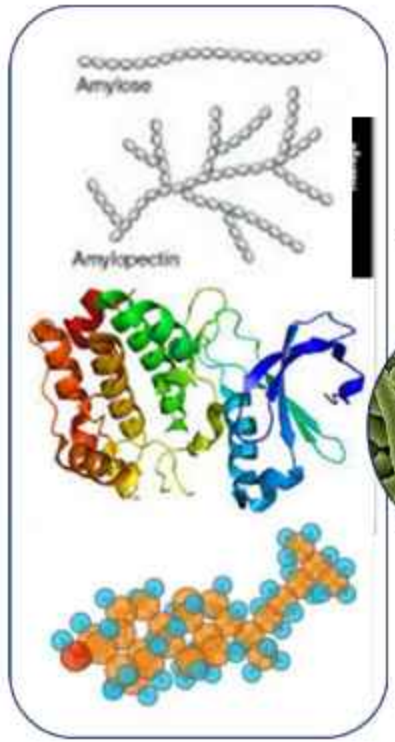
- Konsorsium mikroorganisme:
  - Lebih dari satu jenis mikroorganisme (berbeda jenis, genus, species
  - Tidak diketahui secara pasti jenis mikroorganisme apa yang ada didalamnya
  - Seringkali berbeda antar daerah atau antar produsen
  - Contoh:
    - Ragi tape
    - Kultur starter kefir/granula kefir
    - Kultur starter kombucha
- Tunggal atau campuran dan diketahui jenisnya:
  - Kultur starter yoghurt
  - Laru tempe
  - Kultur starter keju
  - Kultur starter untuk memproduksi senyawa tertentu, termasuk senyawa bioaktif

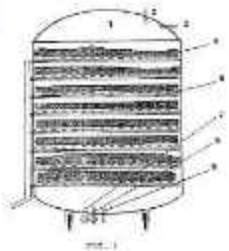
Perbedaan Fermentasi, Probiotik dan Postbiotik

IPB University
Bogor Indonesia

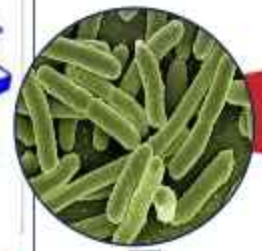
Fermentasi

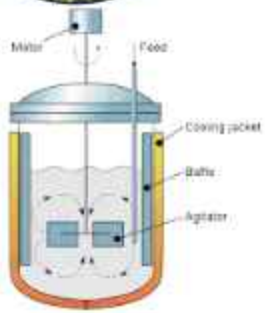
Padat











Padat

Biomassa

Metabolit primer dan sekunder

Komponen sel

Produk fermentasi:

- Utuh
- Diekstrak dan dipisahkan senyawa yang diinginkan

Probiotik

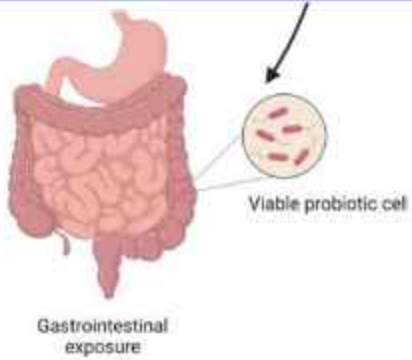
- PERATURAN BPOM No. 1 TAHUN 2022 TENTANG **PENGAWASAN KLAIM PADA LABEL DAN IKLAN PANGAN OLAHAN**
- **PERATURAN BADAN PENGAWAS OBAT DAN MAKANAN NOMOR 17 TAHUN 2025 TENTANG PEDOMAN PENILAIAN PRODUK SUPLEMEN KESEHATAN MENGANDUNG PROBIOTIK**

- Probiotik merupakan mikroorganisme hidup yang jika dikonsumsi dalam jumlah memadai dapat memberikan manfaat kesehatan bagi konsumen.
- Probiotik dapat berupa mikroorganisme tunggal atau campuran yang jika dikonsumsi oleh manusia dapat memberikan manfaat berupa keseimbangan mikrobiota saluran pencernaan.
- Pada prinsipnya Suplemen Kesehatan mengandung Probiotik dapat dibuat dengan bentuksediaan sebagaimana telah diatur dalam peraturan Badan Pengawas Obat dan Makanan.

Manfaat Probiotik

Manfaat tergantung pada galur dan dosis
Perlu didukung hasil uji klinis

Probiotik



- Menyeimbangkan dan memelihara komposisi mikrobiota saluran pencernaan: Kesehatan saluran pencernaan
- Immunomodulasi dan Manfaat Kesehatan lainya
- Efek metabolic (mensekresikan enzim dan menghasilkan SCFA serta senyawa bioaktif)

Prinsip umum dalam penilaian atau pembuatan Probiotik sebagai Suplemen Kesehatan

1. Istilah Probiotik hanya dapat digunakan untuk produk mengandung mikroorganisme hidup yang bermanfaat bagi kesehatan dengan strain spesifik dan dosis tertentu;
2. Jumlah yang tepat untuk setiap strain Probiotik penting ditetapkan untuk memberikan manfaat kesehatan. Jumlah minimum mikroorganisme hidup yang efektif perlu ditetapkan karena Probiotik bersifat strain spesifik, begitu pula kaitannya dengan dosis dan manfaat terhadap kesehatan yang harus dibuktikan dengan hasil uji klinis (efikasi) yang konklusif (valid dan konsisten);
3. Untuk digunakan dalam Suplemen Kesehatan, Probiotik tidak hanya dapat bertahan hidup dalam saluran pencernaan tetapi juga harus mampu berproliferasi (tumbuh dan berkembang biak) dalam saluran pencernaan (kolon);
4. Kemampuan Probiotik untuk bertahan dan berproliferasi pada saluran pencernaan (kolon) sangat tergantung pada strain, profil mikrobiota, dan kondisi lingkungan saluran pencernaan yang banyak dipengaruhi oleh lingkungan dan kebiasaan hidup setempat;

LAMPIRAN IV
PERATURAN BADAN PENGAWAS OBAT DAN MAKANAN
NOMOR 17 TAHUN 2025
TENTANG
PEDOMAN PENILAIAN PRODUK SUPLEMEN KESEHATAN MENGANDUNG PROBIOTIK

5. Penggunaan Probiotik sebagai bahan Suplemen Kesehatan harus didasarkan pada bukti ilmiah yang meliputi identifikasi strain, jumlah, lama pemakaian, keamanan dan manfaat kesehatan yang dihasilkan;
6. Bukti ilmiah manfaat kesehatan harus berupa hasil uji klinik eksperimental dan dilakukan sesuai kaidah Cara Uji Klinik yang Baik (CUKB); dan
7. Untuk mengklarifikasi identitas Probiotik pada Suplemen Kesehatan maka Pelaku Usaha wajib mencantumkan genus, spesies dan strain Probiotik pada penandaan. Efek Probiotik adalah strain spesifik dan efek strain tersebut tidak bisa diekstrapolasi kepada strain lainnya.

Produk Probiotik



Strain Probiotik Tunggal atau Jamak

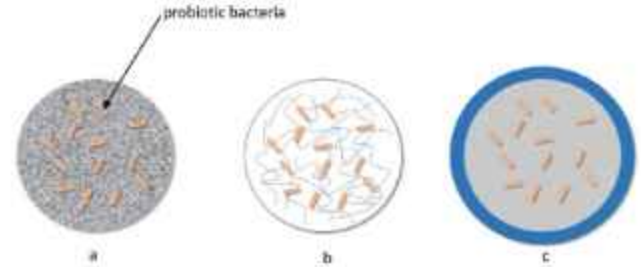


- Makanan dan minuman
  - Fermentasi
    - Kultur starter
  - Non-fermentasi
- Suplemen
  - Capsules
  - Chewable tablets
  - Sachet/ Powder





Mikroenkapsulasi



Daftar Strain Probiotik Yang Telah diijinkan untuk suplemen

- https://standar-otskk.pom.go.id/otskk-db/kategori/daftar-strain-probiotik-yang-telah-diizinkan
- Terdapat 94 strain yang termasuk ke dalam list yang diijinkan sebagai suplemen probiotik

Daftar Strain Probiotik yang telah diizinkan Direktorat Standarisasi Obat Tradisional, Suplemen Kesehatan dan Kosmetik

https://standar-otskk.pom.go.id/otskk-db/kategori/daftar-strain-probiotik-yang-telah-diizin

Daftar Strain Probiotik yang telah diizinkan

No	Nama strain
1	Lactobacillus casei EMRO 213
2	Lactobacillus plantarum LP01 AFID 1171
3	Lactobacillus plantarum EMRO 009
4	Lactobacillus plantarum CBT LP3
5	Lactobacillus lactis BCMC 12451
6	Lactobacillus helveticus R0052
7	Lactobacillus fermentum PCC
8	Lactobacillus fermentum EMRO 211
9	Lactobacillus casei W56
10	Lactobacillus casei subsp. casei ATCC 393
11	Lactobacillus casei subsp. BCMC 12313
12	Lactobacillus casei HA-108
13	Lactobacillus reuteri ATCC PTA 5289
14	Lactobacillus casei EMRO 002
15	Lactobacillus casei ATCC 393
16	Lactobacillus bulgaricus HA-137
17	Lactobacillus bulgaricus EMRO 212
18	Lactobacillus bulgaricus ATCC 11842
19	Lactobacillus acidophilus W55
20	Lactobacillus acidophilus W 22
21	Lactobacillus acidophilus R0052
22	Lactobacillus acidophilus LA-G80
23	Lactobacillus acidophilus LA85
24	Lactobacillus acidophilus LA-5
25	Lactobacillus rhamnosus LR5
26	Streptococcus thermophilus STCC0037
27	Streptococcus thermophilus ST3
28	Streptococcus thermophilus HA-110
29	Streptococcus thermophilus CBT ST3
30	Streptococcus thermophilus ATCC 19258
31	Saccharomyces cerevisiae (boulardii) CBS 5926
32	Saccharomyces boulardii Hansen CBS 5926

No	Nama strain
33	Saccharomyces boulardii CNCM I-745
34	Lactococcus lactis W58
35	Lactobacillus salivarius W57
36	Lactobacillus rhamnosus R0011
37	Lactobacillus acidophilus LA14
38	Lactobacillus rhamnosus LMG25626
39	Lactobacillus rhamnosus HA-111
40	Lactobacillus rhamnosus GR-1TM
41	Lactobacillus rhamnosus GR 1
42	Lactobacillus rhamnosus GG ATCC 53103
43	Lactobacillus rhamnosus EMRO 014
44	Lactobacillus rhamnosus ATCC 7469
45	Lactobacillus reuteri RC-14 TM
46	Lactobacillus reuteri RC-14
47	Lactobacillus reuteri DSM 17938
48	Bifidobacterium bifidum CBT BF3
49	Bifidobacterium lactis W52
50	Bifidobacterium lactis W51
51	Bifidobacterium lactis BL-07
52	Bifidobacterium lactis BL-04
53	Bifidobacterium infantis R0033
54	Bifidobacterium infantis HA-116
55	Bifidobacterium infantis BCMC 02129
56	Bifidobacterium breve HA-129
57	Bifidobacterium breve ATCC 15700
58	Bifidobacterium bifidum R0071
59	Bifidobacterium bifidum CUL-20
60	Bifidobacterium longum ATCC 15707
61	Bifidobacterium bifidum BF3
62	Bifidobacterium bifidum BCRC 11844
63	Bifidobacterium bifidum BCMC 02290
64	Bifidobacterium bifidum BB14
65	Bifidobacterium animalis subsp.lactis HNO19
66	Bifidobacterium animalis subsp.lactis CUL-34
67	Bifidobacterium animalis subsp.lactis BL-04
68	Bifidobacterium animalis subsp.lactis BB12
69	Bacillus mesentericus TO-A

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No	Nama strain
70	Bacillus coagulans SNZ 1969
71	Bacillus coagulans SANK70258
72	Clostridium butyricum TO-A
73	Lactobacillus acidophilus LA1063
74	Lactobacillus acidophilus LA1
75	Lactobacillus acidophilus HA-122
76	Lactobacillus acidophilus CUL-60
77	Lactobacillus acidophilus CUL-21
78	Lactobacillus acidophilus COREE
79	Lactobacillus acidophilus BCRC 14079
80	Lactobacillus acidophilus BCMC 12130
81	Lactobacillus acidophilus ATCC1063
82	Lactobacillus acidophilus ATCC 4356
83	Lactiplantibacillus (Lactobacillus) plantarum Dad-13
84	Bacillus coagulans MTCC 5724
85	Bifidobacterium longum W 108
86	Bifidobacterium longum STCC0986
87	Bifidobacterium longum OLB6001
88	Bifidobacterium longum NCC 3001
89	Bifidobacterium longum BL-G301
90	Bifidobacterium longum BL-05
91	Bifidobacterium longum BG7
92	Bifidobacterium longum BCRC 14634
93	Bifidobacterium longum BCMC 02120
94	Bifidobacterium longum BB536

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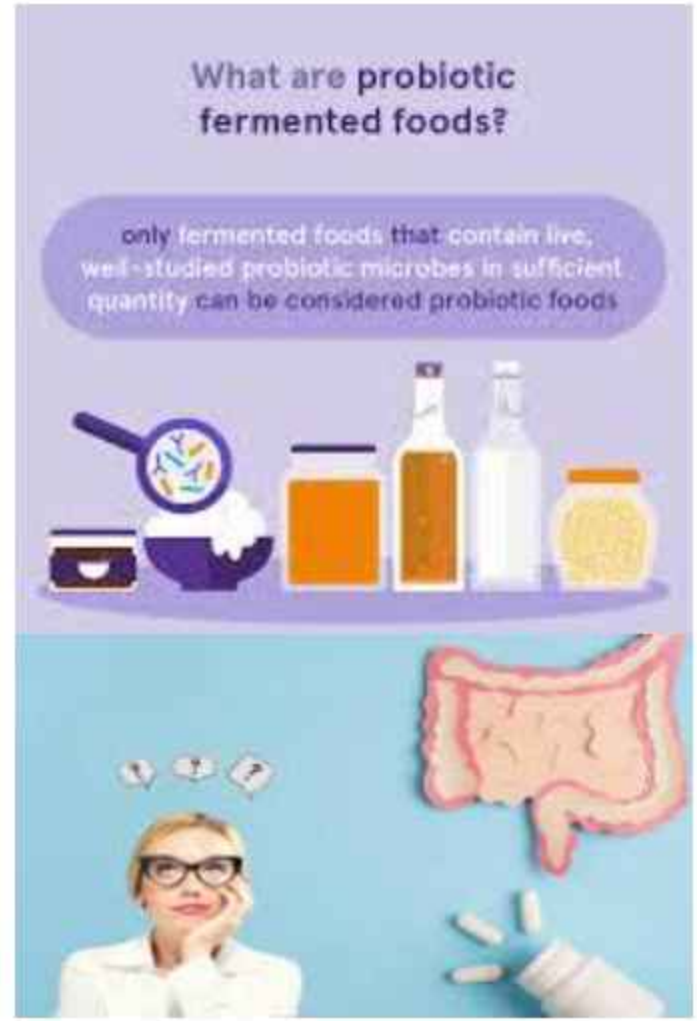
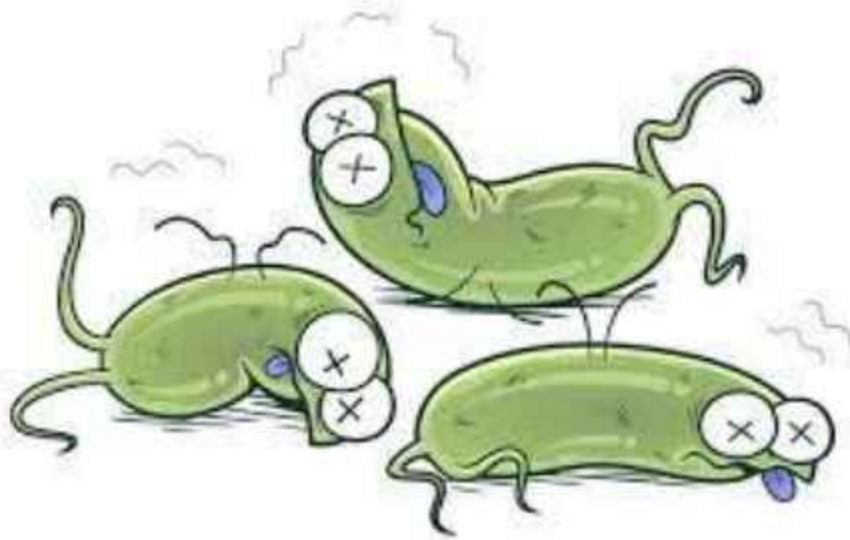
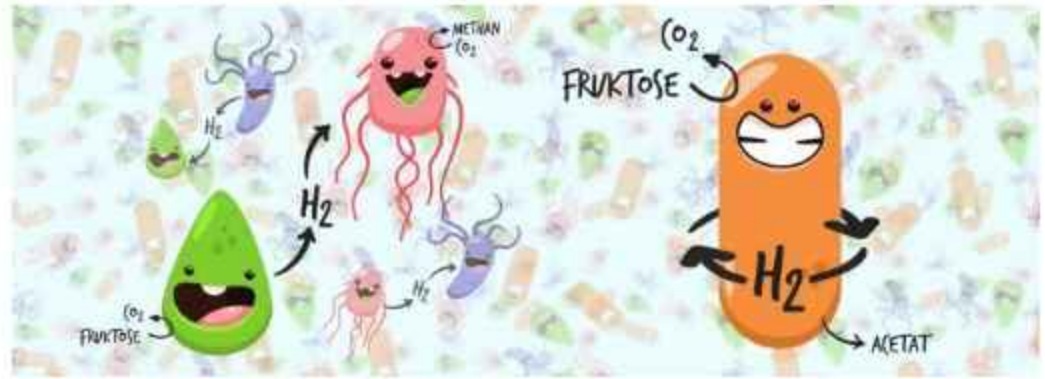
Apakah produk fermentasi merupakan probiotik?

- Jika mengandung mikroorganisme hidup yang telah dibuktikan sebagai probiotik
- Jumlah sel hidup pada saat dikonsumsi sesuai dengan khasiat saat uji klinis
- Rekomendasi konsumsi 10^8-10^9 CFU



Apakah sel mati atau metabolitnya memberikan manfaat kesehatan?





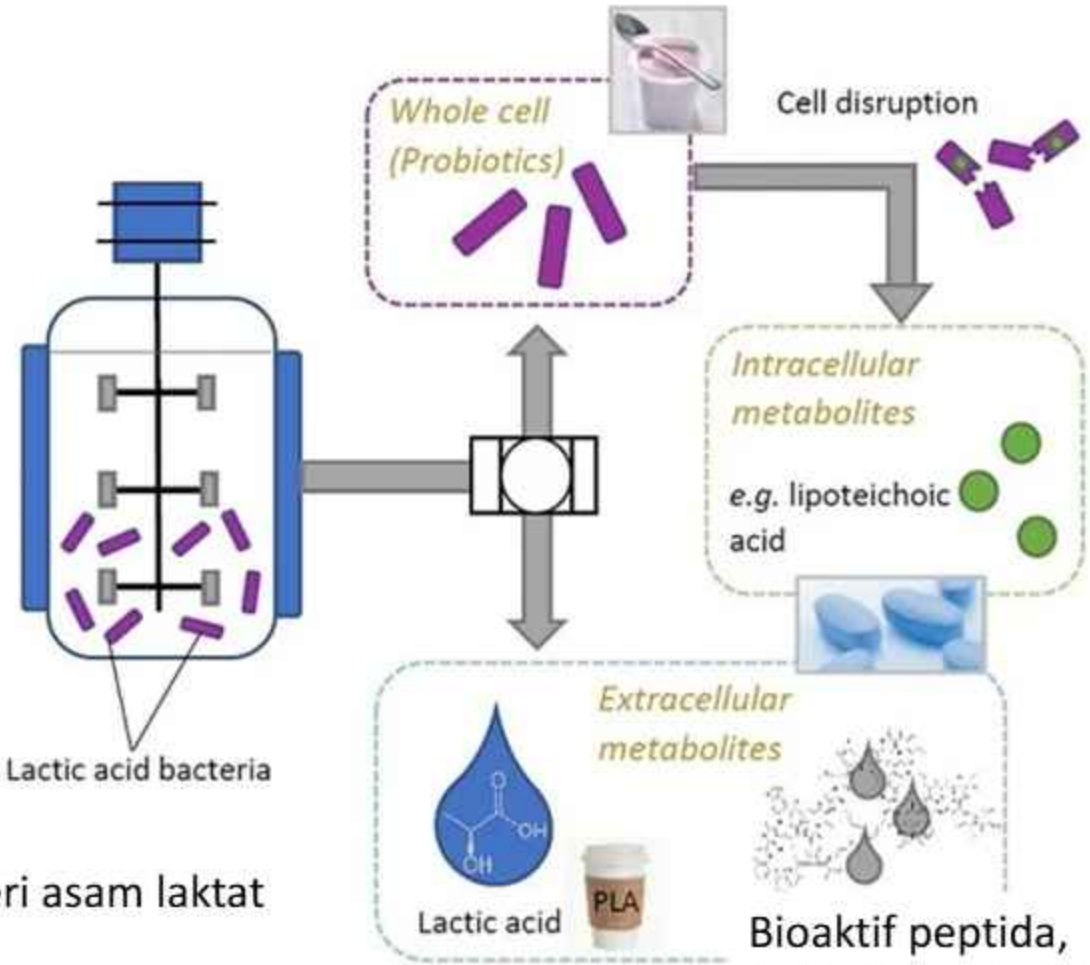
Manfaat kesehatan produk fermentasi

Mikroorganisme:

- Probiotik

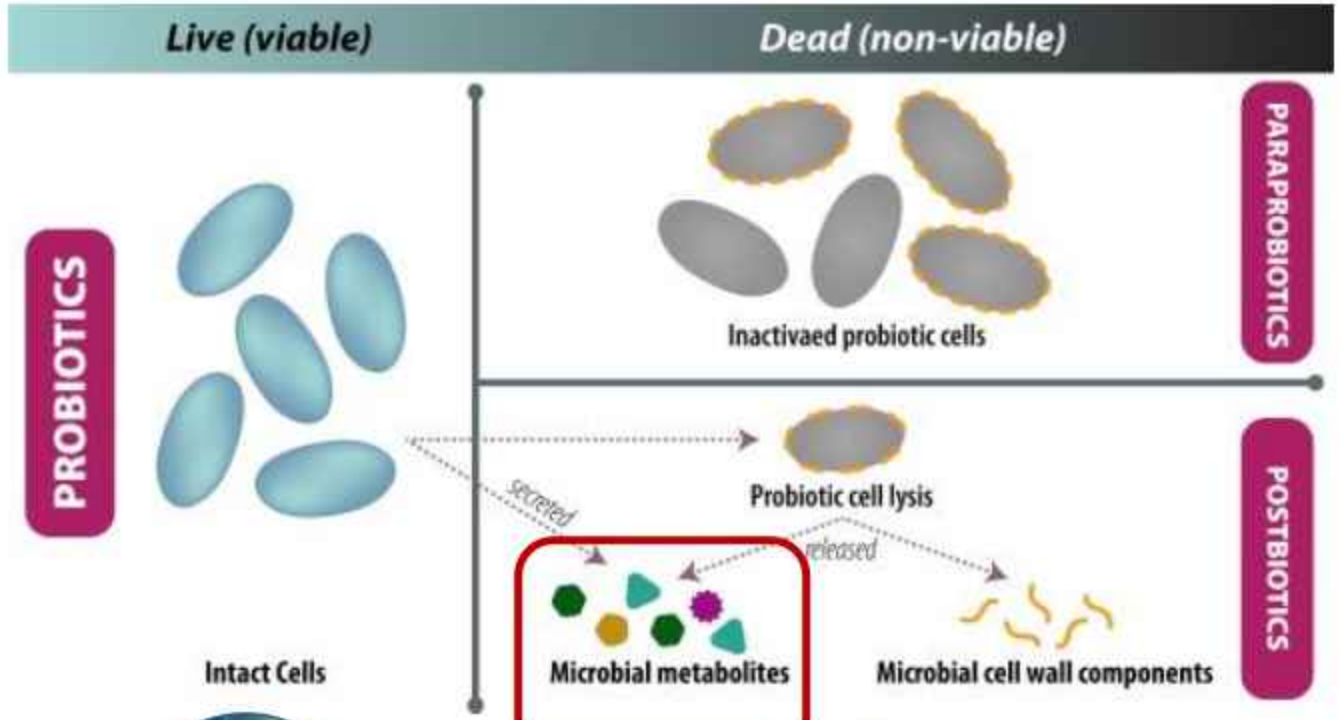
Metabolit:

- Intraseluler
- Ekstraseluler

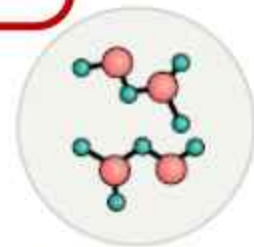


Contoh komponen bioaktif dari bakteri asam laktat

BEBERAPA ISTILAH YANG SERING DIGUNAKAN: PROBIOTIK, PARAPROBIOTIK DAN POSTBIOTIK







Postbiotics

Salah satu atau keduanya dapat berada pada produk fermentasi

Paraprobiotic/ghost probiotics/inactivated probiotics: sel mikroorganisme yang tidak hidup (utuh atau pecah) dalam jumlah yang cukup dan memberikan manfaat kesehatan kepada konsumen.

Pos-biotik: produk mikroorganisme atau metabolit mikroorgansime yang memiliki aktivitas biologis (misalnya: SCFA, EPS, peptida) terhadap konsumen non-viable

BELUM ADA REGULASI YANG MENGATUR DEFINISI POSTBIOTIK, PARAPROBIOTIK

https://www.nature.com/articles/s41575-020-0344-2

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Probiotik vs Postbiotik

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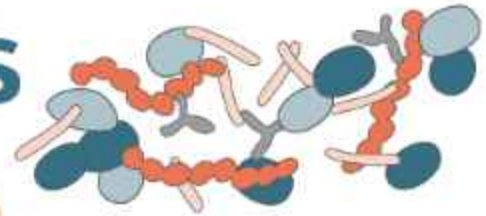
Probiotics



Probiotik merupakan mikroorganisme hidup yang jika dikonsumsi dalam jumlah memadai dapat memberikan manfaat kesehatan bagi konsumen.

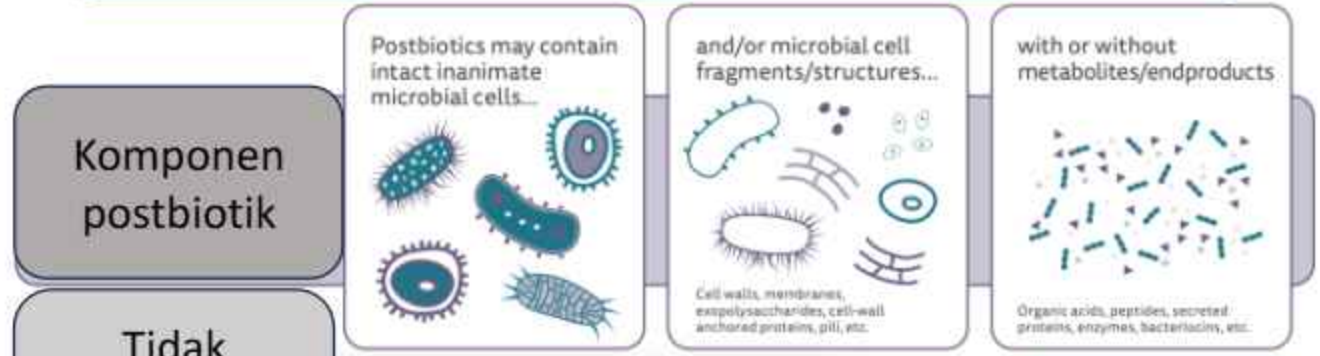
Menghasilkan metabolit dalam saluran pencernaan atau dalam medium fermentasi



Metabolit: Asam organic, peptida, protein, enzim, bakteriosin dll

Postbiotics

Sediaan mikroorganisme inaktif atau telah diinaktivasi dan/atau komponennya yang memberikan manfaat kesehatan kepada konsumen



https://isappscience.org/behind-the-publication-understanding-isapps-new-scientific-consensus-definition-of-postbiotics/

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Mikroorganisme penting pada proses fermentasi:

- Bakteri
  - Bakteri asam laktat: *Lactococcus, Streptococcus, Leuconostoc, Lactobacillus terutama* pada susu fermentasi
  - *Propionibacterium*: pada fermentasi keju Swiss
  - *Acetobacter:* fermentasi asam asetat/vinegar, kombucha dan nata de coco
- Khamir
  - Yang paling penting *Saccharomyces cerevisiae:* roti, bir, wine, kombucha, invertase, ekstrak khamir
- Kapang
  - *Aspergillus, Penicillium, Rhizopus and Mucor:* species yang tidak menghasilkan toksin untuk produksi enzim dan pangan
  - *A. oryzae*: sake, kecap, miso
  - *P. roquefortii, P. camembertii*: keju
  - *A. niger*: produksi asam sitrat

Mikroorganisme penting pada proses fermentasi untuk menghasilkan komponen bioaktif

Berbagai jenis dan species:

- Bakteri
- Kapang
- Khamir

- Mikroroganisme yang digunakan pada fermentasi pangan atau berada pada pangan selama proses fermentasi pangan
- Bukan penyebab sakit atau penghasil racun
- Mampu menghasilkan senyawa yang diinginkan dari substrat yang digunakan

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Contoh mikroorganisme yang meningkatkan senyawa bioaktif setelah fermentasi

Herbal medicine	Microbial strain	Bioactive substances/compounds after fermentation
Codonopsis lanceolata	*Bifidobacterium longum, L. acidophilus, L. mesenteroides*	↑ Gallic acid, caffeic acid, vanillic acid, 4-coumaric acid, trans-ferulic acid, caffeine
Rhodio larosea Lonicera japonica	*Alcaligene spiechaudii*	↑ Total phenolic content
Red ginseng	*Phellinus linteus*	↑ Rg2, Rg3, Rg5, Rk1, CK, Rh1, Rh2, F2
	L. brevis M2	↑ Rg3, Rg5, Rk1, compound K, Rh1, F2, Rg2, flavonoids
	L. brevis	↑ Rg5, Rk1, Rg3, and F2
Ginseng seed	*B. licheniformis subtilis, Pediococcus pentosaceus, L. gasseri*	↑ Total sugar content, acidic polysaccharides, total phenolic compound, p-coumaric acid
Radix astragali	*A. oryzae* M29	↑ Phenolic constituents, antioxidant (3,4-di (40-hydroxyphenyl) isobutyric acid.)
Panax notoginseng	*Streptococcus thermophlius L. helveticus, L. rhamnosus, L. acidophilus, B. longum, B. breve, Bifidobacterium bifidum*	↑ Rh1 and Rg3
Oyaksungisan	*Lactobacillus*	↑ Rutin, naringin, hesperidin, poncirin.
Jaeumganghwa-Tang	*Lactobacillus*	↑ 5-HMF, paeoniflorin, glycyrrhizin, nodakenin and, nodakenetin, berberine and palmatine and hesperidin
Hwangryun-haedok-tang	*Lactobacillus*	↑ Baicalin
Dioscorea zingiberensis	*Trichoderma reesei*	↑ Diosgenin
Rhizoma gastrodiae	*Grifola frondosa*	↑ Parishin ↓ Gastrodigenin, p-hydroxylbenzaldehyde

B; Represents either *Bifidobacterium* or *Bacillus* as described in text, *L*; *Lactobacillus*, *A*; *Aspergillus*.

A. Hussain et al. / Food Research International 81 (2016) 1–16

Senyawa bioaktif yang terdapat pada produk ferementasi berbasis biji-bijian

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Health-Promoting Activity	Health-Promoting Compounds	Raw Food Matrices	Fermenting Microorganism(s)
Antioxidant activity	Phenolic compounds, GABA [1], peptides, CLA [2], folates (vitamin B_9)	Quinoa and buckwheat	*P. pentosaceus* and *Lactobacillus paracasei*
		Wheat germ, barley, rye and buckwheat	*Lb. rhamnosus* and *Saccharomyces cerevisiae*
		Quinoa fermented	*Lb. plantarum* strain T6B10 and *Lactobacillus rossiae* strain T0B10
		Bread supplemented with bioprocessed Bran	Yeast, xylanase enzyme and combination thereof
		Rice bran	*Pediococcus acidilactici*, *L. lactis* and *Pediococcus pentoseous*
		Rice bran	*Saccharomyces boulardii*
		Bread prepared with wheat sourdough	*Lb. brevis* CECT 8183 and a commercial protease
		Sourdough and legume flours	*Lb. brevis* strain AM7 and *Lb. plantarum* strain C48
		Spontaneous fermented quinoa sourdough	*Lb. plantarum* strain CRL1905, *Leuconostoc mesenteroides* strain CRL1907 and *Lb. brevis*
		Rye malt sourdoughs	*Lb. reuteri*
		Lentils	*Lb. plantarum* and Savinase®

https://pubmed.ncbi.nlm.nih.gov/31137859/

Health-Promoting Activity	Health-Promoting Compounds	Raw Food Matrices	Fermenting Microorganism(s)
Anti-hypertensive activity	ACE [3] inhibitory peptides and GABA	Whole meal wheat sourdough	*Lb. brevis* CECT 8183 and protease
Vitamin content	Folate (vitamin B_9), vitamin K, riboflavin (vitamin B_2)	Lupin - tempeh	Co-culture of *Propionibacterium freudenreichii* and *Rhizopus oryzae*
			Rhizopus and Propionibacterium
		Cereal-based matrices (malted barley flour, barley flour and wheat aleurone)	Three strains of *P. freudenreichii*

Produksi antibiotic dengan fermentasi



Fermentasi Herbal

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Bogor Indonesia



Kampoo (variant dari Korea dan China)

Fermentasi herba secara tradisional dan modern: Fermentasi padat dan cair

Ayuverda Unani Siddha



Jamu ferementasi: Anggur kolesom, sari buah ferementasi, dll



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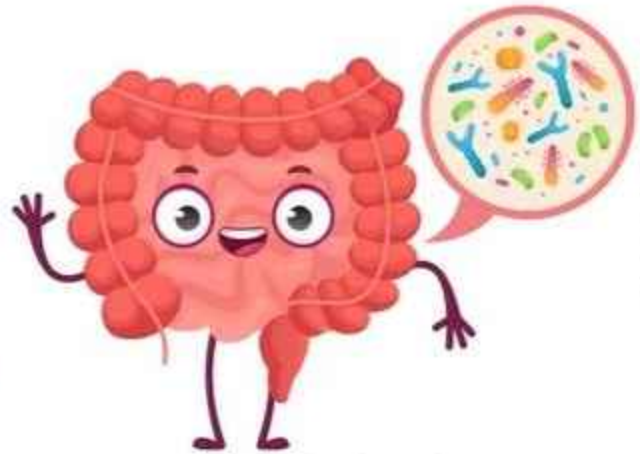
Fermentasi herbal



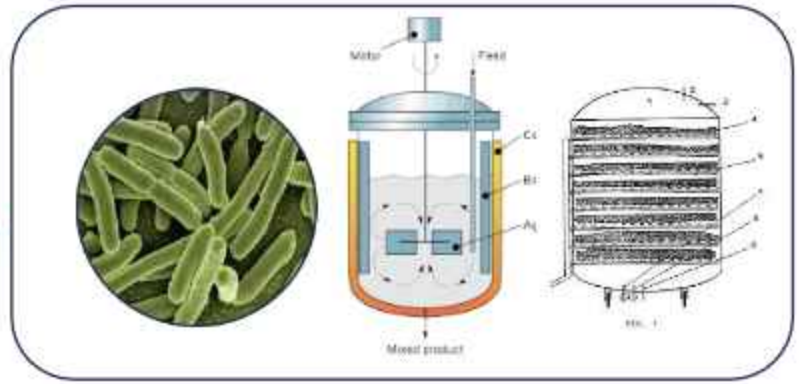
bakteri saluran pencernaan mengkonversi metabolit ke dalam bentuk aktif, namunkeberadaan bakteri ini sangat berbeda antar individu sehingga efek dari obat herbal juga dapat bervariasi



Banyak komponen pada obat herbal yang meruakan glikosida yang sangat polar

Penyerapan oleh tubuh dalam usus halus sangat terbatas, sehingga komponen ini masuk ke kolon dimana terdapat 100 triliunan bakteri



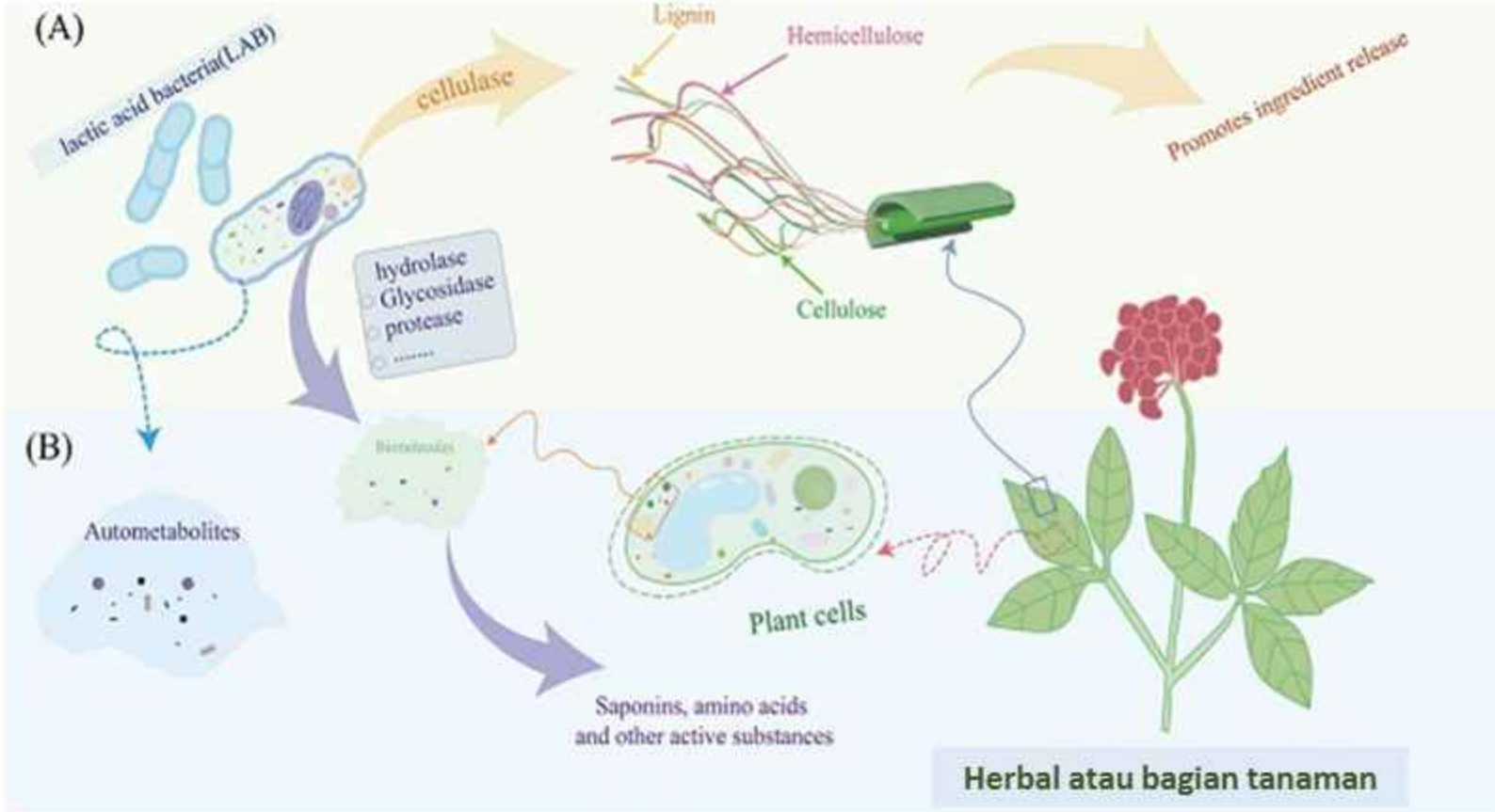


Dilakukan di luar tubuh

- Dekomposisi senyawa kompleks ke dalam komponen dengan BM rendah sehingga lebih mudah diserap
- Biotransformasi senyawa ke dalam bentuk aktif
- Konsentrasi senyawa bioaktif lebih konsisten

Manfaat fermentasi herbal

- Melepaskan senyawa aktif dan meningkatkan bioaktivitas seperti antioksidan, antiinflamatori, antidiare dll:
  - Fermentasi oleh BAL menghasilkan asam organic, anti-oxidant ferulic acid, hidrolisis protein
- Menghasilkan senyawa bioaktif baru
- Mereduksi toksisitas
- Mengurangi limbah



https://www.heraldopenaccess.us/openaccess/research-advances-and-application-prospects-of-lactic-acid-bacteria-fermentation-of-chinese-herbal-medicines

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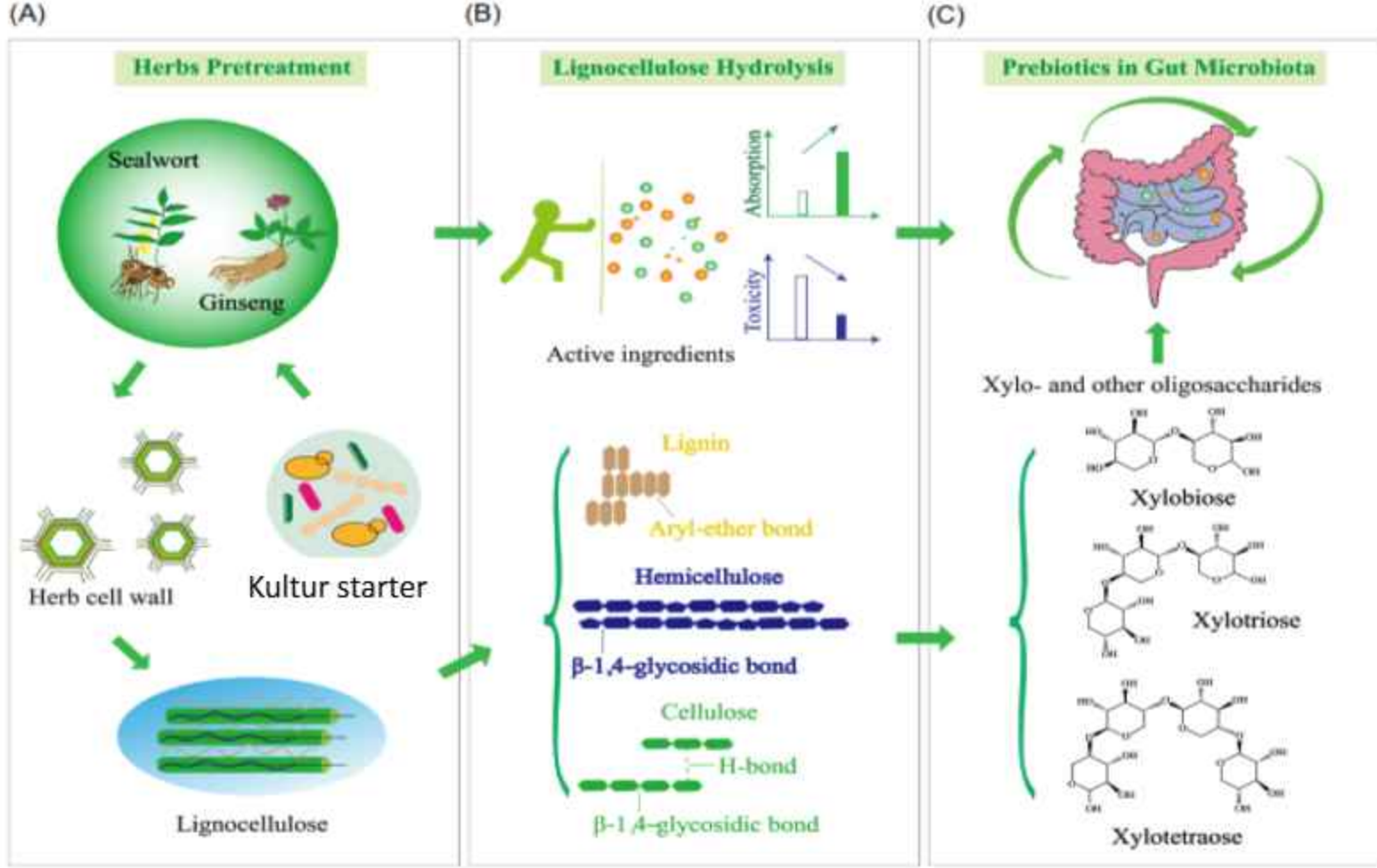
Degradasi komponen kompleks dalam fermentasi herbal





Enzim lignoselulases dari mikrorganisme (kutur starter) dapat mendegradasi lignocellulosa

Hidrolisis lignocellulose melepaskan senyawa bioaktif

Senyawa bioaktif dan oligosakarida bermanfaat bagi mikrobiota saluran pencernaan dan kesehatan.

https://onlinelibrary.wiley.com/doi/full/10.1002/imt2.93

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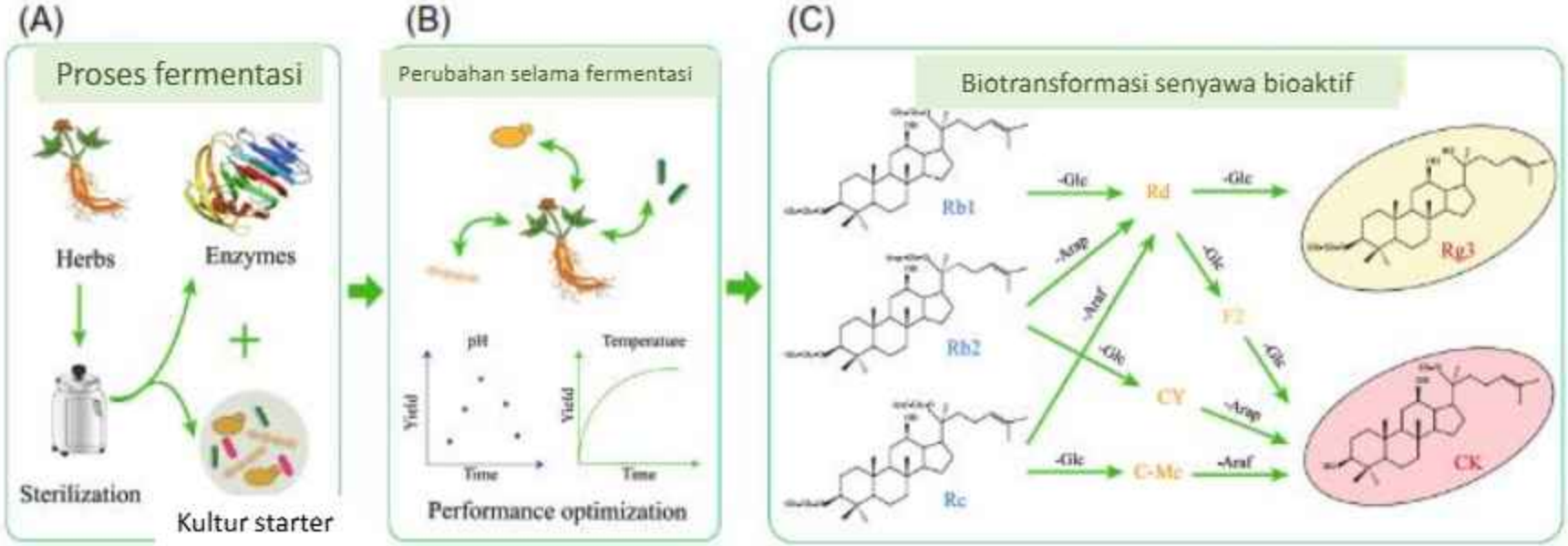

Ginseng terfermentasi memperbaiki penyerapan senyawa K oleh tubuh

- Senyawa K adalah ginsenoside CK atau IH901, metabolite utama pada ginseng terutama ginseng merah.
- Terbentuk melalui biotransformasi pada saluran pencernaan oleh bakteri saluran pencernaan → diganti dengan proses fermentasi
- Senyawa K memiliki manfaat kesehatan antara lain neuroprotective,meningkatkan kognitif dan efek antiinflamatori

https://onlinelibrary.wiley.com/doi/full/10.1002/imt2.93

Contoh lain:

- Fermentasi serealia oleh Aspergillus oryzae menghasilkan antioxidant.
- Fermentasi the menjadi Pu-Erh tea meningkat aktivitas antioxidannya, juga statin, total polyphenol dan GABA
- Fermentasi kunyit, ginseng, bawang putih, jus buah noni meningkatkan Aox dan absorpsi

Mikroorganisme dan produk fermentasi herbal serta manfaat kesehatannya

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Microorganism used in fermentation	Herbal formulation	Effects
L. fermentum NUC-C1	Red ginseng	Antidiabetic effect
B. subtilis natto	*Radix astragali*	Collagen production in human skin fibroblast
L. brevis k-1	*Artemisia princeps*	Anti-inflammatory
B. subtilis NUC1 (KCCM 10839P)	*Achyranthes japonica nakai*	Anti-inflammatory and Anti-osteoarthritis
B. licheniformis	*Rhizoma Atractylodis Macrrocephalae*	Anti-inflammatory
A. niger	*Ginkgo biloba* leaves	Small intestine and function of boiler chick
L. plantarum M1	Red ginseng	Anti-diabetic effect associated with changes in ginsenosides in Korean red ginseng
L. casei KFRI-127	*Hwangryun-Haedok-Tang*	Suppression of ovariectomy-induced bone loss
L. rhamnosus	*Cornus officinalis*	Promoting hair growth
L. fermentum, *L. gasseri*, or *L. casei*	*Ssanghwa-tang*	Hepatoprotective effect
L. casei	*Lonicerae Flos*	Anti-viral effect on A type Influenza virus
Saccharomyces cerevisiae and *L. brevis*	*Panax Ginseng*, *Rehmannia glutinosa*, *Polygonum multiflorum* and *Polygonatum Sibiricum*	Anti-aging effect
L. Pentosus	*Artemisiae Argyi Folium*	Hepatoprotective effect
L. Pentosus	*Artemisiae Argyi Folium*	Effect against hydrogen peroxide production
Eurotium cristatum	*Camellia sinensis L Fuzhuan* tea	Anti-bacterial activity

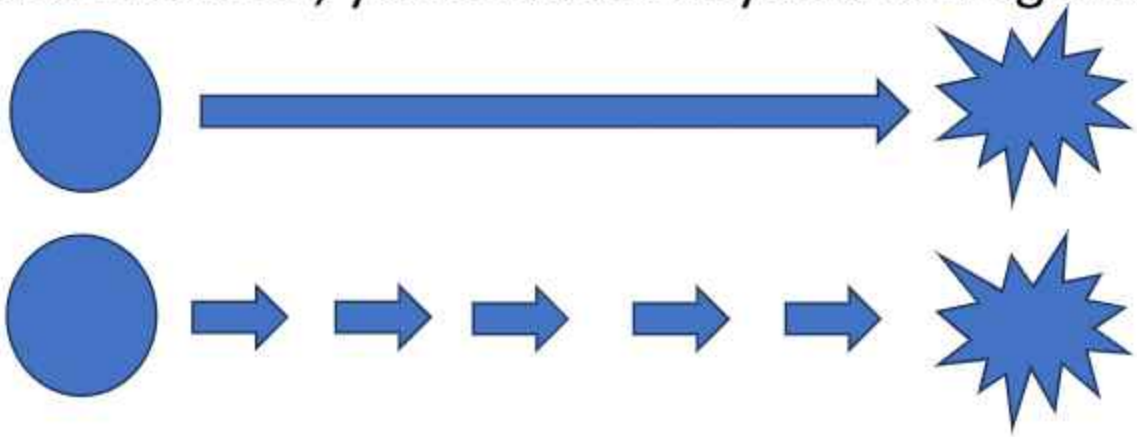
Manfaat Kesehatan dan Potensi sebagai Obat tradisional

A. Hussain et al. / Food Research International 81 (2016) 1–16

B; Bifidobacterium, L; Lactobacillus, A; Aspergillus.

Fermentasi Herba

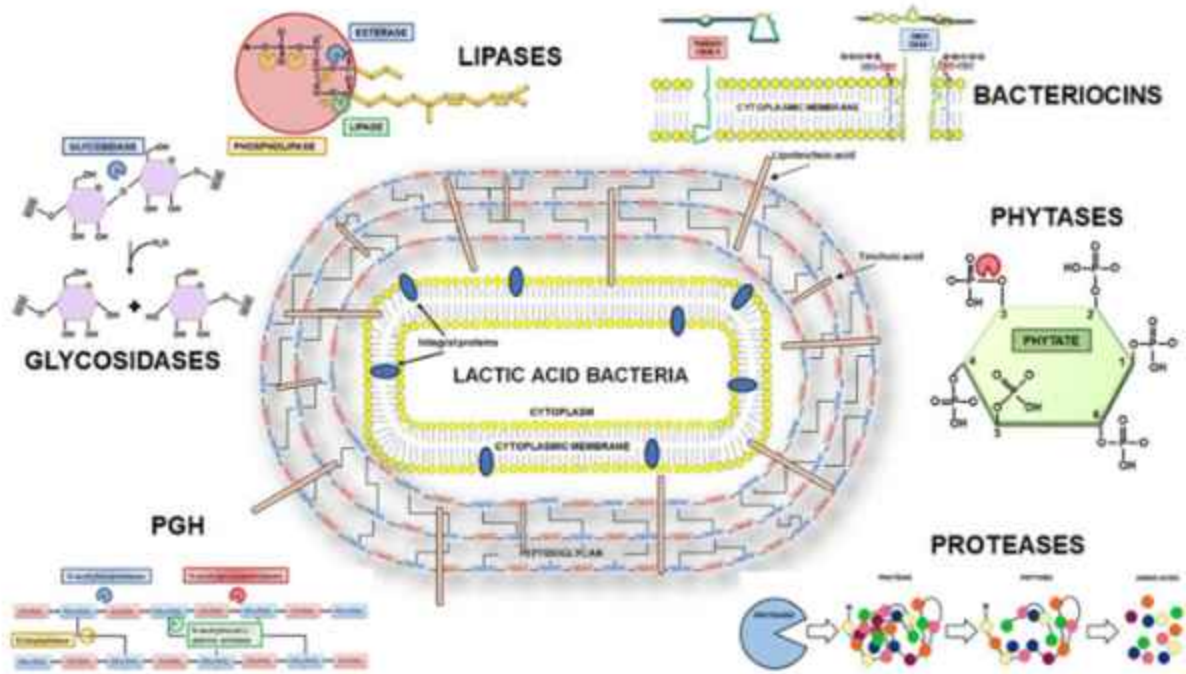
- Pada fermentasi herba, pola metabolit berbeda tergantung jenis mikroorganisme dan jenis tanamannya, sehingga antara satu herba dengan lainnya dapat berbeda
  - Senyawa ginsenosida hanya memerlukan deglikosilasi untuk aktivasi biologisnya
  - Namun banyak herba yang memerlukan berbagai proses metabolism untuk aktivasinya.
  - Trachelosida, senyawa lignan utama pada biji safflower seeds, memerlukan deglukosilasi, demetilasi dan dehidroksilasi untuk mengkonversinya menjadi enterolactone, yaitu suatu senyawa estrogenik



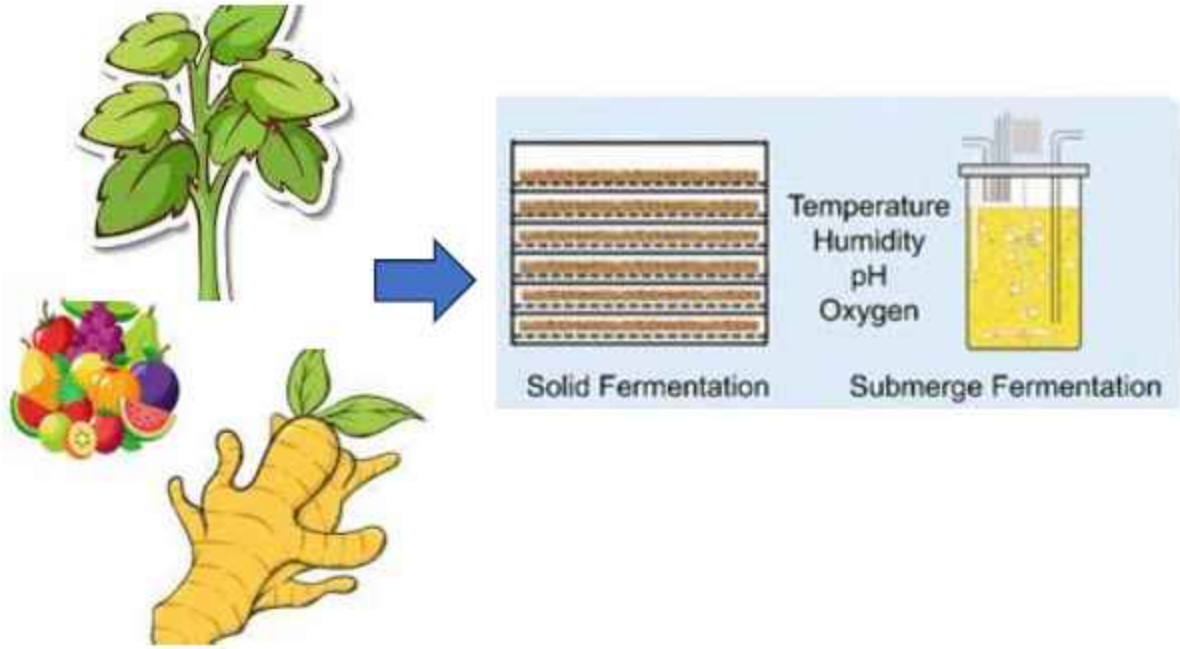
Manfaat tergantung pada konsentrasi senyawa bioaktif pada hasil fermentasi

Mengapa produk yang dihasilkan kelompok mikroba berbeda?

- Setiap kelompok mikroorganisme mempunyai enzim yang umum (atau dimiliki oleh semua/ sebagian kelompok mikroba), dan memiliki juga enzim yang spesifik yang hanya dimiliki oleh kelompok tersebut
- Perbedaan enzim menyebabkan perbedaan cara pemotongan pada substrat



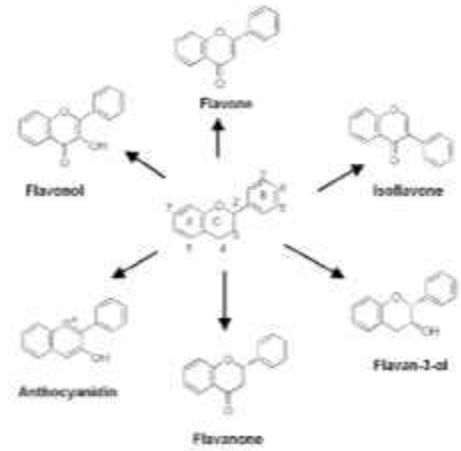
Pemanfaatan produk ferementasi herbal



Utuh



Ekstraksi, separasi dan purifikasi



Pengembangan teknologi fermentasi untuk menghasilkan OBA atau obat tradisional

- Untuk menjamin hasil fermentasi sebagai sumber senyawa bioaktif untuk suplemen atau bahan alami obat, maka berbagai jenis bakteri yang mampu mengkonversi atau menghasilkan senyawa aktif perlu diisolasi dan keamanannya divalidasi
- Produktivitas, konsentrasi senyawa dan kualitas merupakan kriteria utama dalam fermentasi herbal.
- Keamanan dan toksisitas produk memerlukan pengujian
- Untuk penggunaan sebagai obat perlu riset untuk mendukung status farmakologi senyawa aktif

Standarisasi fermentasi herbal sebagai obat tradisional:

- Produk:
  - Komponen bioaktif jelas terindetifikasi
  - Konsentrasi senyawa bioaktif diketahui
  - Aman
  - Memberikan manfaat yang dibuktikan secara klinis
  - Mekanisme farmakologi senyawa aktif diketahui jika digunakan sebagai obat
  - Konsentrasi yang memberikan manfaat saat dikonsumsi sesuai dengan hasil pengujian klinis

Mikroorganisme:

- Identitas mikroorganisme
- Aman:
  - Sejarah penggunaan menunjukkan keamanan
  - Atau data dukung seperti pengakuan keamanan dari Lembaga berwenang

Standarisasi fermentasi herbal sebagai obat tradisional:

- Proses fermentasi:
  - Fermentasi harus dilakukan pada kondisi terstandar yang mencakup:
    - Komposisi medium fermentasi,
    - suhu fermentasi,
    - pH medium,
    - Aerob atau anaerob
    - jenis mikroorganisme yang digunakan untuk fermentasi,
    - mikroorganisme yang terdapat pada bahan,
    - waktu inkubasi.
  - Jika senyawa dipisahkan, jenis pelarut yang digunakan juga sangat menentukan konsentrasi senyawa aktif dan khasiatnya.

CODEX ALIMENTARIUS
INTERNATIONAL FOOD STANDARDS

Food and Agriculture Organization of the United Nations
World Health Organization

E-mail: codex@fao.org - www.codexalimentarius.org

IPB University
Bogor Indonesia

REGIONAL STANDARD FOR FERMENTED NONI FRUIT JUIC

North America and South West Pacific

CXS 356R-2023

Adopted in 2023

2.3 Fermentation of noni fruit juice

Whole fruit or fruit pulp are fermented spontaneously or by starter culture. Juice is extracted from the fermented products. The resultant fermented noni fruit juice is pasteurized or otherwise treated to eliminate pathogens of public health significance.

3. ESSENTIAL COMPOSITION AND QUALITY FACTORS

3.1 Ingredients

The fermented noni fruit juice as defined in Section 2.

3.2 Fermented noni fruit juice

a)	Brix value (soluble solids)	5.5°minimum
b)	pH	3.5-3.9
c)	Ethanol	less than 0.5% v/v
d)	Deacetylasperulosidic acid	Present
e)	Scopoletin	Present[iii]

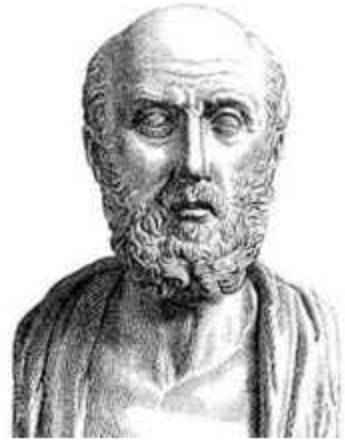


[iii] Scopoletin is present naturally in fermented noni fruit juice. Some reports have shown potential toxicity of scopoletin. Therefore, the scopoletin levels should be kept as low as technologically feasible until a safe level is established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA).

Penutup

- Mikroorganisme memberikan manfaat kesehatan melalui sel hidup (probiotik), sel mati dan metbaolitnya (Postbiotik).
- Probiotik dapat ditambahkan sebagai kultur starter atau dalam bentuk termikroenkapsulasi
- Aktivitas mikroorganisme selama fermentasi herbal merubah karakteristik substrat dan menghasilkan metabolit yang memiliki aktivitas biologis (komponen bioaktif)
- Pemanfaatan mikroorganisme dalam teknologi fermentasi dapat digunakan untuk meningkatkan khasiat herbal.
- Senyawa bioaktif yang dihasilkan tergantung pada jenis mikroorganisme dan substrate yang digunakan.
- Penggunaan hasil fermentasi herbal sebagai bahan untuk obat alami memerlukan identifikasi senyawa aktif dan standarisasi proses termasuk mikroorganisme yang digunakan

Let food be thy Medicine and Medicine be thy food.







Terimakasih

IPB University
Bogor Indonesia

Prof. Dr. Lilis Nuraida, MSc.
SEAFAST Center and
Department Food Science and Technology
IPB University
lnuraida@gmail.com

Lilis Nuraida, 20 Agustus 2025

Research & Development of Modern Herbal Medicine in Indonesia

By
Dexa Laboratories of Biomolecular Science (DLBS)



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Dexa Group State of The Arts Facilities

R&D Centers



Dexa Development Center
Cikarang



Dexa Laboratories of Biomolecular Sciences
Cikarang

Manufacturing Facilities



Solid and Cephalosporin Production PT Dexa Medica
Palembang



Oral Solid & Syrup Production PT Beta Pharmacon
Karawang



Solid, Liquid, Injectables and API Production PT Ferron Par Pharmaceuticals
Cikarang



Oncology Injectables Production PT Fonko International Pharmaceuticals
Cikarang



API OMAI (Herbal/ Protein) and Oral Solid FG OMAI
PT Dexa Medica
Cikarang



Medical Device Production
PT Deca Metric Medica
Cikarang



Oral Solid Pharma and Oral Liquid Herbal
PT Anugrah Amartha Global
Bogor

Distribution Facilities



National Distribution Center
PT Anugrah Argon Medica
Cikarang



Kantor Cabang Palu
PT Anugrah Argon Medica
Palu

Certifications:

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DLBS Our Research Campus

DLBS
DEXA LABORATORIES OF BIOMOLECULAR SCIENCES

CEBS

Biomolecular Research using Indonesian Biodiversity since 2005







Approved by:

BADAN POM

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DLBS Design



DISCOVERY

Research for **new candidate of drug substances** from natural sources that have potencies in pharmacological activities

- Bioactive Fraction
- Bioactive **Protein** Fraction
- Bioactive **Oil** Fraction
- Bioactive **Probiotic** Isolate



BIOLOGY

Study through modern pharmacology by molecular biology basis with approach of ***protein target*** and ***gene expression***

Conduct pre-clinical studies using animal model **for ensure the toxicity and pharmacodynamics** of new candidate of natural drug substances



DEVELOPMENT

Pharmaceutical development for formula and process of manufacturing, incl. analytical method and packaging development, provide stability data for **technical dossier registration**

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Research Facilities

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1st AAALAC Accreditation in 2012











Phyto-chemistry Lab.

Biotech. Lab.

Compound Isolation Lab

Bio-molecular Lab.

Animal Lab.

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Integrated with Herbal Extract Scale-Up & Production IEBA (Industri Ekstrak Bahan Alam)

Two major DLBS Drug Substance scale up and commercial activities:

- Herbal scale up
- Biotech scale up













DLBS

Dexa Medica

Expertise for the Promotion of Health

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Production Facility



Extraction & filtration
[e&e, Germany]



2-effect Evaporation
[e&e, Germany]



Liquid-liquid Extraction
[e&e, Germany]



1-effect Evaporation
[e&e, Germany]



Decontamination (UHT)
[e&e, Germany]



Vacuum Belt Dryer
[e&e, Germany]

- Closed system production facility
- Explosion proof (organic solvent area)
- CPOTB-CPBBAOTB
- CPOB-CPBBAOB
- ISO 22000
- Halal Assurance System

3 produk Fitofarmaka Dexa Group masuk dalam Formularium Fitofarmaka

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No	Kelas Terapi/ Komposisi/ Bentuk Sediaan	Indikasi	Kontra Indikasi	Aturan Pakai
II	**Sistem Metabolik**			
2	Fraksi dari ekstrak campuran **Daun bungur** (Lagerstroemiae speciosae folium) dan **Kulit kayu manis** (Cinnamomi burmannii cortex) Tiap kapsul mengandung 100 mg fraksi dari ekstrak campuran Lagerstroemiae speciosae folium dan Cinnamomi burmannii cortex (1:3)	Sebagai terapi kombinasi dengan obat antidiabetes oral lainnya pada pasien diabetes melitus tipe 2.	Belum diketahui	1x1 kapsul sehari
III	**Sistem Pencernaan**			
3	Fraksi dari ekstrak **Kulit kayu manis** (Cinnamomi burmannii cortex) Tiap kaplet mengandung 250 mg fraksi dari ekstrak Cinnamom burmannii cortex	Meringankan gangguan pada lambung.	Belum diketahui	1-2 kaplet sehari
IV	**Sistem Imun**			
4	Ekstrak **Herba meniran** (Phyllanthi niruri herba) 1. Tiap kapsul mengandung 50 mg ekstrak	Memperbaiki sistem imun.	- Wanita hamil dan menyusui. - Pasien hipersensitif terhadap *Phyllanthus niruri*	Dewasa (diatas 12 tahun): 3 x 1 kapsul sehari
	Phyllanthi niruri herba 2. Tiap 5 ml sirup mengandung 25 mg ekstrak Phyllanthi niruri herba		- Pasien yang menderita penyakit autoimun.	Anak-anak (diatas 1 tahun): 3 x 5 ml sehari Dewasa: 3 x 10 ml sehari

→ **INLACIN**

→ **REDACID**

→ **STIMUNO**

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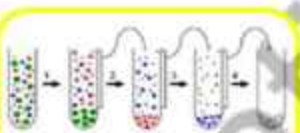
Example of R&D Process on Finding Bioactive Fraction for Modern Herbal Medicine in DLBS

Striatin is produced using complex biotechnological process


Channa striata

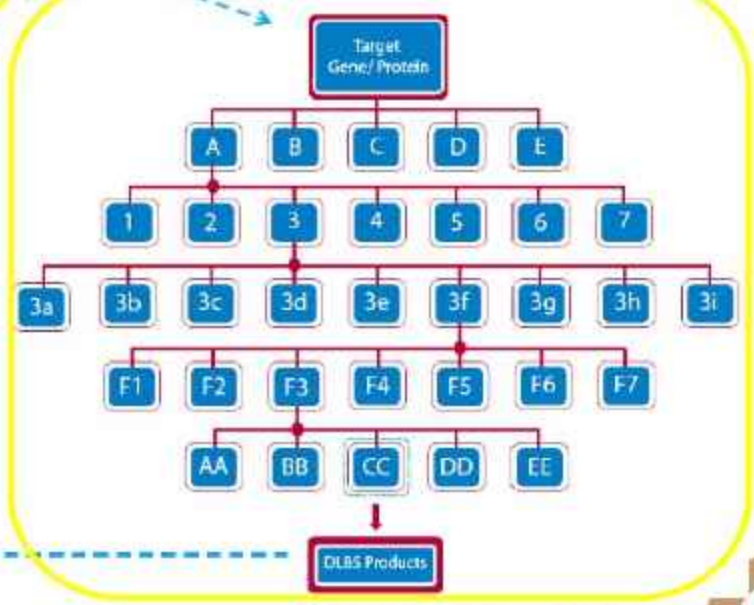

Extraction


Crude extract


Bioactive fractionation








STRIATIN powder


Granulation


Microfiltration


Chromatography


Tableting



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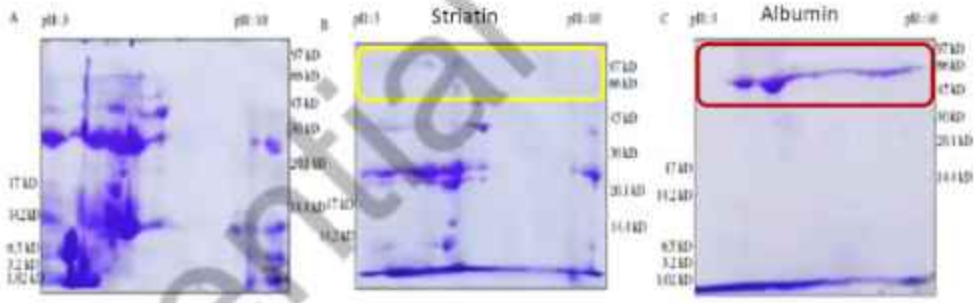
Protein Profile from 2D-Electrophoresis

(A) *C. striata* crude extract
(B) Striatin
(C) Albumin

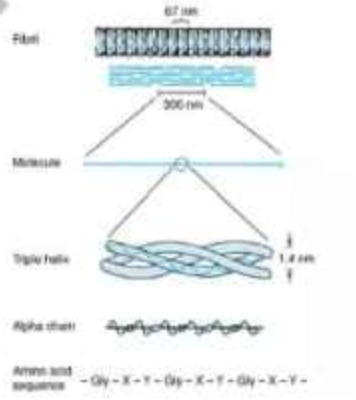


Amino Acid Composition of Striatin

Amino acids		Amino acid content (%)
Essential amino acid	L-arginine	1.74
	L-histidine	0.78
	L-isoleucine	0.99
	L-leucine	2.01
	L-lysine	1.16
	L-methionine	1.07
	L-phenylalanine	1.64
	L-threonine	0.90
	Tryptophan	1.91
	L-valine	0.96
Non essential amino acid	L-alanine	0.81
	L-cysteine	2.26
	Glutamine	1.90
	Glycine	1.29
	L-proline	1.05
	L-serine	0.37
	L-tyrosine	1.00

Rahayu et al. As Pac J Trop Biomed 6(6):930-936, 2016

Glycine promotes wound healing through production of collagenous fibers



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Clinical Trials of DLBS Products



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SITES AND INVESTIGATORS OF OUR CLINICAL TRIALS



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CLINICAL CASES

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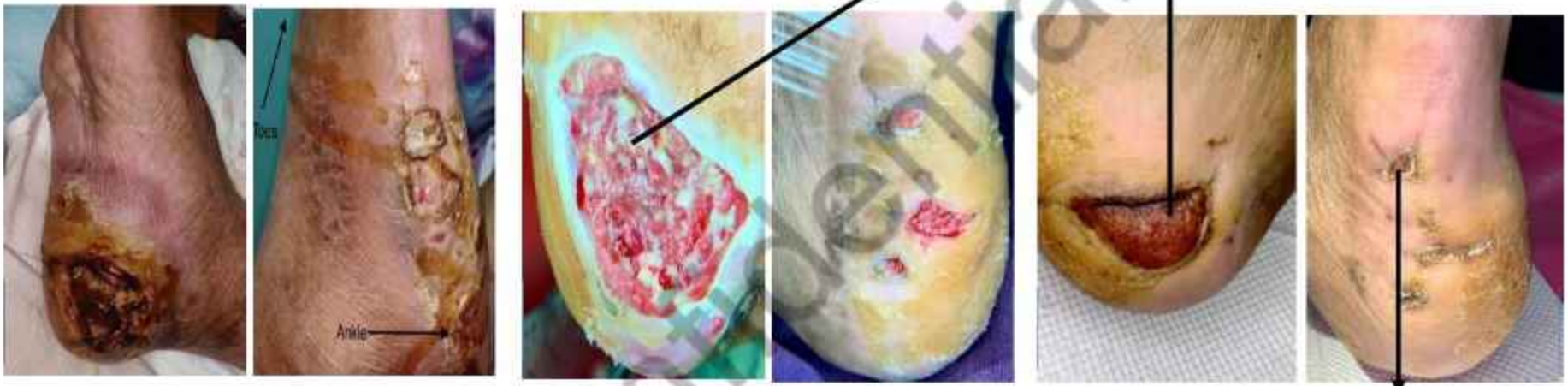
Inbumin
Striatin 250 mg



DAY OF CONSULT | DAY 10 POST DEBRIDEMENT | DAY 35 POST DEBRIDEMENT

57/ M with a chronic and infected non healing wound on his right foot. Known Diabetic and Hypertensive uncontrolled. Maintenance:

- *Ultra long-acting insulin*
- *Antihypertensives*
- *High Intensity Statin*
- ***Disolf 490mg TID*** ***and*** ***Inbumin 250 BID***



DAY 47

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53 Grow Faster & Stronger dexa group

CLINICAL CASES

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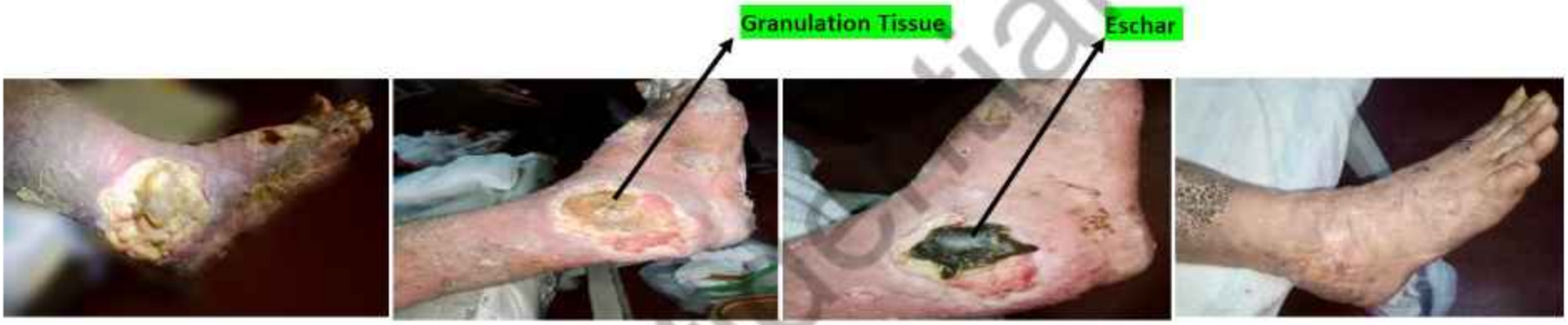
Inbumin
Sitalin 250 mg



DAY OF CONSULT | DAY 21 POST DEBRIDEMENT | DAY 40 | DAY 60

82/F Chronic non healing, infected wound on her right foot and leg. Known Diabetic uncontrolled.

Management:
- Debridement
- Wound care follow ups
- Maintained on: *Oral Hypoglycemic Agents, High Intensity Statin*, ***Disolf TID*** *and* ***Inbumin 250 BID*** *and wound care dressings.*

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- **Inlacin** contains **DLBS3233** 50 mg and 100 mg, derived from the combination of *Lagerstroemia speciosa* folium and *Cinnamomum burmannii* cortex.
- The combination of both has been proven to have pharmacological effects as an **anti-diabetic**.
- Clinical studies show that Inlacin can **significantly** lower **HbA1C** levels by up to **1.13%** in patients with type-2 diabetes.
- Recent studies on PCOS patients have shown that Inlacin demonstrates similar efficacy to metformin, while presenting a lower incidence of side effects as a standar d therapy.
- The patent of Inlacin has been registered in 5 countries, including Indonesia, Europe, the United States, Australia, and Korea, along with numerous other international publications.









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- **Disolf** contains the bioactive protein fraction **DLBS1033 490 mg**, derived from *Lumbricus rubellus*.
- Disolf contains **8 main proteins** known as **Lumbricus Low Molecular Weight Proteins** (LLP).
- Disolf works as an oral **antithrombotic** and **thrombolytic**, promoting better blood circulation.
- The Disolf patent is officially registered in four countries, in cluding Indonesia, Europe, Australia, and the Philippines, along with numerous international publications.







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- Redacid contains the bioactive fraction **DLBS2411** 250 mg, derived from *Cinnamomum burmannii* cortex.
- Redacid works as an **anti-ulcer**, alleviating stomach disorders.
- Patented innovation in the extraction process: a **coumarin-free fraction**.
- The DLBS2411 and DLBS24 coumarin-free patents are registered in six countries, including Indonesia, Europe, Japan, Australia, Taiwan, and Korea, with additional support from various international publications.

REDACID



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Quality Management System



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Simplisia Characterization



- **Plant Origin:** The variant of seedling, identification
- **Growth Environment:**
  - **Location and Climate:** Soil, atmosphere, weather, temperature, light, water, and organic/ inorganic compounds.
  - **Growing Process:** Use of fertilizers, pesticides, organic, etc.
- **Harvesting:**
  - **Conditions:** Age and method of harvesting.
  - **Timing:** The harvesting period influences metabolism and compound formation.
- **Post-Harvest and Preparation:**
  - **Cultivated Plants:** Good Agricultural Practice (GAP) significantly impacts this stage.
  - **Wild Crops:** The drying process, often done in the field, is a key influence
- **Quantitative**: soluble essence

Storage: Affects the material's stability and susceptibility to biotic and abiotic conta mination.

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Extract Standardization

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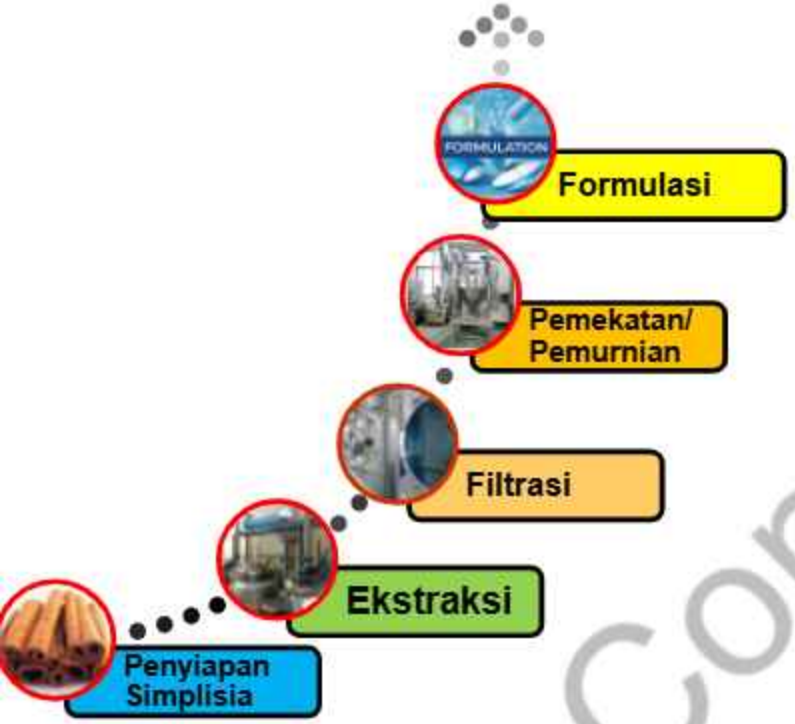

- Farmakope Herbal Indonesia
- PerBPOM No 29 Th 2023 (Persyaratan Keamanan dan Mutu Obat Bahan Alam)
- WHO Guidelines for Selecting Marker Substances for Quality Control of Herbal Medicines(WHO TRS No. 1003, 2017, Annex 1)
- Other reputable reference

Extracts produced by specific extraction methods possess u nique markers, though not all are currently identified within FHI.

For a method to be considered valid, it must meet scientific standards of repeatability and reproducibility, as well as stati stical standards. This means as long as a method has been validated, it can be used.

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QC-Obat Bahan Alam

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- PerBPOM No 29 Th 2023 (Persyaratan Keamanan dan Mutu Obat Bahan Alam)
- ASEAN Traditional Medicine/ Health Supplement
- Other specific country requirement from export destination country



OBAT DALAM

- Sediaan Rajangan
- Sediaan serbuk simplisia
- Sediaan lainnya: Granul, Tablet, Kapsul, cairan obat dalam, dll.



OBAT LUAR

- Sediaan cair: cairan obat luar
- Sediaan semi padat: salep, krim
- Sediaan padat: parem, pilis, tapel, koyo, supositoria

AWARDS

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2022

The Most Phytopharmaceutical Manufacturer

FROM
Ministry of Health



2021

Rintisan Teknologi Industri Award 2021

FROM
MINISTRY OF INDUSTRY

Contribution to Improving National Industry Competitiveness through OMAI Research and Innovation



2020

Innovative Industry Award

FROM
MINISTRY OF RESEARCH AND TECHNOLOGY, INDONESIA

Commitment to developing Native Indonesian Modern Medicine (OMAI)



2019

IIRDI Award

FROM
MINISTRY OF RESEARCH AND TECHNOLOGY, INDONESIA

Contributes to research and development activities

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THANK YOU

DLBS
DEXA LABORATORIES OF BIOMOLECULAR SCIENCES

OMAI

OBAT MODERN ASLI INDONESIA

Berbasis Uji Klinis, Terbukti Efektif dan Aman Untuk Pasien

- Kemandirian bahan baku Indonesia
- Dengan hasil uji klinis
- Berkualitas GMP
- Peluang lisensi ke luar negeri



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Herbal dan *Natural Extract* (Natex)
PT Indofarma Tbk

Bekasi, 21 Agustus 2025



Company Milestones PT Indofarma Tbk

1918

Berawal dari unit produksi kecil di **Rumah Sakit Pusat Pemerintah Hindia Belanda** yang memproduksi salep dan kasa pembalut

1942

Diambil alih oleh Pemerintah Jepang di bawah **Takeda Pharmaceutical**

1950

Diambil alih oleh Pemerintah Republik Indonesia di bawah pengelolaan **Departemen Kesehatan**

1981

Berubah status menjadi Perusahaan Umum Indonesia Farma **(Perum Indofarma)**

2001

Pencatatan Saham Perdana PT Indofarma (Persero) Tbk **(INAF)**

2020

Dibentuknya **Holding BUMN Farmasi**



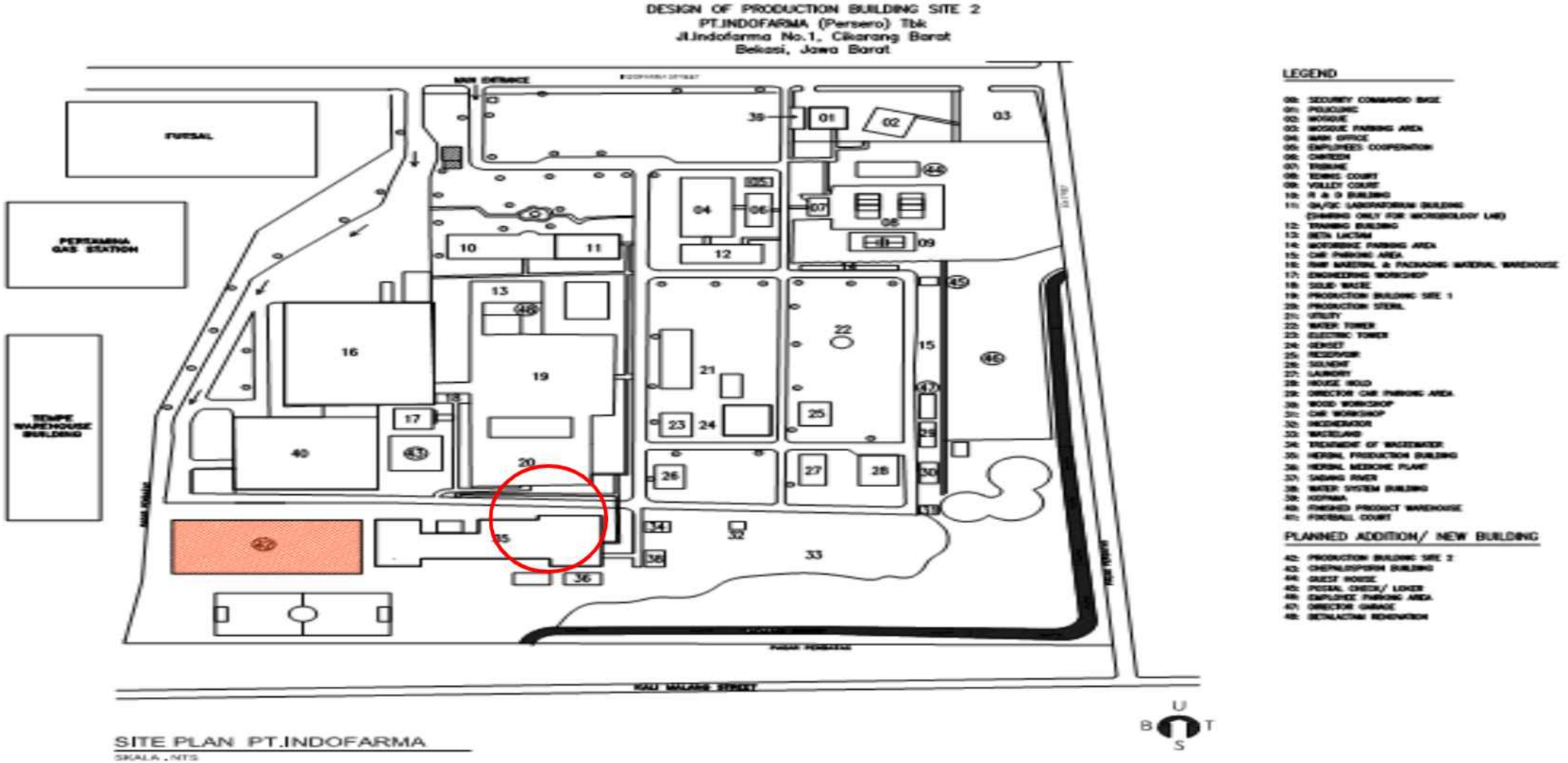








PT Indofarma Tbk – Site Plant



Factory PT Indofarma Tbk

Factory

1. Herbal Production Building	4.284 m^2
2. Main Production Building	8.721 m^2
3. Sterile Production Building	1.615 m^2

Support

1. QC - R&D Building (incl. Microbiology Lab)	2.346 m^2
2. QA Building	400 m^2
3. Technical and Maintenance	360 m^2
4. Raw Material Warehouse	5.346 m^2
5. Finish Product Warehouse	6.000 m^2
6. Utilities	2.000 m^2

Sertifikasi dan NIE Aktif PT Indofarma Tbk

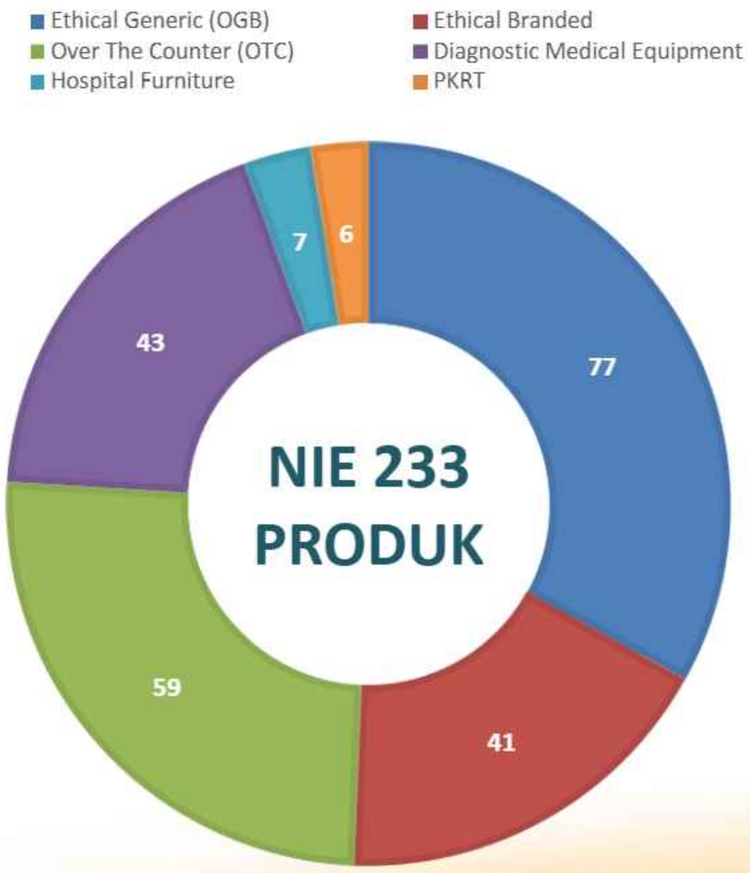
- Produksi dan Pemasaran Produk Obat dan Obat Tradisional

- Peralatan Kimia Klinik dan Toksikologi Klinik
- Peralatan Bedah Umum dan Bedah Plastik

- Ekstrak Kental
- Ekstrak Cair
- Ekstrak Kering
- Tablet
- Kapsul
- Cairan Obat Dalam
- Serbuk Oral
- Cairan Obat Luar
- Tablet Salut

- Rempah, Bumbu dan Kondimen (8 Produk)
- Vitamin, Mineral dan Zat Gizi Lainnya (4 Produk)
- Jamu dan Obat Tradisional (6 Produk)
- Ekstrak (50 Produk)
- Obat Tradisional (4 Produk) – Tambahan
- Obat Tradisional (18 Produk) – Tambahan
- Ekstrak Teh Hijau dan Ekstrak Teh Hitam

- Cairan Oral Nonbetalaktam
- Kapsul Keras Nonbetalaktam
- Serbuk Steril Injeksi Antibiotik Sefalosporin dan Turunannya
- Semisolid Nonbetalaktam
- Serbuk Oral Nonbetalaktam
- Tablet dan Tablet Salut Nonbetalaktam
- Injeksi Volume Kecil Nonbetalaktam



Fasilitas dan Kapasitas Produksi Herbal PT Indofarma Tbk



Extractor
Percolation



Evaporator
1.000 liter/hour



Retrificator
Alcohol purifier

Sediaan	Kapasitas 1 Tahun
Kapsul Herbal	29.342.600
Ekstrak Herbal	54.000
Mixing Herbal	240.000
Sirup Cair Herbal	123.200
TOTAL HERBAL	**29.760.800**



High Speed Mixer
250 liter / use



Capsule Filling
20.000 capsule/hour



Sachetting Machine
18.000 sch/hour



Automatic Counting Machine
15.000 capsule/hour



Vacuum Drier
30 kg / cycle



Spray Drier
20 kg / hour

Produk Ekstrak PT Indofarma Tbk



Turmeric



Java Turmeric



Ginger



Red Ginger



Bangle



Bilberry



Strawberry



Black Tea



Green Tea



Pasak Bumi



Daun Katuk



Meniran



Jati Belanda



Pegagan



Daun Kelor

TERSERTIFIKASI

Produk Herbal PT Indofarma Tbk



Suplemen
Kesehatan Mata



ProLipid®

Obat tradisional untuk
Menurunkan kadar kolesterol



ProBagin® Elixir

Obat tradisional untuk
penanganan batu ginjal



ProAsi®
Membantu Melancarkan ASI

Obat tradisional untuk meningkatkan
produksi ASI



ProliSlim®

Obat tradisional untuk
Menurunkan lemak tubuh



NATURAL bioprost®
Saw Palmetto Capsules

Obat tradisional untuk menjaga
kesehatan prostat

TERSERTIFIKASI

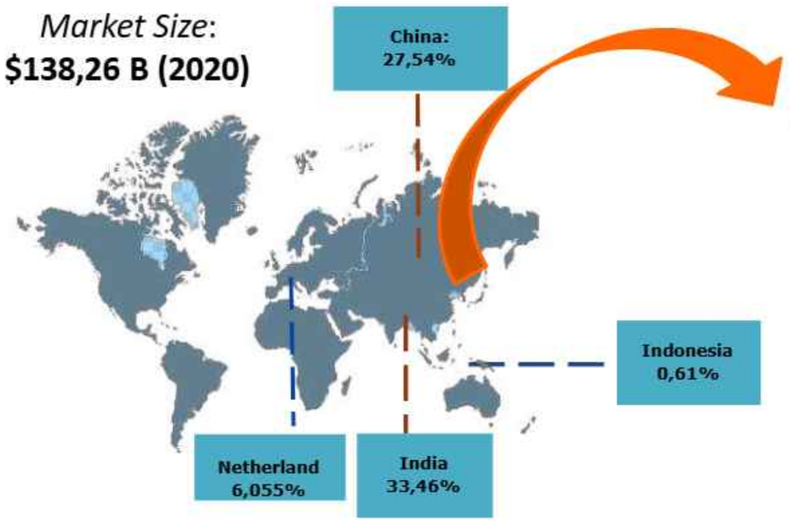
HALAL INDONESIA

STANDARD CPOTB

CERTIFIED ISO 9001:2015 COMPANY

Pasar Herbal Global dan Nasional

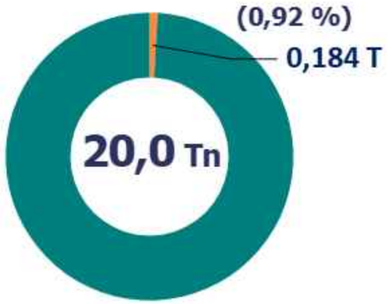
Global Herbal Market Size:
$138,26 B (2020)





Indonesia Herbal Market Size tahun 2019 sebesar **17 T** dan tumbuh menjadi **20 T** tahun 2020.

Market Size & Market Share



Holding Farmasi

Secara konsolidasi, **market size Produk Herbal** Holding BUMN Farmasi **tahun 2020** mencapai **IDR 184,3 Milyar** dengan **market share sebesar 0,92 %**.

Source: TMO Holding Farmasi GP Jamu & Kementrian Perdagangan

- Hingga 2023, terdapat 17–18 Industri Ekstrak Bahan Alam (IEBA) di Indonesia yang telah memperoleh sertifikat CPOTB dari BPOM, termasuk PT Indofarma Tbk
- IEBA berperan penting sebagai penyedia bahan baku ekstrak bagi industri obat tradisional.
- **BPOM mensyaratkan bahwa bahan baku obat bahan alam harus berasal dari IEBA yang telah bersertifikat CPOTB** sesuai dengan Peraturan BPOM No. 25 Tahun 2021 tentang CPOTB dan Permenkes No. 006 Tahun 2012.
- **Tujuan:** Menjamin mutu, keamanan, dan konsistensi bahan baku obat tradisional.

Danantara Indonesia

Strategic Partnership



Kami menawarkan kerja sama pemasaran eksklusif untuk pasar domestik dan ekspor. Kerja sama dapat dilakukan dalam bentuk:

1. Mitra bertindak sebagai pemasar dan distributor produk dengan merek dagang kami.
2. Mitra bertindak sebagai pemasar dan distributor produk dengan merek dagang Mitra dari formula yang sudah ada.

1 Exclusive / Non-Exclusive Marketing Partnership

indofarma

Tanggung Jawab :

1. Dossier holder
2. Registrasi
3. MA holder
4. Trademark holder
5. Manufacturer

Partner

Tanggung Jawab :

1. Marketing
2. Distribution

Biofarma GROUP indofarma

2 Second Brand Partnership

indofarma

Tanggung Jawab :

1. Dossier holder
2. Registrant (tba)
3. MA holder (tba)
4. Manufacturer

Partner

Tanggung Jawab :

1. Registrant (tba)
2. MA holder (tba)
3. Trademark holder
4. Marketing
5. Distribution

Toll Manufacture

Original Equipment Manufacturer (OEM)

	Indofarma	Customer
Dossier (Closed Document)	☑	
Raw Material	☑	
Packaging Material		☑
Brand Owner		☑

Original Design Manufacturer (ODM)

	Indofarma	Customer
Dossier		☑
Raw Material		☑
Packaging Material		☑
Brand Owner		☑



Terima Kasih



सत्यमेव जयते
Ministry of AYUSH
Government of India

Regulatory Framework & Guidelines for evaluating Safety & Efficacy for Innovative Traditional Medicine Products in India

Plenary - II: Ensuring the quality of innovative technology of traditional medicine products

Dr Galib
All India Institute of Ayurveda
New Delhi, India

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Government of India

Outline

- Demands for Traditional Medicine
- TM in India
- Regulatory framework
- Standards for Ayush Products
- Guidelines for evaluating Safety & Efficacy
- Integrating Traditional Knowledge with Science

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Demands for Traditional Medicine

Fig. 1.5. Growth in the number of Member States with national or state level laws or regulations for T&CM, 1999–2018

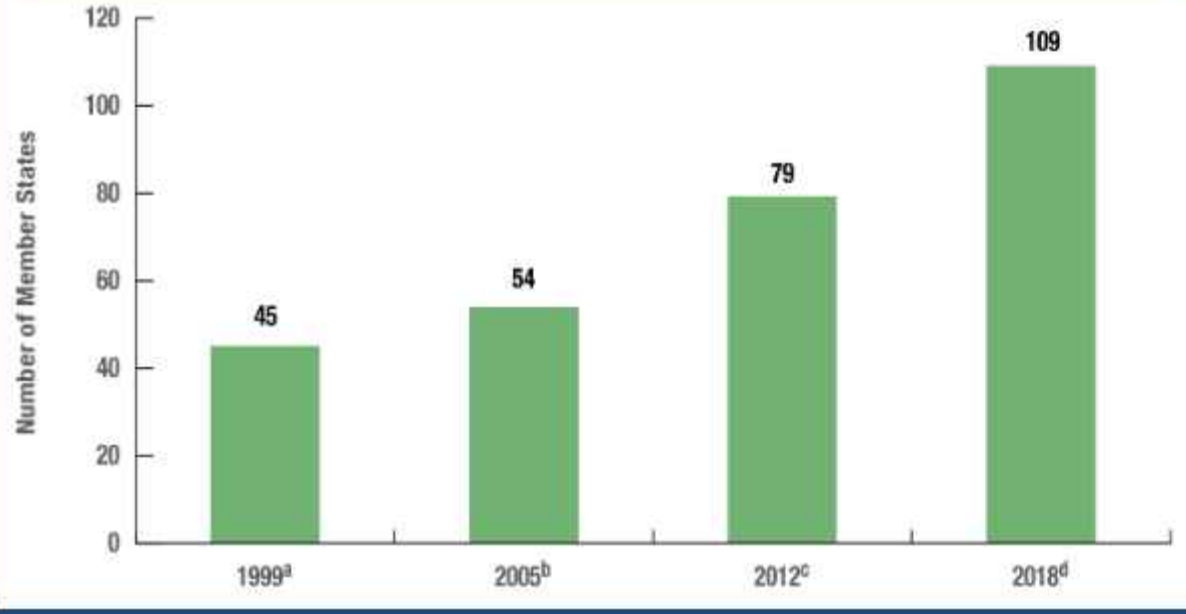
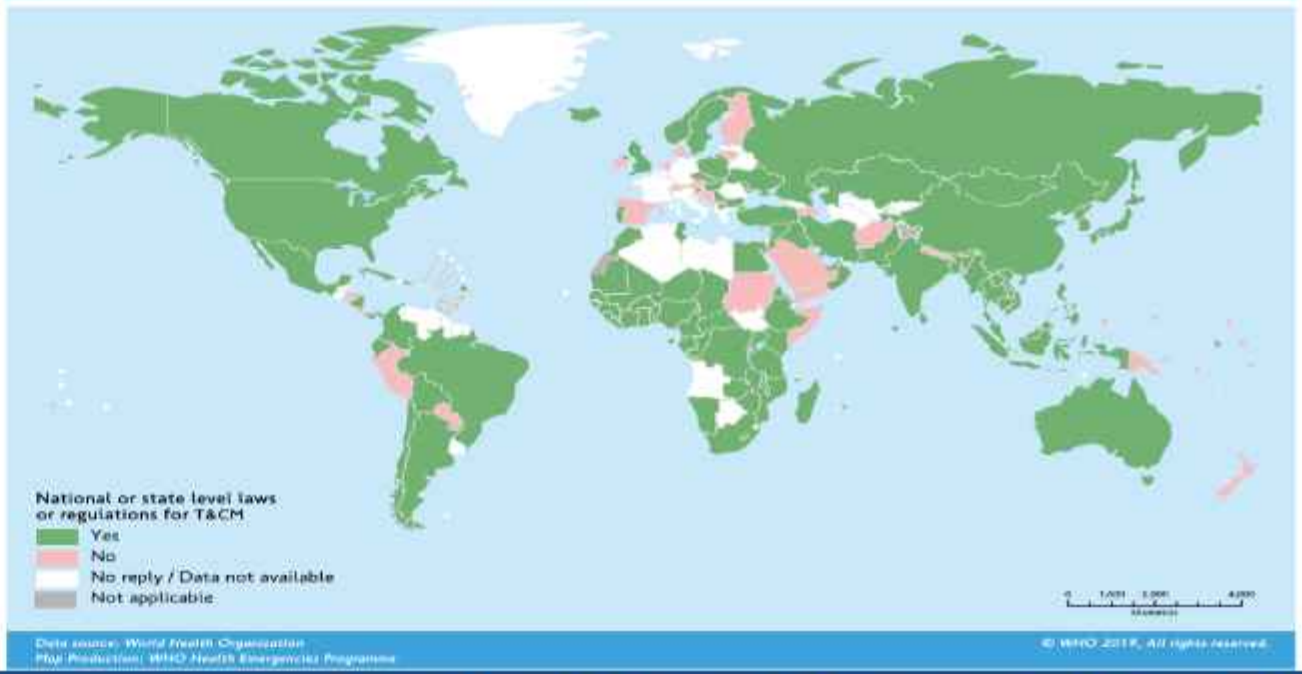


Fig. 1.7. Member States with a national or state level laws or regulations for T&CM, 2018



WHO Global Report on Traditional and Complementary Medicine 2019
https://www.who.int/publications/i/item/978924151536

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Demands for Traditional Medicine

https://apps.who.int/gb/ebwha/pdf_files/WHA78/A78_4Add1-en.pdf

apps.who.int/gb/ebwha/pdf_files/WHA78/A78_4Add1-en.pdf

Draft global traditional medicine strategy 2025–2034 1 / 16 229%

World Health Organization

Seventy-eighth World Health Assembly

Provisional agenda item 13.8

A78/4 Add.1

14 May 2025

Draft global traditional medicine strategy 2025–2034

Introduction

Traditional medicine is used by people across all six regions of WHO.[1]

Traditional medicine refers to codified or non-codified systems for healthcare and well-being, comprising practices, skills, knowledge and philosophies originating in different

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Traditional Systems of Medicine in India



A Y U S H

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Government of India

AYUSH Infrastructure

Academic

AIIA, New Delhi
ITRA, Jamnagar
NIA, Jaipur
NEIAH, Shillong
RAV, New Delhi

AYURVEDA

NIUM, Bangalore

UNANI

NIS, Chennai

SIDDHA

NIH, Kolkata

HOMEOPATHY

MDNIY, New Delhi
NIN, Pune
NEIAFMR, Pasighat

YOGA

NATUROPATHY

11 + 3 Academic Institutes

5 - Research Councils

Research

AYURVEDA — CCRAS - 30 Institutes

UNANI — CCRUM - 22 Institutes

SIDDHA — CCRS - 9 Institutes

HOMEOPATHY — CCRH - 29 Institutes

YOGA NATUROPATHY — CCRYN

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Regulation



- **Central Govt Authority**
  Makes regulatory provisions
- **State Govt Authority**
  Responsible to enforce the provisions

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Drugs & Cosmetics Act, 1940 & Rules 1945
SCOPE



To regulate:

- Pharmaceutical Drugs
- Ayurveda, Siddha and Unani Drugs (ASU Drugs)
- Homoeopathy Drugs
- Cosmetics

Sowa-Rigpa system is recognized as Ayush system in 2010 and yet to be included in under the provisions of D & C Act and Rules thereunder.

- These regulations are applicable to entire country.

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DEFINITION OF Ayush Products



- (3a) Classical/Traditional:
- (3h) Patent and Proprietary:
  - Phyto Pharmaceuticals

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Regulation
schedule T

Chapters	I - V
Sections	1 - 38
Schedules	I & II

Chapters	IV-A
Sections	33 B-O
Schedules	I & II

Part XVI to IX (Rule 151-169)
Schedules in Rules-1945
(A, B-1, E-1, T, U, V, Y)



Part in Rules 1945	Dealing with	Rules
Part XVI	Manufacture of Ayurveda Drugs. License, Loan license, Renewal etc....	151 - 160
Part XVI-A	Approval of Institutions for carrying-out tests of Ayurveda Drugs	160 A - 160 J
Part XVII	Labelling, Packing & Limit of Alcohol	161 - 161 A
Part XVIII	Government Analysts and Inspectors / Qualifications / Functions	162 - 167
Part XIX	Standards of ASU drugs	168 - 170

general recommendations
Part 1 - Schedule T
Location,
Surroundings,
Buildings,
Water,
Disposal,
Raw material,
Packaging,
Working space,
Machinery & Equipment
Health & Hygiene,
Records,
QC

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Few provisions in D&C Act 1940

- Misbranded drugs
- Adulterated drugs
- Spurious drugs
- Regulation of manufacture for sale of ASU drugs
- Penalty for manufacture, sale etc of ASU drugs in contravention of this chapter
- Power of Central Govt to make rules

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Quality Control Measures

- Pharmacopoeias are mandatory to follow
- Standards of identity, purity & quality and permissible limits of heavy metals, Aflatoxins, microbial load, pesticide residue are prescribed in Pharmacopoeias.



https://pcimh.gov.in/

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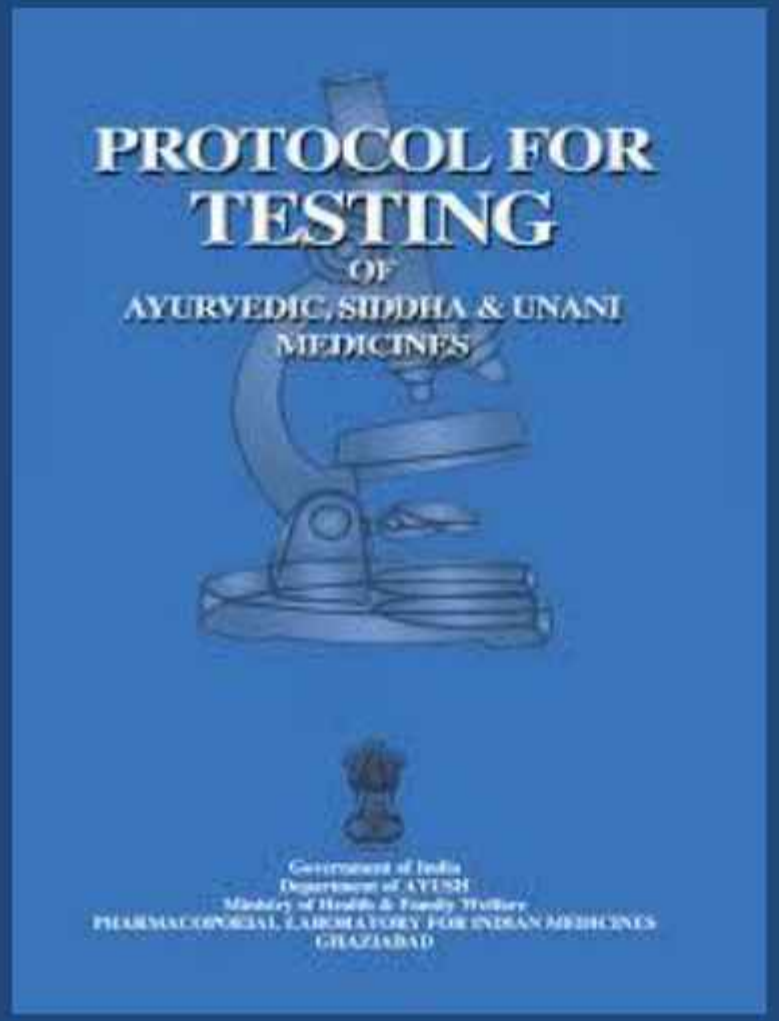
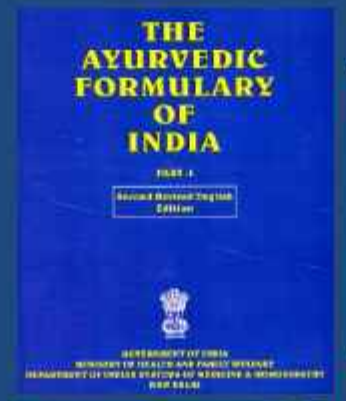
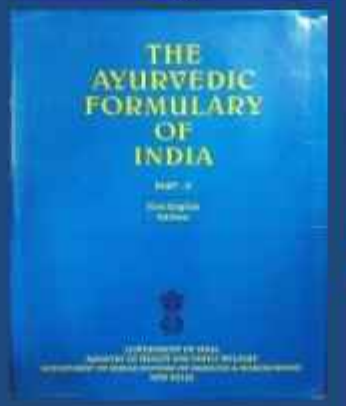
Quality Control Measures











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formularies & pharmacopoeias ..

https://pcimh.gov.in/show_content.php?lang=1&level=1&ls_id=56&lid=54

Ayurvedic Formulary of India

Volume 1	:	444
Volume 2	:	191
Volume 3	:	350
Volume 4	:	50

1035

Ayurvedic Pharmacopoeia of India Part I

Volume 1 – 1986	:	80
Volume 2 – 1999	:	78
Volume 3 – 2001	:	100
Volume 4 – 2004	:	68
Volume 5 – 2006	:	92
Volume 6 – 2008	:	101
Volume 7 – 2008	:	21
Volume 8 – 2011	:	60
Volume 9 – 2016	:	45
Volume 10 – 2022	:	20

656

Ayurvedic Pharmacopoeia of India Part II

Volume 1 – 2007	:	50
Volume 2 – 2008	:	51
Volume 3 – 2010	:	51
Volume 4 – 2017	:	50
Volume 4 – 2025	:	21

223

TLC Atlas

API Part 1, Volume 1 – 2007:	80
API Part 1, Volume 3 – 2016:	99
API Part 1, Volume 2 – 2025:	41

Macroscopy & Microscopy Atlas

API Part 1, Volume 5 – 2009:	92
API Part 1, Volume 1 – 2011:	80

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formularies & pharmacopoeias ..

https://pcimh.gov.in/show_content.php?lang=1&level=1&ls_id=56&lid=54

Unani Pharmacopoeia of India Part I

Volume 1 – 2007	:	45
Volume 2 – 2007	:	50
Volume 3 – 2007	:	53
Volume 4 – 2007	:	50
Volume 5 – 2008	:	52
Volume 6 – 2009	:	48

298

Unani Pharmacopoeia of India Part II

Volume 1 – 2009	:	50
Volume 2 – 2010	:	50
Volume 3 – 2016	:	50
Volume 4 – 2019	:	50

200

National Formulary of Unani Medicine

Part 1 – 1984	:	441
Part 2 – 1994	:	202
Part 3 – 2001	:	103
Part 4 – 2006	:	166
Part 5 – 2008	:	178
Part 6 – 2011	:	139

1229

Siddha Pharmacopoeia of India Part I

Volume 1 – 2008	:	73
Volume 2 – 2011	:	66

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Siddha Formulary of India

Part I – 1984	:	248
Part II – 2011	:	151

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Homoeopathy Pharmacopoeia of India Part I

Volume 1 – 1971	:	180
Volume 2 – 1974	:	100
Volume 3 – 1978	:	105
Volume 4 – 1984	:	107
Volume 5 – 1987	:	114
Volume 6 – 1990	:	104
Volume 7 – 1999	:	105
Volume 8 – 2000	:	101
Volume 9 – 2006	:	100
Volume 10 – 2013	:	101

1017

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Quality Certification Systems

Voluntary certification of quality of AYUSH products through Quality Council of India (QCI) scheme

- **Ayush Standard Mark:** domestic regulatory requirements.
- **Ayush Premium Mark:** international norms.



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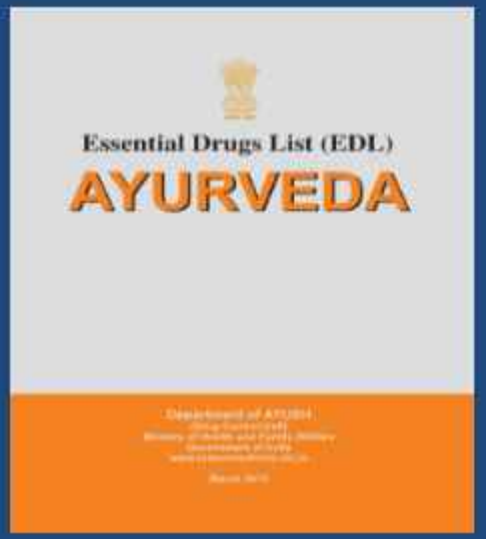
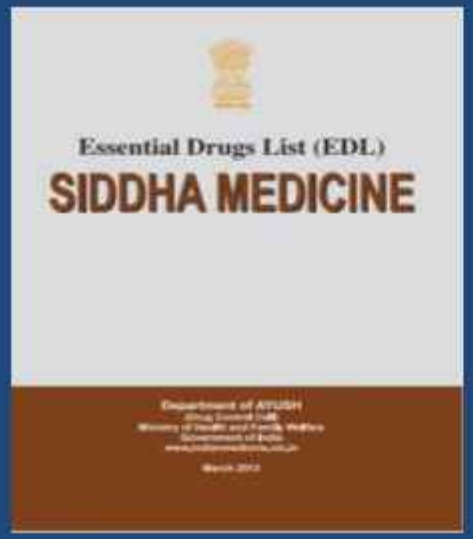
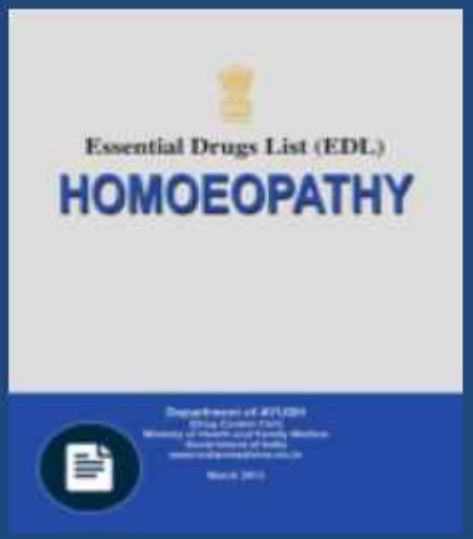
Quality Control Measures

- Essential Drug Lists is published.











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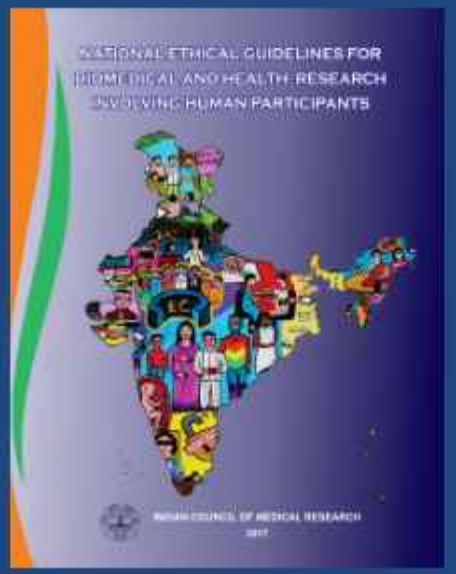
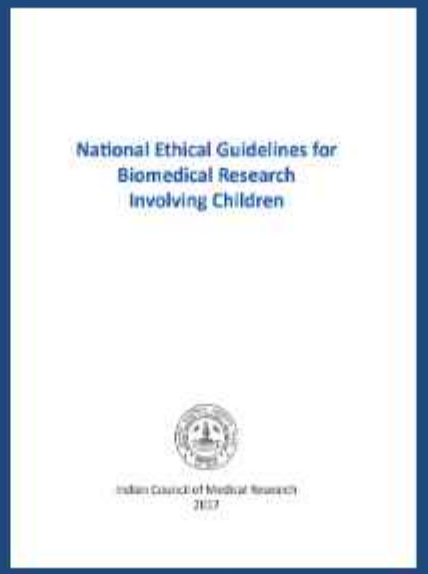
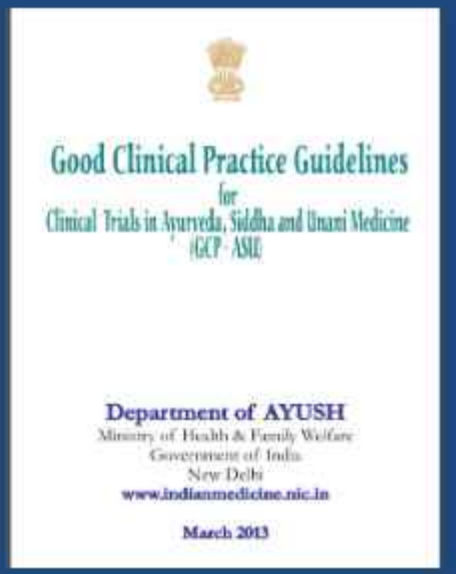
Evaluating Safety & Efficacy
ETHICS











IRB – IAEC/ IEC – DSMB

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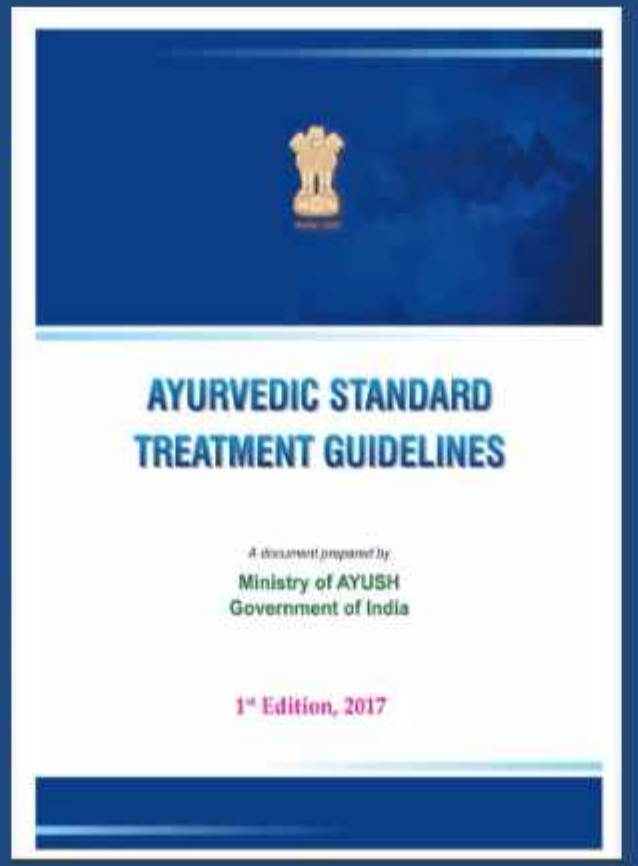
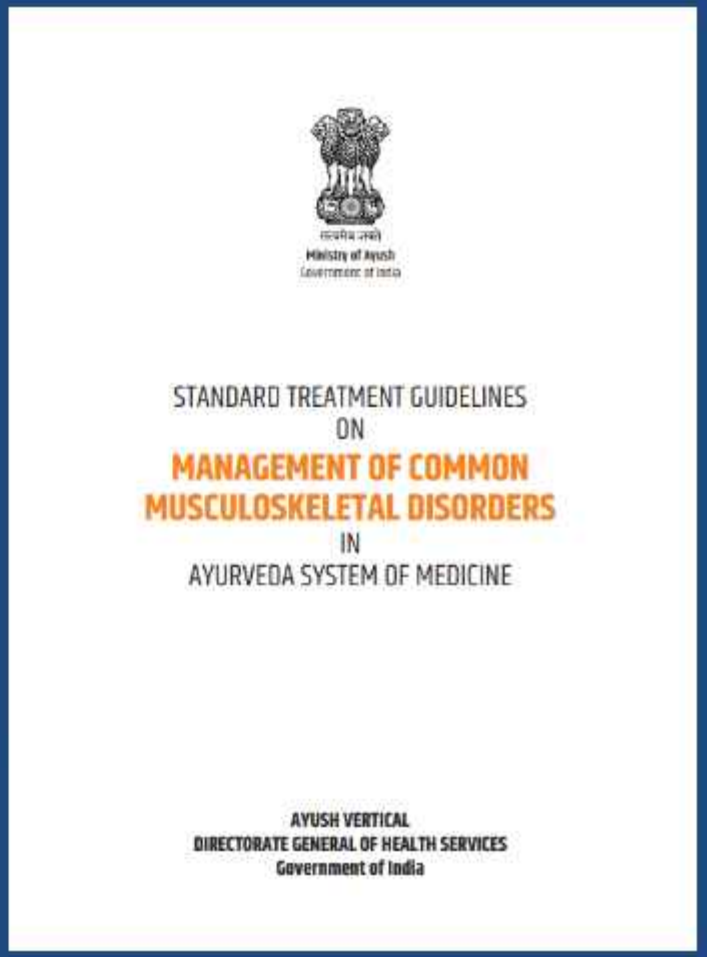
ETHICS







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Clinical trials Registry

https://ctri.nic.in/Clinicaltrials/login.php

ctri.nic.in/Clinicaltrials/login.php

CLINICAL TRIALS REGISTRY - INDIA

ICMR - National Institute of Medical Statistics



Attention: Please note that CTRI only registers trial prospectively i.e. registration befor

Kind Attention: Company trials/studies should be registered under the name of the company and not under the name of an individual account of the employee, to avoid complicated and time taking task of trial transfer if the employee leaves the organization.

Click here for providing CTRI Web Application Revamp Suggestions

SIGN IN TO CTRI

Username

Password

y2j2r

Login

Forgot Password | New Applicant

Trial Registration Data Set Download:[Pdf]

Total Number of Trials Registered in CTRI: 93289

New in CTRI

Health Condition of trial participants is now coded as per ICD-10 classification and must be chosen from the drop down list provided up to a maximum of 4 levels to the nearest disease category possible.

E-Tutorial click here

WHO ICMR DST

Clinical Trials Registry-India (CTRI)

The Clinical Trials Registry- India (CTRI), hosted at the ICMR's National Institute for Research in Digital Health and Data Science (https://nims.icmr.org.in), is a free and online public record system for

Safety & Efficacy

Herbal Medicine: TCIM Safety Monitoring

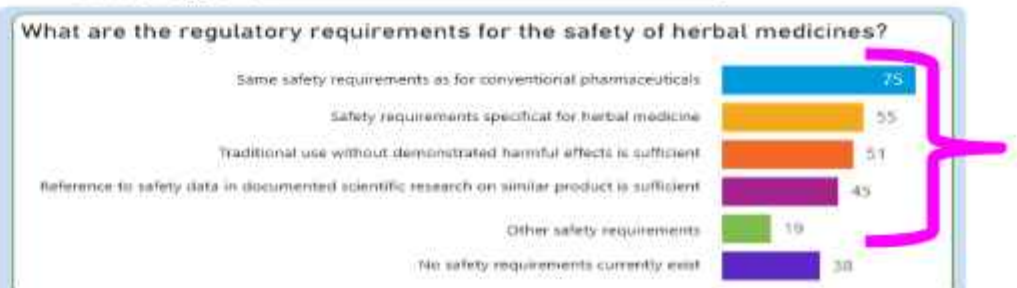
World Health Organization

Thematic Areas: Safety Monitoring | Post-market surveillance

Regions: AFRO | AMRO | EMRO | EURO | SEARO | WPRO

Survey Toggle: Show only results from the Third Global Survey

WHO Region	Count
AFRO	**47**
Algeria	1
Angola	1
Benin	1
Botswana	1
Burkina Faso	1
Burundi	1
Cabo Verde	1
Cameroon	1
Central African Republic	1
Chad	1
Comoros	1
Congo	1
Côte d'Ivoire	1
Democratic Republic of the Congo	1
Equatorial Guinea	1
Eritrea	1
Eswatini	1
Ethiopia	1
Gabon	1
Gambia	1
Ghana	1
Total	**194**



https://app.powerbi.com/view?r=eyJrIjoiZjVmZGYyZGItZjYyMS00NzBiLWJkNWYtMmQ1NGFmYWVhN2JhIiwidCI6IjQ2Y2Y3ZjgxLTljMjMtNGExMC1hOTMyLTRjZDU3Yjg2NzkxZSJ9

Hover over here for additional disclaimers about Serbia, Montenegro, and South Sudan

WHO Third Global Survey on Traditional, Complementary and Integrative Medicine

Powered by: BAI + ANALYTICS

Microsoft Power BI 8 of 16

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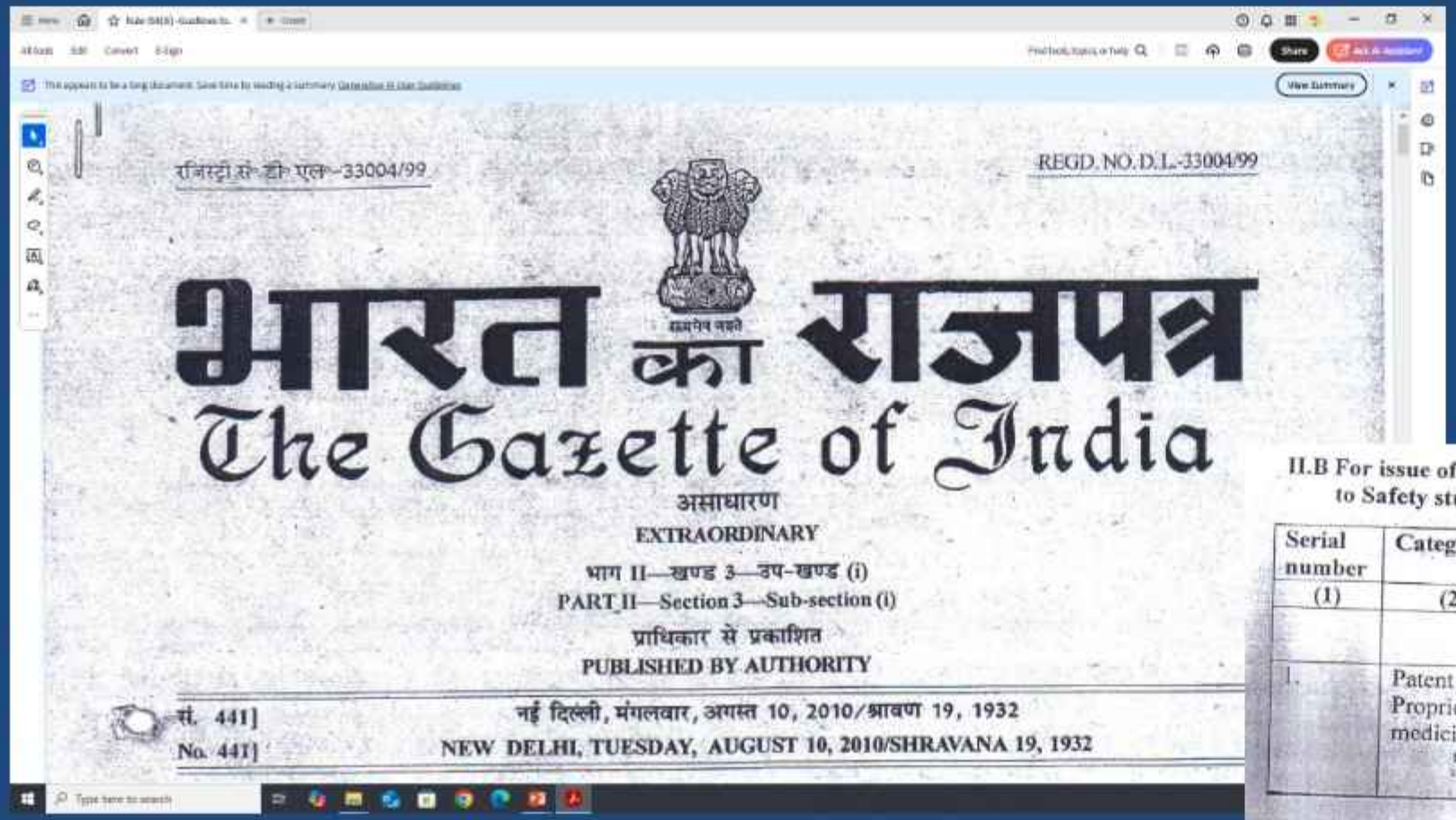
License Requirements
158-B



रजिस्ट्री सं० डी० एल०-33004/99

REGD. NO. D. L.-33004/99

भारत का राजपत्र

The Gazette of India

असाधारण

EXTRAORDINARY

भाग II—खण्ड 3—उप-खण्ड (i)

PART II—Section 3—Sub-section (i)

प्राधिकार से प्रकाशित

PUBLISHED BY AUTHORITY

सं. 441] नई दिल्ली, मंगलवार, अगस्त 10, 2010/श्रावण 19, 1932

No. 441] NEW DELHI, TUESDAY, AUGUST 10, 2010/SHRAVANA 19, 1932

II.B For issue of license with respect to Patent or Proprietary medicine. The condition relating to Safety studies and experience or evidence of effectiveness shall be specified as follows:-

Serial number	Category	Ingredient (S)	Indication (s)	Safety study	Experience/ Evidence of Effectiveness	
(1)	(2)	(3)	(4)	(5)	(6)	
					Published Literature	Proof of Effectiveness
1.	Patent or Proprietary medicine	As per text	Textual rationale	Not Required	Of Ingredients	* Pilot study as per relevant protocol for Ayurveda, Siddha and Unani drugs.

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Pharmacovigilance for Ayush Products

https://www.ayushsuraksha.com/
https://suraksha.ayush.gov.in/about

Programme Management Unit (PMU) → Ministry of Ayush

National Pharmacovigilance Coordination Centre (NPvCC) → AIIA, New Delhi

5 Intermediary Pharmacovigilance Centres (IPvC)

- NIA, Jaipur
- ITRA, Jamnagar — 52
- NIUM, Bangalore — 15
- NIS, Chennai — 15
- NIH, Kolkata — 16

Peripheral Pharmacovigilance Centres (PPvC) — 98+1



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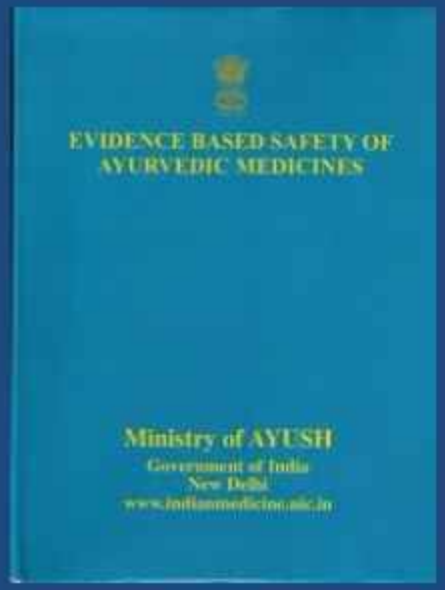
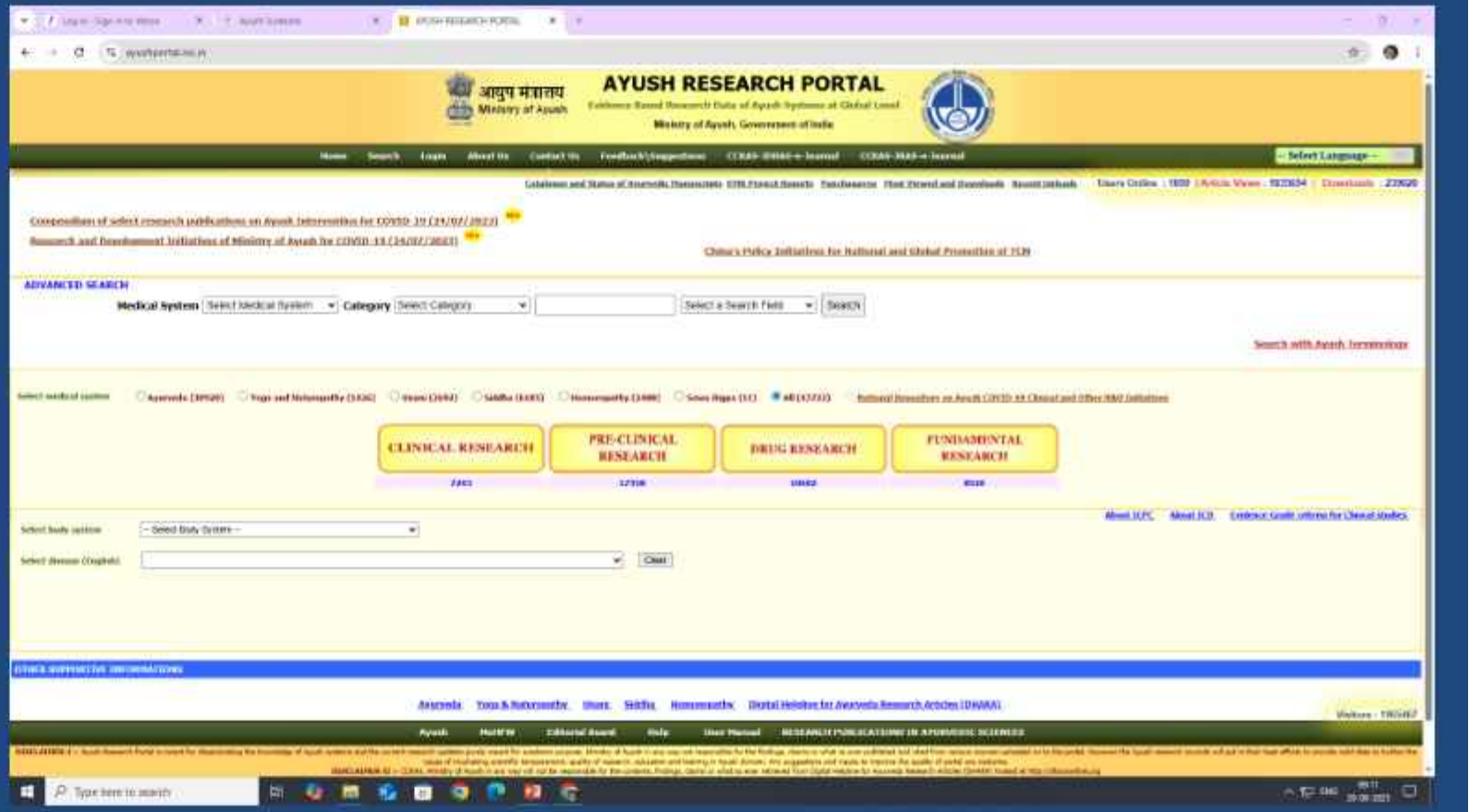
Publications on Safety

https://ayushportal.nic.in/







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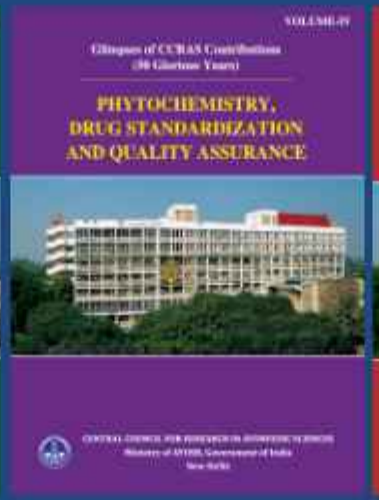
Publications on Safety

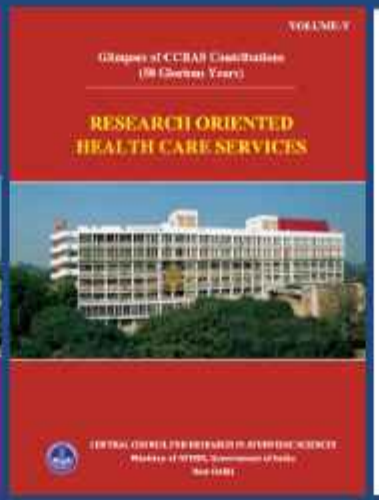
Glimpses of 50 Glorious Years















http://www.ccras.nic.in/content/glimpses-ccras-contributions-50-glorious-years

Ministry of AYUSH
Government of India

Integrating TM

- The Ministry of Ayush (MoA) and the Department of Science and Technology (DST)
- Ayurtech for Integrative Precision Health and Medicine – IIT
- Ayurgenomics

- Council for Scientific and Industrial Research
- Indian Council of Agricultural Research
- Department of Biotechnology
- Indian Council for Medical Research
- Ministry of Defence

Ministry of AYUSH
Government of India

The International Organization for Standardization (ISO)
has officially formed a dedicated
Ayurveda and Yoga Subcommittee
under ISO/TC 249 (Traditional Medicine)

ISO/TC 249/SC 2

Ayurveda and Yoga

मानकः पथप्रदर्शकः



सत्यमेव जयते

Ministry of AYUSH

Government of India

THANK YOU

WHO'S QUALITY ASSURANCE EFFORT FOR TCIM PRODUCTS



Dr Eileen Eunkyung Han

Technical Officer, HPS/DHS/WPRO

WHO Global Core Indicator Framework for Traditional and Complementary Medicine (T&CM), 2022

System Determinants | **Service Delivery** | **Health Objectives**

Structures

Governance

T&CM governance

- Existence of a national policy, strategy, or plan on T&CM[1,2]

Financing

Funding and allocation

- Total current expenditure on T&CM (per capita, % GDP)[1,2,3]
- Total expenditures on T&CM as % of total current health expenditures[1,2]

Purchasing and payment systems

- T&CM services included in the essential health service package[1,2]
- T&CM services reimbursed by health insurance programs[1,2]

Inputs

Physical infrastructure

T&CM facility density

- Nr and density of health facilities offering T&CM[1,2,3]

Health workforce

T&CM health workforce availability

- Nr and density of registered formally trained T&CM practitioners[1,2,3]

Accreditation mechanism for T&CM education and training institutions

- Existence of a national mechanism to ensure quality of T&CM education and training[1,2]

Continuing professional development

- Existence of a continuing professional development programme for T&CM practitioners[1,2]

Information and research

T&CM indicator monitoring

- Nr of T&CM indicators included into national health information system[1]

T&CM research

- Existence of a national body to oversee T&CM-related researches[1,2]
- Total government budget allocated for T&CM research[1,2,3]

T&CM products

Availability of T&CM products

- Nr of T&CM products included in the national essential medicines list[1,2,3]

Manufacturing of T&CM products

- T&CM products are regulated by national medicines regulatory authorities[1,2,3]
- Proportion of licensed T&CM manufacturers that meet good manufacturing practice (GMP) standards[1,2,3]
- Existence of a reference laboratory for testing of T&CM products[1,2]

T&CM safety monitoring

- Existence of a national adverse event reporting system for T&CM products[1,2]

Advertising of T&CM products

- Existence of a regulatory mechanism to oversee advertising and labelling of T&CM products[1,2]

T&CM resource protection and promotion of sustainable use

- Existence and continuing development of a mechanism and database to protect traditional knowledge and associated genetic resources[1,2]
- Existence of conservation and cultivation programme to protect biodiversity and endangered species of medicinal plants and non-plants[1,2]

Processes

Models of care

Integrated care

- Protocol or guidelines for referral between T&CM and allopathic medical services[1,2]
- Nr and density of health facilities providing both T&CM and allopathic medicine services[1,2,3]

Community linkages

- Existence of a communication mechanism to provide public information related to T&CM[1,2]

Improving quality

- Existence of T&CM practice guidelines[1,2,3]
- Percentage of health facilities offering T&CM that implement or receive supportive supervision[1,3]

Outputs

Access and availability

Accessibility of T&CM services

- Percentage of population who report problems in accessing T&CM services when they have a healthcare need[1]

Utilization of T&CM services

- Nr of outpatient department visits for T&CM services per capita[1,2,3]
- T&CM outpatient department visits as a percentage of all outpatient department visits[1,2,3]
- Top 10 health problems as reasons for seeking T&CM services[1,2,3]
- Top 5 T&CM modalities[2]

Quality care

Safety

- Nr of reported T&CM-related adverse events for T&CM products[1,3]

Continuity of care

- Percentage of patients who report having a regular T&CM provider[1]

Integrated care

- Percentage of patients on pain medications with adjunctive traditional and complementary medicine services to assist pain relief[3]

People-centered care

- Percentage of patients who report being involved in decisions about their T&CM care and treatment[1]

Outcomes & Impact

Service coverage

- Percentage of population that use T&CM services[1,2,3]

Responsiveness

- Percentage of patients satisfied with T&CM services and outcomes[1,2,3]

World Health Organization

35 Core Indicators

Legend: Aligned to

1 WHO SEARO indicators
2 WHO WPRO indicators
3 WHO HQ indicators

World Health Organization

Seventy-eighth World Health Assembly

Agenda item 13.8

WHA78(14)

27 May 2025

WHO traditional medicine strategy: 2025–2034

The Seventy-eighth World Health Assembly, having considered the report by the Director-General,[1]

Decided:

(1) to adopt the WHO traditional medicine strategy: 2025–2034;

(2) to request the Director-General to report on the progress made in the implementation of the WHO traditional medicine strategy: 2025–2034 to the Eighty-third World Health Assembly in 2030 and the Eighty-seventh World Health Assembly in 2034.

Seventh plenary meeting, 27 May 2025
A78/VR/7

GLOBAL TM STRATEGY 2025 – 2034

Strategic Objective 1: Strengthen the Evidence Base for TCIM



Facilitate High-Quality Research

Establish national research agendas, conduct scientific studies, and studies, and allocate resources for TCIM.



Explore Research Approaches

Utilize digital technologies and innovative methods for TCIM TCIM research, including non-codified traditional medicine. medicine.

Further investment in TCIM research is needed to leverage its potential in improving health and well-being.

Strategic Objective 2: Support the provision of safe and safe and effective TCIM through **appropriate regulatory regulatory mechanisms**

Direction 1

Regulatory Mechanisms for Products

Establish norms and standards for TCIM products, ensuring ensuring safety, quality, and efficacy.

Direction 2

Regulatory Mechanisms for Practices

Adapt frameworks for diverse TCIM practices and practitioners, prioritizing patient safety.

Appropriate regulatory mechanisms are crucial to safeguard the public from unsafe or substandard TCIM products and services.

Strategic Objective 3: Integrate Safe and Effective TCIM into Health Systems



Incorporate into Frameworks

Include TCIM in national and sub-national health frameworks and frameworks and policies to permit integration at all levels. levels.



Facilitate Across Care Continuum

Integrate TCIM services across health promotion, disease prevention, treatment, and palliative care.

Integration of safe and effective TCIM into health systems is key to reorienting health services, with primary healthcare as a natural entry point. natural entry point.

Strategic Objective 4: Optimize Cross-Sector Value of Value of TCIM and empower communities

Include TCIM in Cross-Sector Policies

Integrate TCIM into policies for health, well-being, One Health, Health, and Sustainable Development Goals.

Promote Approaches to Protect Traditional Knowledge

Develop inclusive approaches for protection, access, and fair **sharing of benefits** from traditional medical knowledge.

TCIM's unique value addresses challenges across health, culture, environment, and socio-economic factors.

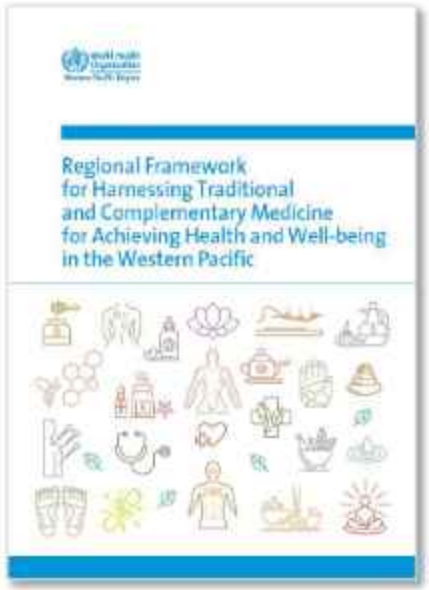


The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
Data Source: WHO | Map Production: WHO WPRO DSI | Map Date: 18 June 2025 | © WHO 2025, All rights reserved.

World Health Organization
Western Pacific Region

REGIONAL FRAMEWORK FOR HARNESSING THE T&CM IN THE WESTERN PACIFIC

World Health Organization
Western Pacific Region



1. Promote and define T&CM in national policies

2. Strengthen context-specific mechanisms to ensure quality and safety

3. Improve coverage and equitable access to T&CM services

4. Promote documentation, research and innovation for T&CM services

COMPONENTS OF REGULATORY SYSTEM

- Legal Framework
- Structure of the Regulatory Authority
- Core regulatory functions (MA, VL, MC, LI, RI, LT, CT, LR)
- GXPs and quality management system (QMS)

COMPONENTS AND CHALLENGES OF TCIM PRODUCT REGULATION (1)

National Regulatory System	
Pre-market	Post-market
Clinical Trial Oversight	
Licensing Premises	
Registration and marketing authorization	Market surveillance and control
Laboratory access and testing	
Inspection and enforcement	
Vigilance	

Herbal Medicine: Good Manufacturing Practices

Thematic Areas

Manufacturing | Manufacturing Quality/Regulation | Compliance | Lab Testing

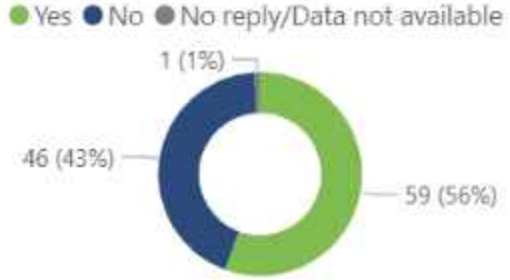
Regions

AFRO | AMRO | EMRO | EURO | SEARO | WPRO

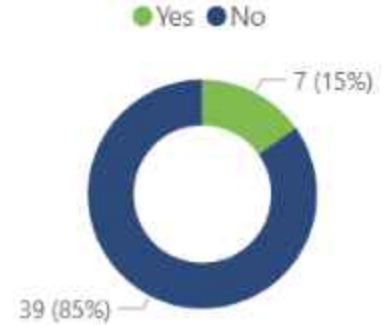
Survey Toggle: Show only results from the Third Global Survey

WHO Region	Count
Maldives	1
Myanmar	1
Nepal	1
Sri Lanka	1
Thailand	1
Timor-Leste	1
WPRO	**16**
Australia	1
China	1
Japan	1
Lao People's Democratic Republic	1
Malaysia	1
Mongolia	1
New Zealand	2
Papua New Guinea	1
Philippines	1
Republic of Korea	1
Samoa	1
Singapore	1
Solomon Islands	1
Vanuatu	1
Viet Nam	1
Total	**106**

Are good manufacturing practices (GMP) available for herbal medicines in your country?



If no, are GMP for herbal medicines being established?



If yes, is it aligned with WHO guidelines?



If yes, what are the number and percentage of licensed TCIM manufacturers that meet the domestic GMP requirements?



Hover over here for additional disclaimers about Serbia, Montenegro, and South Sudan

WHO Third Global Survey on Traditional, Complementary and Integrative Medicine

Powered by: KAI ANALYTICS

Herbal Medicine: Good Manufacturing Practices

Thematic Areas

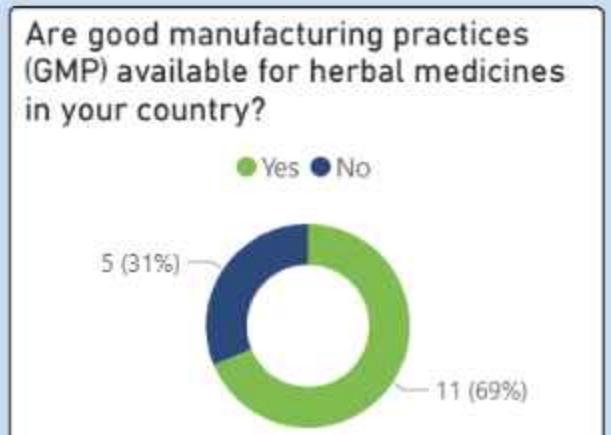
Manufacturing | Manufacturing Quality/Regulation | Compliance | Lab Testing

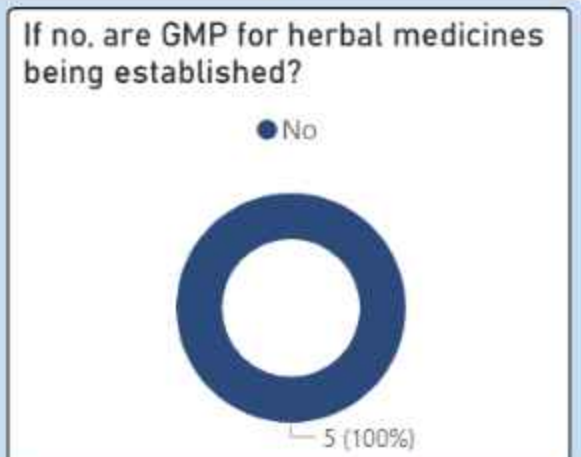
Regions

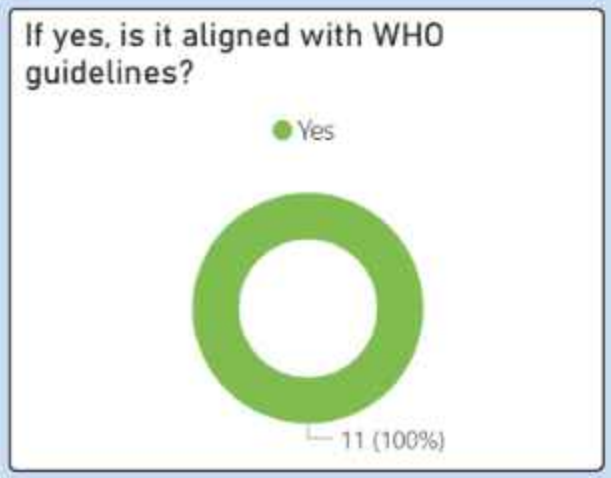
AFRO | AMRO | EMRO | EURO | SEARO | WPRO

Survey Toggle: Show only results from the Third Global Survey

WHO Region	Count
WPRO	**16**
Australia	1
China	1
Japan	1
Lao People's Democratic Republic	1
Malaysia	1
Mongolia	1
New Zealand	2
Papua New Guinea	1
Philippines	1
Republic of Korea	1
Samoa	1
Singapore	1
Solomon Islands	1
Vanuatu	1
Viet Nam	1
Total	**16**









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World Health Organization

Herbal Medicine: Manufacturing Regulation/Quality

Thematic Areas

sting

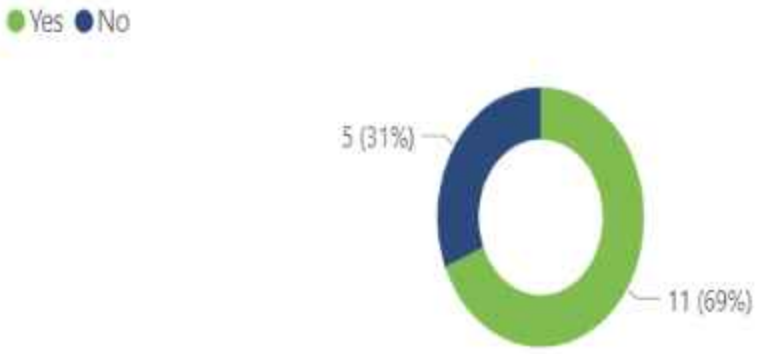
Regions

AFRO | AMRO | EMRO | EURO | SEARO | WPRO

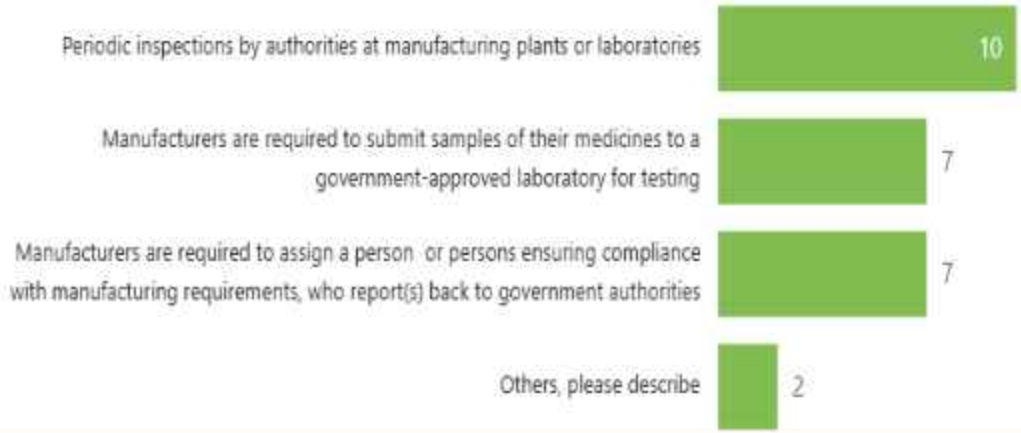
Survey Toggle

Show only results from the Third Global Survey

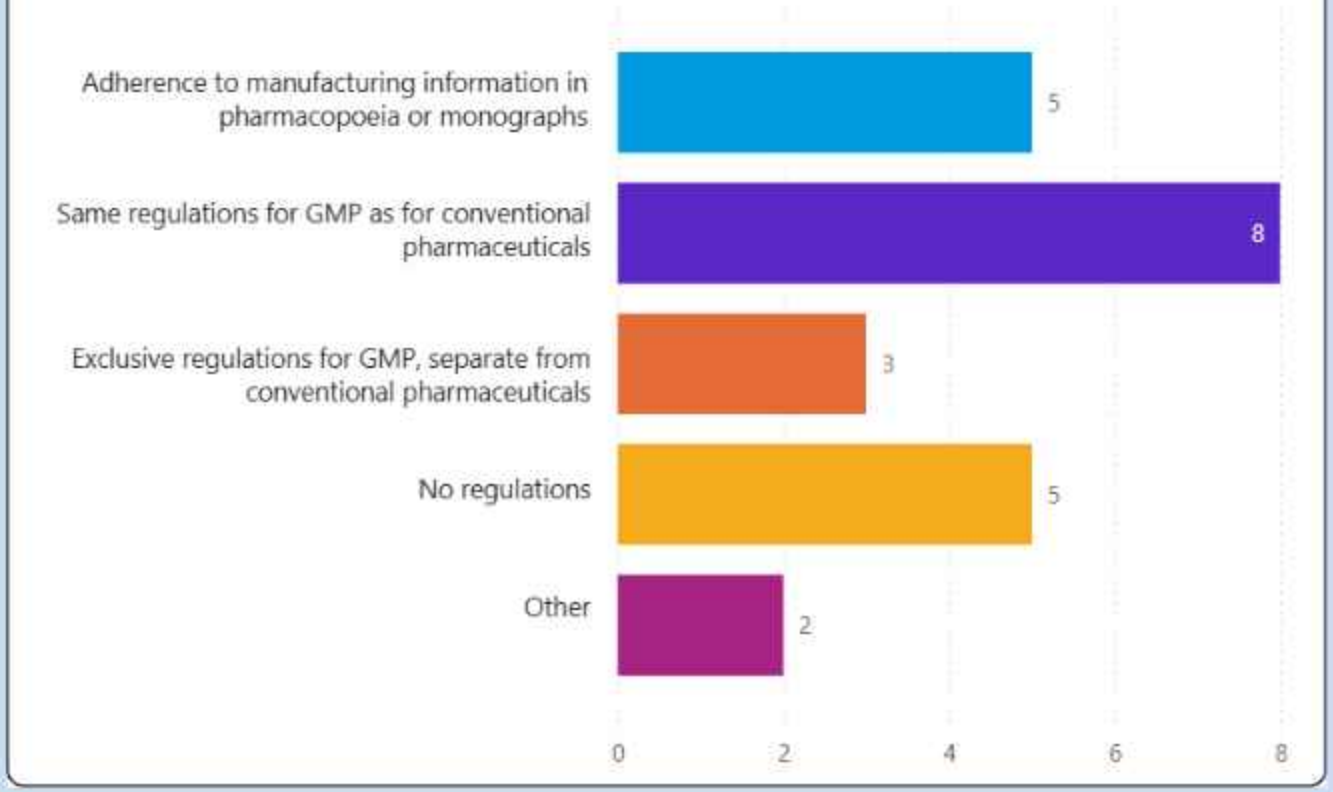
Are mechanisms in place to ensure compliance with these or other manufacturing requirements?



How is compliance ensured? Check all that apply.



What regulations apply to the manufacture of herbal medicines to ensure their quality? Check all that apply.



COMPONENTS AND CHALLENGES OF TCIM PRODUCT REGULATION (2)

Regulation and quality assurance system



ROLE OF WHO SECRETARIAT: ENHANCING REGULATORY MECHANISM OF TCIM PRODUCTS

- Develop standards for herbal medicines in the form of the International Herbal Pharmacopoeia and other such documents.
- Develop, update and disseminate guidelines, technical documents and tools to support TCIM regulatory mechanisms, including pharmacovigilance.
- Develop standardized terminologies and an international classification of TCIM products.
- Enhance the WHO International Regulatory Cooperation on Herbal Medicines network.

WHO GUIDELINES

- WHO Guidelines on **good agricultural and collection practices (GACP)** for medicinal plants
- *WHO guidelines on **good herbal processing practices (GHPP)** for herbal medicines*
- WHO guidelines on **good manufacturing practices (GMP)** for herbal medicines
- WHO guidelines on **safety monitoring of herbal medicines** in pharmacovigilance systems
- WHO **monographs** on selected medicinal plants, Volume 1-4
- WHO guidelines on assessing quality of herbal medicines with **reference to contaminants and residues**
- WHO guidelines for **selecting marker substances of herbal origin** for quality control of herbal medicines

https://www.who.int/publications/m/item/trs1003-annex1
WHO guidelines on good manufacturing practices (GMP) for herbal medicines
https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/production/trs1010-annex1-herbal-processing.pdf?sfvrsn=80b60ae5_0

DEVELOPMENT OF AN INTERNATIONAL HERBAL PHARMACOPOEIA (IHP)

- Member States emphasized the need for establishing a WHO International Herbal Pharmacopoeia (IHP) to ensure the quality of traditional medicine raw materials and the resulting products.
- The IHP, like the WHO International Pharmacopoeia, is designed to provide international recommendations and is expected to be particularly valuable for countries where established standards are lacking.
- The shared goal between WHO and its Member States is **to harmonize quality standards while respecting the unique herbal traditions of each country**. Structurally, experts including representatives from existing pharmacopoeias contributed their expertise to help establish a unified international standard.
- As the next step, an expert group and technical task force will be convened under the Strategic Technical Advisory Group for TCIM to support the development of the WHO IHP.

https://www.who.int/news/item/26-11-2024-towards-global-harmonization--who-s-international-herbal-pharmacopoeia-meeting-in-hong-kong-sar#:~:text=The%20WHO%20IHP%20is%20envisioned,%2C%20consequently%2C%20traditional%20medicine%20products.

WPRO'S LABORATORY CAPACITY BUILDING FOR QUALITY CONTROL TESTING OF TCIM PRODUCTS

- Contextualized to Member States' needs
- Consists of hands-on training, theoretical training, and facilitated group discussions

TOPICS COVERED IN THE TRAINING (2025)

The training covered the following topics of **Active Ingredients and Contaminants:**

- **Day 1:** Determination of moisture content in medicinal herbs (dry weight)
- **Day 2:** Analysis of heavy metals in herbal materials (total heavy metals, Pb, As, Cd, Hg)
- **Day 3:** Detection of pesticide residues in medicinal herbs
- **Day 4:** Detection of mycotoxins (aflatoxin) in herbal medicinal herbs
- **Day 5:** Quantification of active ingredients in medicinal herbs

WHO EFFORTS IN REGULATORY HARMONIZATION

To reduce gaps in safety and quality due to regulatory differences

To strengthen regulatory capacity in resource-limited settings

To expand access to medicines to end-users and tackle public health issues

ASEAN GUIDELINES AND REGIONAL COLLABORATION

Association of South East Asian Nations (ASEAN)

ANNEX VIII - ASEAN GUIDELINES ON GOOD MANUFACTURING PRACTICE FOR TRADITIONAL MEDICINES

https://asean.org/wp-content/uploads/2017/09/ASEAN-Guideline-on-GMP-for-TM-Appendices-2-june-2015-with-disclaimer....pdf



INTERNATIONAL REGULATORY COOPERATION FOR HERBAL MEDICINES (IRCH)

World Health Organization

Health Topics | Countries | Newsroom | Emergencies | Data

Home / Initiatives / International Regulatory Cooperation for Herbal Medicines (IRCH)

International Regulatory Cooperation for Herbal Medicines (IRCH)

International Regulatory Cooperation for Herbal Medicines (IRCH), established in 2006, is a global network of regulatory authorities responsible for regulation of herbal medicines. Its mission is to collaborate and share the best practices to help WHO in its recommendations to the members on improving the regulation of herbal medicines as well as raise awareness regarding their safe use in health and wellbeing.

Membership is open to any national regulatory authority responsible for the regulation of herbal medicines and regional/sub-regional bodies responsible for the regulation of herbal medicine.

FORUM FOR HARMONIZATION OF THE HERBAL MEDICINES (FHH)

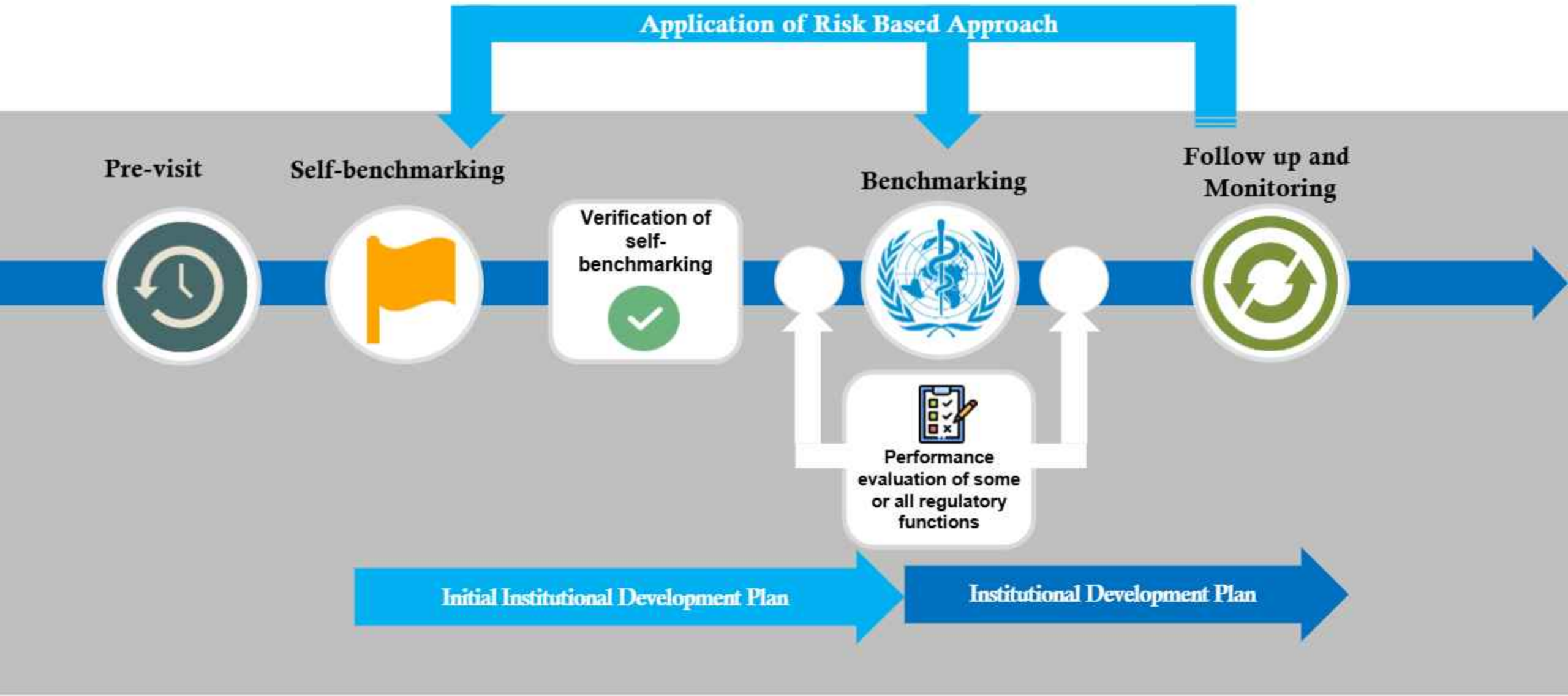
- FHH facilitates the exchange of regulatory information on herbal medicine standards, analytical methods, and quality assessment technologies, promoting harmonized quality and safety standards to enhance global public health.
- **Sub-committies**

- Nomenclature and Standardization (Pharmacopeia, Testing Methods, Reference Standards)
- Quality Assurance
- Pharmacovigilance and Adverse Reaction Reporting

- **Work scope: Pharmacopeia, FHH Atlas, Reference Material of Medicinal Plant Material**

- http://fhh.or.kr/

WHO BENCHMARKING PROCESS



PROPOSED ACTIONS TO STRENGTHEN TCIM REGULATORY SYSTEM

- For Member States with WHO-GBT experience



Review the existing Self-Benchmarking Report in critical regulatory functions



Identify common or TCIM-specific regulatory gaps



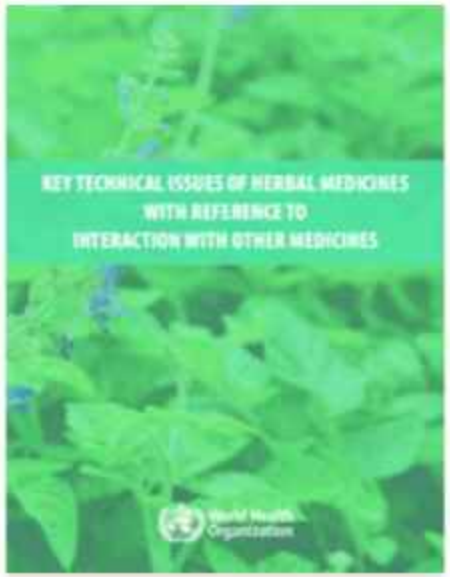
Establish common and TCIM-specific IDPs, priorities, and time-bound action plan



Monitor the progress regularly

Key technical issues of herbal medicines with reference to interaction with other medicines

19 May 2021 | Technical document



Download (1.6 MB)

Overview

This document provides information on the critical technical issues related to interactions between herbal medicines and other medicines for health-care professionals, regulators, researchers, pharmacovigilance centres, manufacturers and consumers. The intention of this document is to provide as much concise information as possible, and to give direction and guidance on capitalizing resources to support informed decision-making and maximize the safe concurrent use of herbal medicines and other medicines.

The concepts of beneficial and harmful herb-drug interaction (HDI)s are introduced, with documented examples from the published literature. Types of HDI and their mechanisms are outlined, and the relevance of in vitro, general screening and in vivo tests is included. Challenges faced in evaluating and monitoring HDIs, data collection, assessment and dissemination of information are briefly discussed. The education and training of health professionals and consumers are addressed, together with potential research strategies for further investigation of the mechanisms, incidence, monitoring and management of HDIs.

Key technical issues of herbal medicines with reference to interaction with other medicines
https://www.who.int/publications/i/item/9789240019140

BIODIVERSITY

- In line with the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) and other applicable international conventions and national legislation

THANK YOU

ehan@who.int