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Phyto-pharmacological review on bioavailability enhancer [Trikatu]

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Abstract
Trikatu is a blend of Ayurvedic herbs, including dried fruits of *Piper nigrum* (Maricha), *Piper longum* (Peepli), and dried rhizomes of *Zingiber officinale* (Sunthi). Trikatu balances the three doshas—vata, pitta, and kapha—calming Vata and Kapha while raising Pitta. Its spicy taste, hot potency, and digestive effects enhance the bioavailability of phytoconstituents and drugs. This concept originates in Ayurveda and has been used in the medical system for millennia. When Trikatu is provided in small dosages with the main medicine as bio-enhancers it increases the bioavailability or biological activity of the drug. Modern studies confirm immunomodulatory, antiviral, and anti-inflammatory properties, making it valuable in medicinal formulations. Information from authentic Ayurvedic texts and related research articles ensures the authenticity of Trikatu.

Keywords: *Piper longum*, *Piper nigrum*, *Zingiber officinale*, Trikatu

Introduction
Over the last century, chemical and pharmacological investigations have been conducted to understand plant extracts' composition better and validate them for traditional uses. Ayurveda's contribution to drug discovery through reverse pharmacology has dramatically reduced development costs. Recent advancements focus on improving drug bioavailability and transforming administration methods [1]. Despite the in-vitro potential, lipid solubility is the challenges that lead to poor bioavailability for many herbal drugs. Emerging delivery systems like liposomes and lipid-based approaches offer hope in overcoming these issues by facilitating better absorption through lipid-rich biomembranes. Notably, phospholipid-based drug delivery systems ensure efficient delivery of active herbal compounds for optimal efficacy [2]. There is a medical interest in improving the bioavailability of costly, dangerous, and poorly absorbed medications, especially those requiring prolonged use. Poorly bioavailable drugs may remain sub-therapeutic unless administered at high doses, leading to significant adverse effects. Factors contributing to poor oral bioavailability include low solubility, intestinal barriers, and drug degradation in the gastrointestinal system. Addressing this issue requires compounds that enhance bioavailability when combined with other medications without altering their therapeutic effects. Bioenhancers, often derived from natural plant substances, contribute to the improved effectiveness of poorly bioavailable medications without causing synergistic effects [3].

The concept of enhancing bioavailability originated in Ayurveda and has been utilized for centuries in this traditional system of medicine. Ayurveda employs bio-enhancers like *Piper longum*, *Zingiber officinale*, and *Piper nigrum* to boost the biological activity of drugs when co-administered with the main drug at low doses. This approach reduces the therapeutic dose of the primary drug, minimizing the risk of toxicity and side effects while improving efficacy. Ayurvedic methods such as Shodhana, and properties like Yogavahi and Rasayana, contribute to bio-enhancement, reducing treatment costs and benefiting the global economy [4]. Utilizing bio-enhancers is an interesting approach for increasing the therapeutic effect of orally delivered medications and improving formulations. Bio-enhancers, which come from traditional Indian medicine, offer a unique technique that could potentially lower drug prices, reduce toxicity, and decrease adverse consequences. Ongoing research on expensive, poisonous, or poorly bioavailable medications emphasizes the significance of finding an optimal bioenhancer—one that is safe, effective, cost-effective, easily accessible, and non-addictive [5]. In Ayurvedic medicine, incorporating bio-enhancers can potentially reduce treatment costs by enhancing drug bioavailability. The present global emphasis lies on ways that lower drug dosage, making pharmaceuticals more inexpensive for a wider demography,

including individuals with financial constraints [6]. In Ayurveda, the term for bio enhancement is “Yogvahi”. It refers to the collaborative influence of mixing various biomolecules to increase a drug's effectiveness. Ayurvedic polyherbal formulations leverage Yogvahi to enhance drug bioavailability, tissue distribution, and overall efficacy, particularly for drugs with limited oral bioavailability. “Anupaan” is the simultaneous eating of food and a medicament to increase its effectiveness, for example by taking "Amrit Dhara" drops over sugar for gastrointestinal disorders. Common “Yogavahi” includes- Trikatu (long pepper, black pepper, ginger), sesame/til, gold/swarn bhasam, heerak bhasm, and cow urine distillate [7].

Method of preparation

To make Trikatu, an Ayurvedic combination, gather equal amounts of three pungent herbs dried fruits of *Piper longum* (Long Pepper), *Piper nigrum* (Black Pepper), and the dried rhizomes of *Zingiber officinale* (Ginger). Carefully dry these herbs and grind them individually into fine powders using a mortar-pestle, or grinder. Once the individual powders are obtained, ensure equal proportions by precise weighing and thoroughly blending them [8]. The resulting mixture is then sifted through a fine mesh, typically employing a sieve with a mesh size of 80. This sieving method produces an extra-fine powder, which has been shown to have higher therapeutic potential due to its increased surface area. Store the finely powdered Trikatu in moisture-free, airtight containers to protect the efficacy and prevent degradation. This Ayurvedic formulation is valued for its possible medicinal effects, which are due to the synergistic qualities of the three spicy herbs [9].

Dosage

Powders, which are finely separated medications or chemicals in dry form, have a variety of internal and external applications, particularly for patients who struggle with solid forms. Ayurvedic literature recommends consuming 1-3 g of Trikatu churn with honey or warm water to mask its harsh taste and maximize therapeutic effects. While powders are not only widely utilized in therapeutics, they also play an important role in the development of various dosage forms such as ointments, suppositories, and tablets. Churna is a popular powdered dosage form in Ayurvedic medicine. Key considerations in powder formulations involve particle properties, bulk characteristics, interactions, morphology, and mixing features [10].

Chemistry of Trikatu

Table 1: Trikatu Churna's Origin [11]

Name	Botanical name	Synonyms	Therapeutic action	Pharmacological properties	Formulation
Pippali	*Piper longum linn*	Kana, Tiksna, Capala, Tandula	Used for treating cholera, respiratory conditions, discomfort in the teeth, reiteration of acid, discomfort in the stomach, reduced high temperature, etc.	Virya-ushna, Guna-laghu, Rasa-katu, and Vipaka-madhura.	Gurna Trikatu, Gurda *Pippali*.
Adraka/ Sunthi	*Zingiber officinale*	Nagara, Sri Vajra, Visva, Visvabhejasa, and Kathudra.	Anorexia, Fluid retention, Gas, Rheumatism, Colitis, and abdominal discomfort.	Rasa – katu. Guna laghu, The Virya-ushna Madhur Vipaka, Kapha vata samak dosha karma.	Among them are Samasarkara and Panchaka.
Maricha	*Piper nigrum Linn*	Sakanga, Venlaja, Usana, Krsna, Dhanvantari, and Dharmapattana.	Appetizer Carminative and Resistance Microbial.	The Rasa-katu Laghu, guna tikshna, Virya -ushna, Vipaka-katu Kaphavatahara Doshakarma.	Marichadi taila, Talisadi taila, and Trikatu churna.

Chemical composition and structure

The three herbs *P. longum*, *P. nigrum*, and *Z. officinale* are found in trikatu. Ginger contains the following: inorganic fat (10%), volatile oil (1-4%), starch (40–60%), fiber (5%), and substance (6%), wetness that is still present (10%), and pungent resinous stuff (5-8%). Monoterpene hydrocarbons, sesquiterpene hydrocarbons, oxygenated mono- and sesquiterpenes, and phenylpropanoids make up ginger oil. Volatile oil, alkaloids, resin (6%), piperidine, and starch (30%) are all present in black pepper [12].

The pepper aroma is attributed to the volatile oil, which is made up of sesquiterpenes, dipentene, α and β-pinene, and terpenes such as phellandrene. In addition to 1% volatile oil, long pepper fruits also include resin, the waxy alkaloids N-isobutyl trans 2: trans 4 decadienamide, the alkaloids piperine and piperlonguminine, sesamin, a lignin derivative, and a terpenoid material. It was established that piperlonguminine is an isobutylamide of piperic acid [13].

***Pippali* (*Piper longumlinn*)**

Piper longum Linn, an essential medicinal plant in the Piperaceae family, holds significance as a key element in Ayurvedic preparations like trikatu and Panchkula. Its widespread use in Ayurveda contributes to overall health and tissue nourishment [14]. *Pippali* is recognized in Ayurvedic literature for its versatile medicinal properties, encompassing anti-inflammatory, cough-suppressant, antibacterial, and immunostimulatory effects. It has been valued for generations and appears in 324 formulas in the Ayurvedic Formulary of India, where it is widely used as a complementary element. [15].

An explanation of the plant

Piper longum Linn is a creeping, rooted plant with thin stems that trail under plants. The leaves are rectangular and cordate, measuring 5 to 9 cm in length [15]. It is rich in secondary metabolites, including amides, alkaloids, lignans, flavonoids, esters, essential oils, and organic acids. Alkaloids are prevalent in seeds, fruit, stems, leaves, and roots, influencing the plant's characteristics. A unique component, piperine, identified as the initial amide in Piper species, plays a key role in imparting spicy and robust Flavors to *P. longum* [16].

Chemical Structure

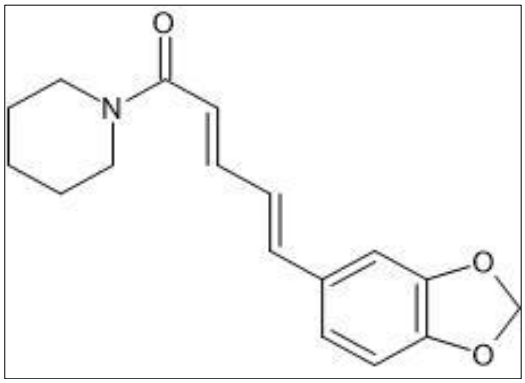


Fig 1: Piperine chemical structure.

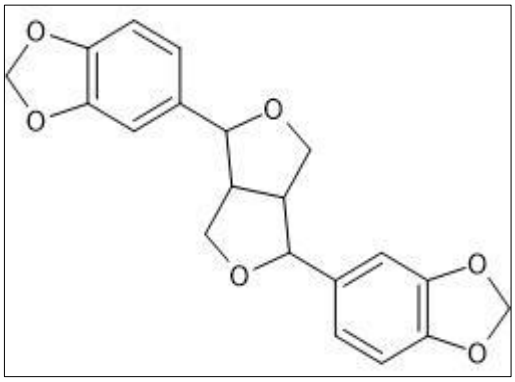


Fig 2: (+)-Asarinine chemical structure

S. No	Pharmacological activity	Part of plant	Action	References
1.	Contra proliferative.	*Piper longum* fruit extract,	When tested on human and immunocompromised animals, it damaged cancer cell mitochondria, caused caspase-independent death, and slowed colon cancer tumor development with minimal toxicity.	[17]
2.	Activity against Alzheimer's disease.	*Piper longum* fruit.	Piper longumine, which improves Sirt-1 activity in hippocampus neurons and reduces Aβ1-42 toxicity. Piper longumine taken orally reduced β-amyloid in APP/PS1 mice increased VGLUT1 in the hippocampus, and reduced active microglia and astrocytes, showing potential.	[18]
3.	Activity against Parkinson's disease.	*P. longum* seeds	The 85% ethanol extract from *P. longum* seeds, containing piperine and *piper-linguine*, showed neuroprotection in mice with MPTP-induced Parkinson's disease, enhancing GSH, SOD, and increasing dopaminergic neurons and GABA levels.	[19]
4.	Nootropic action.	*P. longum* fruit extract	Swiss Albino mice showed positive cognitive enhancement of *P. longum* fruit extract, requiring further investigation into its nootropic effects and the signaling pathways involved.	[20]
5.	Antiepileptic and anticonvulsant properties.	Fruit extract from *Piper longum*	It protects against pentylenetetrazole-induced convulsions, but not strychnine or 4-aminopyridine. Reduction in GABA levels in treated mice suggested the GABAergic processes' role.	[21]
6.	Antihistamine and anti-serotonin properties.	A leaf extract from *Piper longum*	On Wistar rats they reduced carrageenan and dextran-induced paw edema and cotton pellet granuloma, preventing inflammation and possessing antihistamine and anti-serotonin properties.	[22]
7.	Anti-ulcer properties.	*Piper longum* leaf extract.	Scientists found it effectively prevents stomach ulcers in rats exposed to aspirin, pylorus ligation, and cold restraint stress, reducing cell shedding, controlling mucin secretion, and limiting acid release.	[23]

Adraka/ Sunthi (*Zingiber officinale*)

Zingiber officinale, commonly referred to as ginger, is an evergreen herb that belongs to the Zingiberaceae family. Originating from tropical Asia, it is extensively cultivated in different regions of India. Ginger holds a prominent place in traditional medicine, including Ayurveda and Chinese medicine, valued for its antiemetic, stomachic, expectorant, anti-inflammatory, and aphrodisiac properties. As identified in phytochemical analyses, the herb contains volatile oils and oleo-resins, such as gingerol, zingerone, and zingiberol [24]. Numerous experimental and clinical experiments have demonstrated ginger's varied therapeutic effects. These include antibacterial, antidiabetic, antiemetic, hypolipidaemic, and hepatoprotective effects. Beyond its use as a spice, ginger is recognized for its efficacy in treating various conditions associated with the gastrointestinal, respiratory, cardiovascular, and sexual systems [25]. *Zingiber* plants include 447 known phytochemical components, including volatile oils, diarylheptanoids, gingerols, flavonoids, and terpenoids. Particularly, gingerols serve as the potent and aromatic essential elements. Extracts reveal a range of advantages, including anti-inflammatory, anticancer, antibacterial, larvicidal, antioxidant, and hypoglycemic effects [22].

An explanation of the plant

Determining the optimal time to harvest ginger requires consideration of both age and bulb size. Harvest the rhizomes at 5 months, when soft and mild, for maximum freshness. Harvesting around 7-9 months yields stronger-flavored ginger, which is good for drying due to its high oil content. Harvesting late leads to fibrous ginger with a shorter storage life. The optimal harvesting time depends on the intended use, whether for fresh consumption, preservation, or drying [26]. The genus *Zingiber*, ranking as the third largest within the Zingiberaceae family, encompasses 141 primarily edible and medicinal plant species, with 12 indigenous to China. These perennial herbs feature fibrous rhizomes, utilized for food, medicine, and the extraction of aromatic oils from stems, leaves, and roots. Various chemical compounds, including volatile oils, organic acids, gingerols, and terpenoids, have been identified within this genus. Noteworthy species *like Zingiber zerumbet*, *Zingiber officinale (ginger)*, *Zingiber corallum*, *Zingiber myoga*, and *Zingiber striolatum* exhibit diverse biological activities, demonstrating antimicrobial, antioxidant, anti-inflammatory, and anti-tumor effects. Historically, these plants have been employed to address a range of ailments, including nausea, joint pain, and cardiovascular issues [27].

Chemical Structure

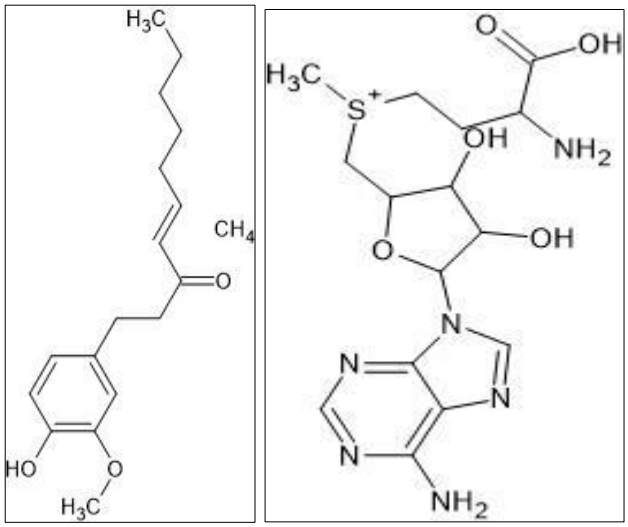


Fig 3: 6-GINGEROL **4** - 6-SHOGAOL

S. No.	Pharmacological activity	Part of plant	Action	Reference
1.	Antiviral activity.	The fresh rhizome of *Zingiber officinale.*	It has antiviral properties against HRSV, stimulating mucosal cells to release IFN-β, a crucial cytokine for viral infection prevention and reduction.	[28]
2.	Effect of gastrointestinal as anti-inflammatory.	*Zingiber officinale* rhizome.	It is rich in key elements like PI3K, Akt, NF-κB, and 6-shogaol, which significantly impacts gastrointestinal inflammation, especially in colitis disorders, protecting against TNF-α-induced intestinal dysfunction.	[29]
3.	Effect of radioprotection.	Hydroalcoholic suspension of *Zingiber officinale* rhizome.	The oral hydroalcoholic suspension of *Zingiber officinale* rhizome, containing phytochemicals like dehydrogingerone and zingerone, has been found to protect mice from gamma radiation-induced illness and mortality.	[30]
4.	Anti-tumor effect.	*Zingiber officinale* plant.	With anti-inflammatory and anti-tumorigenic properties, it may help prevent or control colon, stomach, and ovary cancers through its bioactive components, including 6-gingerol, 6-shogaol, 6-paradol, and zerumbone.	[31]
5.	Activity of antioxidants.	*Zingiber officinale* rhizome.	Ginger's anti-inflammatory properties and antioxidant actions, which reduce C-reactive protein levels and increase renal superoxide dismutase activity, contribute to a renoprotective effect in renal failure cases.	[32]
6.	Anti-diabetic activities.	*Zingiber officinale* rhizome.	With anti-inflammatory properties and antioxidant actions, which reduce C-reactive protein levels and increase renal superoxide dismutase activity, contribute to a renoprotective effect in renal failure cases.	[33]
7.	Antisemitic properties.	Ginger's active components include diterpenoid ginger, galanolactone, and ginger.	They have purifying and detoxifying effects, potentially treating vomiting and nausea. Animal studies show anti-serotoninergic effects.	[34]

Maricha (*Piper nigrum* Linn)

Black pepper, scientifically known as *Piper nigrum*, is a member of the Piperaceae family with an extensive history in traditional medicine. It has been used to treat a variety of conditions, including piles, coughs, colds, dyspnea, dysentery, stomachache, and worms. The medicinal benefits of black pepper are derived from compounds called phenolics. Black pepper seeds contain a wide range of chemicals, including carotenoids, terpenoids, flavonoids, alkaloids, and more. Both conventional and modern medical viewpoints recognize black pepper's numerous health benefits [35]. Black pepper contains a high concentration of essential vitamins, minerals, and nutrients. Black pepper seeds have notable quantities of essential minerals such as calcium, magnesium, potassium, and phosphorus, complemented by traces of sodium, iron, and zinc. These minerals play a crucial role in supporting daily human activities. Additionally, black pepper comprises carbohydrates (66.5 g), protein (10 g), and fat (10.2 g). Noteworthy concentrations of vitamins B1, B2, B3, and C further enhance its nutritional profile, making black pepper a valuable dietary addition [36].

An explanation of the plant

Black pepper is widely embraced in world cuisine and carries a rich history in traditional medicine. Its versatile uses extend to therapy, flavorings, preservatives, cosmetics, and the perfume industry. Scientifically recognized as *Piper nigrum* L., black pepper is highly regarded for its therapeutic qualities, encompassing antioxidant, hepatoprotective, antibacterial, antihypertensive, and anti-inflammatory properties. The pepper is an annual plant that climbs and spreads, with a crown size of up to 1.5 meters and a plant height of 10 meters. The plant consists of roots, stalks, branches, flowers, leaves, fruit, and seeds. There are two

types of roots those that grow through hoops in the soil to absorb nutrients and those that belong to the ground's surface. The lateral roots, known as taproots, are filamentous near the stem base, with approximately 10–20 roots per meter, each measuring around 3–4 meters in length [37]. Black pepper contains approximately 5–9% alkaloids, including piperine and piperidine, as well as around 1.2–5% volatile oil. The essential oil, responsible for the characteristic aroma and flavor, primarily consists of terpenes and sesquiterpenes. Phytochemical studies have identified various constituents in Piper plants, such as piperolides, propenylphenols, amides, neolignans, flavonoids, terpenes, and steroids. Piperine, the primary chemical in black pepper, exhibits diverse activities, including central nervous system depression, cytotoxicity, anti-inflammatory properties, and hepatoprotective effects. Additionally, piperine enhances bioavailability. Nakatani *et al* 1986 discovered five phenolic amides in *Piper nigrum*, these phenolic amides exhibited strong antioxidant activity, exceeding that of the natural antioxidant alpha-tocopherol. Notably, one specific amide, feruperine, showed antioxidant effects similar to synthetic antioxidants like BHT (butylated hydroxytoluene) and BHA (butylated hydroxyanisole) [38]. The initial active compound discovered in the Piperaceae family was piperine. *P. nigrum* also contains phenolics, flavonoids, alkaloids, amides, steroids, lignans, neolignans, terpenes, chalcones, and more. Specific compounds like piperine, piperamide, and piperamine have been associated with various pharmacological properties. Notably, piperine has isomers: piperine, isochavicine, and cha vicine. Among these, piperine exhibits pharmacological activity, highlighting the richness of black pepper's bioactive constituents [39].

Chemical structure

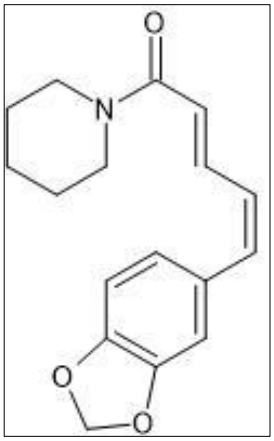


Fig 5: 3-Piperamide

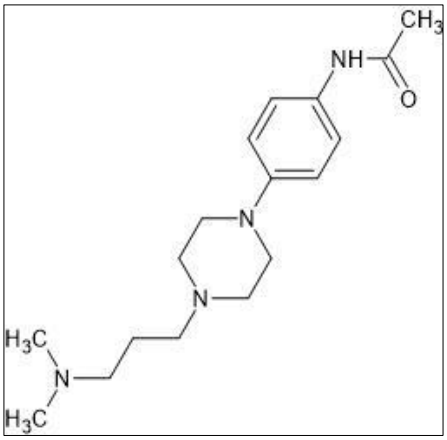


Fig 6: Isochavicine.

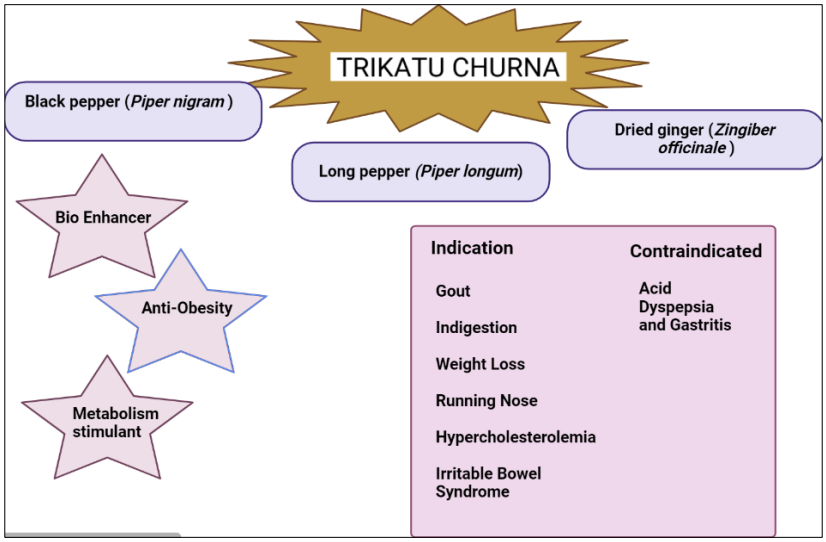
S. No	Pharmacological activity	Part of plant	Action	References
1	Antimicrobial efficacy.	Infusions include bay leaf, anise, coriander, and black pepper.	Han and Siddiqui *et al*. (2007) investigated the antimicrobial properties of infusions like bay leaf, anise, coriander, and black pepper on 200 participants, finding black pepper to have the highest activity.	[40]
2	Activity of antioxidants.	*Piper nigrum*.	*Piper nigrum*, found in animal studies, inhibits lipid peroxidation and human lipoxygenase, and neutralizes hydroxyl and superoxide free radicals, protecting against oxidative stress and reducing lung cancer risk.	[41]
3	Anti-inflammatory properties.	Piperine.	Piperine, a black pepper component, has been found to have anti-inflammatory, analgesic, and anti-arthritic properties, effectively reducing inflammatory markers and hindering protein movement within cells.	[42]
4	Hepatoprotective properties.	Piperine.	A black pepper compound has been found to protect the liver by lowering serum GPT and GOT levels and restoring normal liver markers in rats.	[43]
5	An enhancer of bioavailability.	Piperine.	It is a potent medication metabolism inhibitor and bioavailability enhancer, which improves drug and nutrient absorption by modifying membrane mechanics and enhancing permeability.	[43]
6	Pain-relieving action.	Piperine.	when injected intraperitoneally, significantly reduced acetic acid-induced writhing in mice, outperforming indomethacin. It also delayed reaction times in the tail-flick assay, suggesting its opioid-related role in pain reduction.	[44]
7	Action of anticonvulsants.	Piperine.	Piperine, a potent anti-convulsant agent, reduces seizure duration, mortality, and intensity in mouse models, highlighting its potential as a treatment for TRPV1-selective antagonism.	[45]

Need for bioavailability enhancer

Phytochemical studies demonstrate the potential of plant products for overall health which addresses a significant medical demand. Some herbal medications have difficulty in absorption due to factors such as insufficient lipid solubility and improper molecular size, which reduce their bioavailability. Water-soluble plant components, notably phenolics, have difficulty interacting with lipid-rich intestinal walls which limits bioavailability. Innovative delivery technologies such as liposomes, macropinosomes, and lipid-

based strategies address these challenges by improving release rates and allowing for the bridging of lipid-rich biomembranes. Phospholipid-based drug delivery systems hold the potential to improve the efficacy of herbal medicine delivery by ensuring the correct administration of active components by involving "Trikatu" in Ayurvedic formulations [46]. The term "bioavailability enhancers" originates in the ancient Ayurvedic system, sometimes known as the "science of life". Bose *et al*. (1929) developed the concept of bio-enhancers- Ginger, long pepper, and black pepper combination is known as "Trikatu," which means "three acrids" in Sanskrit. These compounds improve the therapeutic effectiveness of medicine by increasing their bioavailability across membranes, increase their molecular interactions, and receptivity in target cells. These agents, also known as "absorption enhancers," boost a drug's absorption and efficacy when combined with formulation. The term was introduced in 1979 by researchers at the Regional Research Laboratory, Jammu, who identified piperine as the first bioavailability enhancer [47].

Action mechanism of herbal-origin [TRIKATU] bio-enhancers: Herbal bio-enhancers TRIKATU function in a variety of ways. Nutritional bio-enhancers improve gastrointestinal absorption, whereas antimicrobial bio-enhancers affect medication metabolism. These herbal bioenhancers operate through mechanisms such as: (a) reducing hydrochloric acid secretion and increasing blood supply to the gastrointestinal tract, (b) slowing down gastrointestinal transit, gastric emptying time, and intestinal motility, (c) changing the permeability of the gastrointestinal epithelial cell membrane, (d) exhibiting a cholagogous effect, (e) possessing bioenergetics and thermogenic properties [48].



Medicinal Properties of Trikatu

Trikatu showed the Bio-stimulant, Protective against chemo, Antiviral, Anticipating, Carminative, Both an appetizer and a digestive aid.7. Low-glycemic.8. Burner of Fat.9. Gentle anodyne, Lower the blood sugar level, Counter-emet and Anti-inflammatory.

Table 2: Trikuta formulation

S. No	Formulation	Indication	Reference
1.	Trikatu churna	Enhance digestion and metabolism	[2]
2.	Trikatu guggulu	Anti-inflammatory properties and this combination is often used for joint and musculoskeletal issues.	[50]
3.	Trikatu rasayana	Ayurvedic rejuvenating tonics	[51]
4.	Trikatu tablets and capsules	Digestive support, weight management, or respiratory health.	[8]
5.	Trikatu arishta	Digestive disorders.	[52]
6.	Trikatu kwath	Support respiratory health.	[53]
7.	Trikatu ghrita	Digestive and metabolic properties, managing Anaemia	[54]
8.	Trikatu avaleha	Digestive and respiratory benefits	[55]
9.	Trikatu taila	Reproductive oddities, hypercholesteremia, sluggish metabolism, and obesity.	[56]
10.	Trikatu linctus	Soothe the throat and support respiratory health.	[57]
11.	Astangavleha	Cough and Asthma	[58]
12.	Panchnimba churn	Skin diseases	[59]
13.	Vyagriharitaki	Cough and Rhinitis	[60]
14.	Arkadi kwacha churn	Lockjaw and Cold cough	[61]

Table 3: Literature review pharmacological activity of tikatu

S. No	Scientist	Pharmacological activity of trikatu	Reference
1.	P.R. Mavlankar *et al* 2012.	Trikatu Churna's antibacterial activity was tested using an *in vitro* agar well. The extract showed significant activity, nearly matching the effects of a conventional ampicillin solution. The plant extract-filled wells showed clear circular zones of inhibition, eliminating *S. aureus* and *E. coli*.	[62]
2.	Amrutha C. S *et al* 2012.	The antibacterial qualities of Trikatu, a combination of *Z. officinale*, *P. nigrum*, and *P. longum*, were investigated in this study. Different levels of suppression against bacterial strains were demonstrated by the extracts. *P. longum* and *Z. officinale* demonstrated the least amount of action against all species, whereas *P. nigrum* exhibited the highest. Trikatu's use in intestinal bacterial infections appears to have some preliminary proof as methanol extracts demonstrated good action against all species.	[63]
3.	Dwivedi *et al*., 2008.	Earthworms, resembling human intestinal roundworm parasites, were used in a study. Petri dishes were prepared with different concentrations of saline, Piperazine citrate solutions, and ethanolic extracts from different plants. Six earthworms were introduced into each dish, and the time until paralysis and death were recorded. The experiment was replicated for validation.	[64]
4.	Mukherjee and Wahile, 2006; Ponnusankar *et al*., 2011a)	The study investigated cytochrome P450 inhibition in male rat liver microsomes using a method by Ponnusankar *et al*. (2011b). The liver was isolated, treated with KCl, and homogenized. The supernatant was collected and centrifuged, and microsomal fractions were collected. Protein estimation was performed using the biuret method with bovine serum albumin as the standard. The experiment followed ethical guidelines approved by the Institutional Animal Ethical Committee and the Committee for Control and Supervision of Experiments on Animals.	[65]
5.	Amrutha C. S *et al*.,2022.	The study involved washing, drying, and powdering fruits of *P. nigrum*, *P. longum*, and *Zingiber officinale* rhizomes. Extracts were extracted using various solvents and refrigerated. Preliminary phytochemical tests showed alkaloids, carbohydrates, phenols, flavonoids, tannins, terpenoids, steroids, saponins, amino acids, proteins, and cardiac glycosides in all extracts. The extracts showed antibacterial activity against bacteria like B. cereus, *S. aureus*, *E. coli*, and *V. harveyi*, with specific extracts showing significant inhibition zones.	[63]
6.	S. V. Suresh Kumar *et al*.,2004	In research examining the influence of the ethanolic extract of Trikatu Churna on normal liver functions, the administered dose of 150 mg/kg demonstrated non-toxicity, with SGOT, SGPT, AP, and TB levels remaining within normal ranges. Conversely, normal rats treated with CCI4 exhibited a substantial increase in these parameters, indicative of acute liver damage. Rats treated with Trikatu Churna extract and a positive control displayed a significant decrease in the heightened biochemical markers induced by CCI4, mirroring the positive control's effect.	[66]
7.	Madhukar S. Dama *et al*.2008.	A study on mountain Gaddi goats found that trikatu, an herb-al bio-enhancer, significantly influenced the pharmacokinetics of pefloxacin. It reduced plasma concentration during absorption and increased concentrations during elimination, enhancing bioavailability and prolonged pharmacological action. Trikatu treatment also decreased the elimination half-life, indicating quicker drug clearance. The recommended dosage for goats is 6.0 mg/kg priming and 2.21 mg/kg maintenance at 8-hour intervals.	[67]

S.NO	Adverse effect	Activity
1.	Burning aftertaste.	Consuming too much Trikatu may cause a lingering burning sensation in the mouth or throat after ingestion.
2.	Acid reflux.	Trikatu tends to cause stomach acid to reflux back into the esophagus, which can cause pain and irritation.
3.	Burning sensation in the throat.	Excessive intake of Trikatu may trigger a burning feeling in the throat, contributing to overall discomfort.
4.	Increased perception of body heat.	Known for its heating properties, an overdose of Trikatu may intensify the sensation of warmth within the body.
5.	The rare occurrence of mouth ulcers.	In certain instances, an overdose of Trikatu may be linked to the development of mouth ulcers, although this is considered a rare side.
6.	Infrequent sweating.	Overconsumption of Trikatu may result in sporadic episodes of sweating.
7.	Occasional redness in eyes.	In rare cases, an overdose of Trikatu might lead to redness or a burning sensation in the eyes.

Side effect: Trikatu is a popular herbal remedy in traditional medicine that is generally considered safe. On the other hand, excessive consumption may have certain adverse effects [68].

Contraindications

There are conditions like acid reflux, dyspepsia, and Pitta dosha imbalances. Burning sensation in any part of the body, such as the throat, hands, feet, or abdomen, vomiting, bloodshot eyes. conditions affecting the skin that manifest as burning feelings. Stools that are hard, dry, or bleed when a person has diarrhea are common contraindications of TRIKATU [69].

Acid reflux and heartburn: Trikatu churna is a mixture of ginger, an herb that has been used in traditional medicine for the facilitation and relief of discomfort related to the stomach. But for those with predominant symptoms like severe acid reflux or heartburn, the heating abilities of ginger may worsen the illnesses. However, it is significant that the healthcare professional gets consulted to determine whether Trikatu churna is suitable to ease these symptoms [70].

Burning sensations: When heat or indigestion becomes apparent in the bodies of those suffering from congestive heart failure, the production of heat is probably the primary cause of the issue. Thus, Ginger has the potential to be the best Trikatu churna. On the other hand, until the patients are cleared to consume the powder, the consumption of Trikatu churna is not recommended for those suffering from skin conditions, knee and joint discomfort, or other issues that are likely being treated by professionals. One such instance of the "robust-ness" concept in action is the dosha imbalance condition because Trikatu churna is feeble and is unable to cure a disorder fully. In this case, the likelihood of developing increasingly severe and critical symptoms is increased [71].

Gastrointestinal issues: It will improve digestive problems, However, excessive use can have

negative consequences as well, like acidity, scorching aftertaste, heat feeling, burning in the throat, and rare cases, oral ulcers. To prevent these possible adverse effects, it's crucial to utilize this medication sparingly [72].

Abortion threats

In general, during pregnancy trikatu is not recommended, especially in the case of high-risk pregnancies or conditions where an abortion is a possibility. While Ginger which is among the components in Trikatu churna ingredients is possibly used in pregnancy for treating morning sickness its safety is not established thereby warranting precautionary measures and therefore seeking advice from health care providers is pertinent [73].

Conclusion

In Ayurveda, Trikatu is called the "Heating Formulation" because it increases the maharani, or digestive fire, which enhances digestion and metabolism. Made up of *Pippali*, Sunthi, and Maricha, it balances immunity, energizes the digestive and respiratory systems, and gets rid of harmful substances. For Kapha dominance, trikatu is used seasonally, particularly for water-related illnesses of liver, spleen, and lung issues. It helps respiratory issues as an expectorant because of its bronchodilator qualities. Trikatu improves appetite and digestion by increasing the synthesis of digestive enzymes. It supports heart health by lowering cholesterol and triglycerides. Moreover, Trikatu's purifying properties help relieve joint pain associated with gout. Recognized for a variety of health advantages, it includes properties that are antibacterial, anti-inflammatory, antidiabetic, anti-cancer, nephroprotective, hepatoprotective, larvicidal, and immunomodulatory.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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