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Review Article

Ayurveda Section

Trikatu and its Therapeutic Potential: A Narrative Review of its Bioactive Compounds and Pharmacological Mechanisms

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ABSTRACT

Trikatu is an essential Ayurvedic formulation of *Piper nigrum*, *P. longum*, and *Zingiber officinale*, traditionally revered for balancing the body's humours and enhancing digestion. Its therapeutic value is supported by a rich array of bioactive phytochemicals. The present narrative review aimed to thoroughly synthesise the available pharmacological and clinical data on *Trikatu's* health benefits. Specific objectives included summarising its active components, evaluating its antimicrobial and anti-inflammatory properties, and reviewing its effectiveness in managing metabolic and endocrine disorders. Major databases, including PubMed/Medline, Google Scholar, Scopus, and Cochrane Library, were searched. Retrieved studies were qualitatively assessed and synthesised to summarise the therapeutic potential and activities. Preclinical findings confirmed potent antimicrobial activity against common pathogens, often rivaling standard antibiotics, and significant anti-inflammatory action. It also demonstrated protective effects on the liver and heart. Clinical studies provided strong support for its role in metabolic health, showing significant improvements in lipid profiles for patients with dyslipidaemia, alongside positive outcomes in managing symptoms of hypothyroidism and Polycystic Ovarian Syndrome (PCOS). *Trikatu* exhibits a strong, multi-faceted therapeutic potential consistent with its traditional applications. However, despite compelling evidence, the formal integration of *Trikatu* into contemporary medicine requires further rigorous, high-quality Randomised Controlled Trials (RCTs) to confirm its efficacy and ensure standardised clinical safety.

Keywords: Aromatic, Body humours, Endocrine disorders,Traditional medicines, Three acrids

INTRODUCTION

India's traditional medical systems- Ayurveda, Siddha, and Unani- are a testament to a long-standing reverence for nature's pharmacy. Within this heritage, *Trikatu* stands out. Its name, literally meaning "three acrids" in Sanskrit, perfectly captures its essence: a fiery blend formulated to restore harmony to the body's *doshas* (*Kapha*, *Vata*, and *Pitta*), whose imbalance is traditionally seen as the root of disease [1-5]. *Trikatu* is disarmingly simple, yet immensely potent. It's prepared by grinding and mixing equal parts of the dried powders of these three kitchen staples: *Piper longum* (Long pepper), *Piper nigrum* (Black pepper), *Zingiber officinale* (Ginger) [Table/Fig-1-3]. This specific triad has secured its place in the 6,000-year-old Ayurvedic Materia Medica [1,3,5]. Contemporary science now helps explain this ancient wisdom identifying a cocktail of active compounds- especially alkaloids like piperine and piperlongumine, alongside flavonoids that underpin *Trikatu's* therapeutic actions. This narrative review compiles the body of preclinical and clinical knowledge to offer acomprehensive look at the pharmacological and healing potential of this time-honored formulation.

[Table/Fig-1]: *Pippali* (*Piper longum* Linn).

[Table/Fig-2]: Shunthi (Zingiber officinalisRosc).

Chemical Composition

Trikatu's effectiveness isn't from one hero ingredient, but a collaborative effort among its components: *Zingiber officinale* (Ginger): Beyond its aromatic resins and starch content, ginger is rich in phenylpropanoids and various mono and sesquiterpenes [6]. These compounds are responsible for its distinctive taste and powerful bioactivity. *Piper nigrum* (Black Pepper): The volatile oils and alkaloids are key here [7]. The pungent flavour comes from compounds like piperine, while the scent involves terpenes like phellandrene [7]. *Piper longum* (Long Pepper): This spice contributes not only piperine but also unique alkaloids such as piperlonguminine and the lignin derivative sesamin [7]. The potent

[Table/Fig-3]: *Marich* (*Piper nigrum* Linn).

alkaloid piperine, present in both peppers, is particularly significant. It's well-known for its ability to enhance the bioavailability of other compounds, which is likely central to *Trikatu's* powerful, synergistic effects.

Pharmacological and Clinical Activities of *Trikatu*

Anthelmintic activity: *Trikatu* extracts have displayed activity against parasites, showcasing anthelmintic potential in in-vitro tests [8]. The ethanolic extract typically proves more potent than the aqueous extract in these studies. *Trikatu* exhibits strong anthelminthic action. Its active ingredients, such as gingerol and piperine, paralyse intestinal worms, interfere with their metabolism, and harm their protective cuticle, which facilitates their ejection. Effectiveness against tapeworms, roundworms, and pinworms has been demonstrated in experimental investigations. The three herbs work together to improve gastrointestinal motility and lower the load of worms, making it an effective natural treatment for helminth infections [9,10].

Antimicrobial and Antifungal activity: *Trikatu,* which has strong antibacterial and antifungal qualities. Both Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis*) and Gram-negative (*Escherichia coli*, *Salmonella typhi*) bacteria are inhibited in their development by ethanol and aqueous extracts. *Aspergillus niger*, *Candida albicans*, and Mucor species are all successfully inhibited by the antifungal action. Bioactive substances like gingerol, chavicine, and piperine are thought to be responsible for its effectiveness since they interfere with protein synthesis, break down microbial cell walls, and impede enzymatic activity [11-16].

Anti-inflammatory and Antiarthritic activity: *Trikatu* exhibits strong anti-inflammatory [17-19] and antiarthritic properties. Its active ingredients, including as gingerol and piperine, reduce joint pain and swelling by blocking pro-inflammatory mediators such prostaglandins, IL-1β, and TNF-α. In models of arthritis, studies have demonstrated that it improves mobility and reduces swelling [20,21]. The three herbs' combined activity intensifies the treatment's impact on joint and inflammatory conditions.

Hepatoprotective activity: Preclinical studies have indicated *Trikatu's* protective role for the liver [22]. The extract successfully mitigated damage by normalising elevated liver enzymes and inhibiting liver peroxidation in animal models. *TrikatuChurna* (200-400 mg/kg) reduced bilirubin, enhanced liver morphology, and improved liver function markers (e.g., Serum Glutamic Oxaloacetic Transaminase (SGOT),Serum Glutamic Pyruvic Transaminase (SGPT) ,Alkaline Phosphatase (ALP)) in an in vivo model of alcoholic liver diseases [23].

Cardioprotective activity: Evidence from rat models of cardiac injury suggests that *Trikatu* offers a protective effect for the heart [24]. Pretreatment with the formulation was observed to markedly reduce myocardial necrosis. In animal models of cardiovascular stress, *Trikatu* (*Piper nigrum*, *Piper longum*, *Zingiber officinale*) has shown cardioprotective benefits. According to studies, it lowers oxidative stress, lipid peroxidation, myocardial antioxidant enzyme levels (SOD, catalase, and GSH), and keeps cardiac biomarkers like Creatine Kinase–Myocardial Band (CK-MB) and Lactate Dehydrogenase (LDH) at normal levels. Its bioactive components, gingerol and piperine, are principally responsible for these effects. They enhance heart function and shield cardiac tissue from ischemia-reperfusion damage.

Analgesic activity: The extract has been reported to exhibit mild pain-relieving effects [25]. This activity was observed using heat-sensitive mouse models.In experimental models including acetic acid-induced writhing and tail-flick tests in rats, *Trikatu*dis plays notable analgesic benefits. Its ability to reduce pain is ascribed to both the modulation of central pain neurotransmitters and the inhibition of prostaglandin synthesis through the cyclooxygenase and lipoxygenase pathways. In contrast to traditional Non-steroidal Anti-inflammatory Drugs (NSAIDS), the formulation also exhibits gastroprotective properties [26].

Bioavailability enhancement/Pharmacokinetic modulation: *Trikatu* has been shown to enhance the oral bioavailability of certain drugs: e.g., it increased absorption of ciprofloxacin, and altered Tmax (time to maximum concentration) of carbamazepine. However, in the case of rifampicin it reduced Cmax and delayed Tmax, showing that its effects can vary depending on the drug [27].

Antioxidant activity: *Trikatu* syrup formulations have been investigated and demonstrated to have the capacity to scavenge free radicals (for example, through the use of hydrogen peroxide and 2,2-Diphenyl-1-picrylhydrazyl (DPPH) assays), indicating the possibility of neutralising reactive oxygen species and lowering oxidative stress [28].

Antitumour/Anticarcinogenic potential (as adjunct)

In a study of chemical carcinogenesis (20-methylcholanthrene induced) in animals, combination of *Trikatu* and mercaptopurine (a chemotherapy-agent) showed enhanced antitumour effect vs mercaptopurine alone, along with better haematological and antioxidant profiles [29].

Respiratory activity: *Trikatu* shows notable respiratory activity. Its bioactive compounds help clear respiratory passages, reduce mucus, and alleviate bronchial congestion. It acts as a mild bronchodilator and expectorant, supporting relief from cough, cold, and asthma symptoms. The synergistic action of the three herbs enhances overall respiratory function and strengthens the respiratory system [30].

Gastroprotective activity: *Trikatu* demonstrates a strong gastroprotective effect. Its bioactive ingredients, such gingerol and piperine, lessen acid production, shield the stomach mucosa, and stop ulcers from developing. Additionally, by strengthening the gastrointestinal lining and increasing the activity of digestive enzymes, the formulation promotes overall digestive health. Its anti-inflammatory and antioxidant qualities also help to lessen stomach inflammation and oxidative stress [31].

Management of dyslipidaemia (*Medoroga*) (clinical): A clinical trial found that *Trikatu* significantly improved serum lipid profiles in patients [32]. It led to a robust reduction in harmful lipids, including total cholesterol, triglycerides, Low-Density Lipoprotein (LDL) and Very Low-Density Lipoprotein (VLDL). The formulation also enhances lipid metabolism and prevents lipid peroxidation, supporting cardiovascular health. Additionally, its antioxidant and anti-inflammatory effects help protect against atherosclerosis and other lipid-related complications.

Management of hypothyroidism (clinical): Clinical trials reported considerable symptomatic improvement for hypothyroid patients [33]. A notable majority of patients were able to reduce or stop their hormone replacement therapy dosage. *Trikatu* enhance basal metabolic rate, which can indirectly benefit hypothyroid conditions. Additionally, their antioxidant and anti-inflammatory effects may protect thyroid tissue from oxidative stress. However, more experimental and clinical studies are needed to establish a clear anti-hypothyroid effect.

Management of PCOS (clinical): *Trikatu Churna* has shown promise in managing symptoms of Polycystic Ovary Syndrome (Artavakshaya) [33]. It was particularly noted for its positive impact on regulating menstrual cycles.Its bioactive ingredients, including as gingerol and piperine, aid in enhancing insulin sensitivity, lowering oxidative stress, and improving metabolism- all of which are critical components in the treatment of PCOS. Additionally, the composition might help control menstrual cycles and lessen inflammation linked to ovarian dysfunction. Although its use is supported by Ayurvedic scriptures, there aren't many clinical trials to back it up, therefore more research is required to determine its effectiveness.

Appetite stimulant (clinical): Consistent with its traditional use, *TrikatuChurna* was found to be effective in treating impaired digestion (Agnimandya) [34]. It acts as a reliable appetite stimulant, enhancing digestive functions. *Trikatuchurna* and *AgnitundiVati,* another Ayurvedic medication, were compared in a human clinical randomised trial for people with *Agnimandya* symptoms (low appetite and digestive weakness). Over the course of roughly three weeks, *Trikatu* was found to increase appetite and decrease symptoms such as indigestion, heaviness in the head (Shirogaurav), lack of appetite (Kshudhamandya), and other associated symptoms, demonstrating its impact on boosting digestive fire ("Agni") and appetite in general [35].

Toxicity/safety profile (preclinical): *Trikatu's* effects were investigated in a comprehensive acute and sub-acute toxicity study conducted on Charles Foster rats. No mortality, morbidity, or notable alterations in vital organs, haematological markers, or biochemical markers were seen in the acute trial (single oral dose up to 2000 mg/kg). Although there were some dosage-dependent alterations, including an increase in LDL, a drop in HDL, a rise in SGPT at certain levels, and a decrease in white blood cell count at the higher dose, most parameters stayed within normal ranges during the 28-day sub-acute dosing (at doses of 5, 50, and 300 mg/kg/day). Overall, *Trikatu's* safety in these animal models was deemed adequate [36].

DISCUSSION

The array of evidence confirms that *Trikatu* is far more than an accidental success. Its powerful antimicrobial and anti-inflammatory properties substantiate its ancient use in treating infections and chronic conditions. Furthermore, its role in improving digestion and offering significant benefits in metabolic conditions like dyslipidaemia likely ties back to piperine's unique role as a bioavailability enhancer and metabolic modulator. However, a crucial note of caution remains: much of this promising data is rooted in in-vitro or animal-based preclinical studies. While these findings validate the concepts, they aren't substitutes for rigorous human testing. The observed toxicity signals at higher doses in rat studies also underscore the necessity for precise dosage guidelines [36]. To truly bring *Trikatu* into modern healthcare, we must transition from preliminary studies to high-quality, double-blind, RCTs. These definitive studies will be the key to establishing validated safety margins, optimal dosages, and clear guidelines for its effective integration into clinical medicine.

CONCLUSION(S)

Trikatu stands as a compelling example of traditional wisdom supported by emerging science. The formulation shows exceptional promise across multiple therapeutic areas, particularly in antimicrobial defense, managing inflammation, and supporting metabolic health. To move forward responsibly, the scientific community must commit to robust RCT to fully confirm *Trikatu's* efficacy and secure its place as an evidence based therapeutic agent.

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