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ADVANCED HERBAL DRUG TECHNOLOGY OF TRIPHALA

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ABSTRACT

Sichuan pepper a signature spice of Chinese cuisine, is renowned for its distinctive tingling and numbing sensation an effect attributed to active compounds such as hydroxy-α-sanshool. Beyond its culinary significance, Z. bungeanum holds an esteemed place in traditional medicine and has been extensively studied for its phytochemical, pharmacological, and industrial potential. This review provides an integrated overview of its botany, chemical constituents, biological activities, and diverse applications. The plant contains a rich array of volatile and non-volatile compounds, including terpenes, alkylamides, and polyphenols, responsible for its aroma, flavor, and therapeutic properties. Pharmacological investigations have revealed potent antioxidant, antibacterial, anti-inflammatory, and antiviral activities. Despite significant progress, further research is needed to elucidate its molecular mechanisms, improve compound stability, and establish standardized quality evaluation systems. Overall, Z. bungeanum represents a versatile bioresource with broad scientific, medicinal, and commercial prospects.

KEYWORD: Sichuan pepper, antioxidant activity, antibacterial properties, pharmacological effects, volatile components, non-volatile compounds, traditional medicine, food applications, flavor modulation, essential oil, phytochemistry, medicinal plants.

INTRODUCTION

Sichuan, known as the "land of abundance," is famous for its vibrant cuisine, especially the distinctive "ma" sensation a tingling numbness on the tongue.[1,2] When paired with chili heat, it forms the classic "ma la" flavor seen in dishes like Ma La Hotpot. This numbing effect comes from Huajiao, the dried fruits of Zanthoxylum species.[3] The genus Zanthoxylum consists of more than 200 species of aromatic shrubs and trees distributed mainly across subtropical and temperate zones, with a strong presence in Asia, particularly the Himalayas, East, Central, South, and Southeast Asia.[4]

Owing to its distinctive fragrance and flavor, extracts of Sichuan pepper have been utilized as a flavor-enhancing component in food innovation.[5,6] Its fruits typically emit a pleasant aroma described as spicy, floral, green, and refreshing. However, variations in sensory qualities and chemical composition exist among different species, even though the tingling sensation remains a defining trait (Yang, 2008).In China and other parts of East Asia, Sichuan pepper recognized in the Chinese Pharmacopoeia as Huajiao has long been applied in traditional medicine, appearing in over 35 classical formulations to address ailments such as stomach pain, nausea, diarrhea, toothache, trauma, and parasitic infection.[7] Modern studies attribute these therapeutic effects to bioactive constituents like sanshool and hyperoside, which are known to trigger neurobiological responses and help alleviate pathological conditions.[8,9] Beyond its medicinal relevance, Sichuan pepper also holds promise in the food, pharmaceutical, cosmetic, and agricultural industries, thanks to its diverse properties, including antioxidant, antibacterial, antifungal, lipid-lowering, fragrance, and even skin-firming effects.[10,11]

Botanical Description

Its woody stems, measuring 3–8 centimeters in diameter, are greyish or brownish-grey and covered with tough, sharp thorns.[12] The plant bears compound leaves ranging from 1.5 to 7 centimeters long and 1 to 3 centimeters wide, varying in color from light to deep green. The flowers are unisexual, fragrant, and appear in clusters. These flowers are white to pale yellow and grow in branched clusters at the ends of branches, measuring about 2–6 cm. The main stalk of the cluster is densely hairy. The fruit a spherical follicle, approximately 4–5 millimeters in diameter, covered with numerous small oil glands that give it a rough texture. When ripe, the outer surface appears red to purplish-red, while the inner surface turns yellowish. The pericarps emit a pleasant aroma and produce a characteristic tingling or numbing sensation on the tongue due to the presence of active compounds. Regarding its distribution, Z. bungeanum demonstrates strong ecological adaptability, enabling it to prosper in diverse habitats. The plant is also extensively cultivated across East and South Asia, including Japan, Korea, India, and neighboring regions.

Figure 1: Stem(A), Leaves(B), & the Pericarps(C,D).

Chemical Composition

Volatile components

In contrast, ripe fruits contained higher levels of oxygenated terpenes such as citronellal and geranial, which generated a strong citrus-like aroma.[13] The milder fragrance observed in dried fruits was attributed to heat-induced alterations in volatile composition during processing. The findings demonstrated that physical disruption, including crushing, greatly increased the release of volatiles compared with intact leaves. Yang.[14,15] investigated the essential oil aroma profiles of two Zanthoxylum species Z. bungeanum and Z. simulans using hydrodistillation and identified approximately 120 compounds in each oil. In Z. simulans, linalool, limonene, and sabinene were most abundant, constituting 56% of the oil, while Z. bungeanum contained higher levels of linalyl acetate, linalool, and limonene, together accounting for 40%. Aroma Character Impact (ACI) analysis indicated that linalool was the dominant odor-active compound in both species also contributing substantially in Z. bungeanum. These observations agree with the findings who demonstrated act as mild TRPM8 (menthol) receptor agonists, producing a cooling sensation. Furthermore, solvent extraction methods used to reduce thermal degradation typically associated with hydrodistillation revealed hydroxyl-α-sanshool as the primary compound responsible for the characteristic tingling and numbing effect.[16]

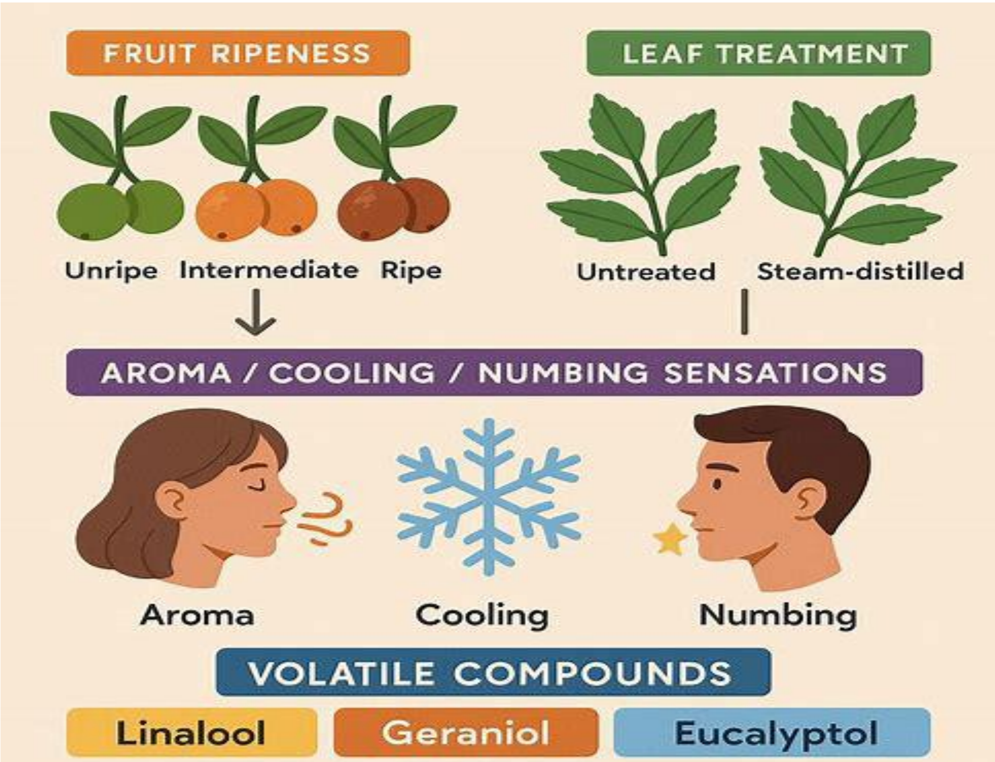

Figure 2: Effect of fruit maturity &leaf processing on volatile sesonary compounds.

Non volatile Components

alklymaides

Alkylamides especially the sanshool group represent the key bioactive and pharmacologically important constituents of Zanthoxylum bungeanum. Within the field of herbal drug technology, alkylamides have attracted considerable interest owing to their distinctive sensory effects, therapeutic potential, and relevance in formulation development.

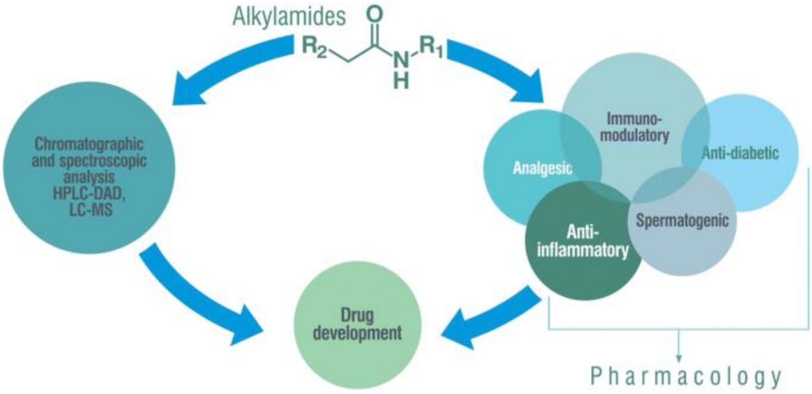

Figure 3: Bioactive alkylamides & their therapeutics actions.

Pharmacology Action

Antioxidant Activity

Carbohydrates derived from the pericarps of Zanthoxylum bungeanum have demonstrated notable antioxidant potential.[17] showing strong activity in vitro. Polysaccharides extracted from the pericarps displayed strong antioxidant potential, demonstrated by high reducing ability, notable ferrous ion chelating activity, and efficient scavenging of both DPPH and hydroxyl radicals, all reflected in low EC_{50} values across the four assay systems.[18] In a comparable investigation, Li, Wang, Li, and Peng (2015) examined the lipid-protective properties of Z. bungeanum leaves and their key polyphenols hyperoside, quercitrin, and chlorogenic acid during the processing of salted fish.[19] Both crude leaf extract & the purified polyphenols exhibited significant antioxidant capacity, particularly through pronounced DPPH radical scavenging. Fish treated with the leaf extract retained higher levels of intrinsic antioxidant enzymes and showed lower TBARS and peroxide values than untreated samples.

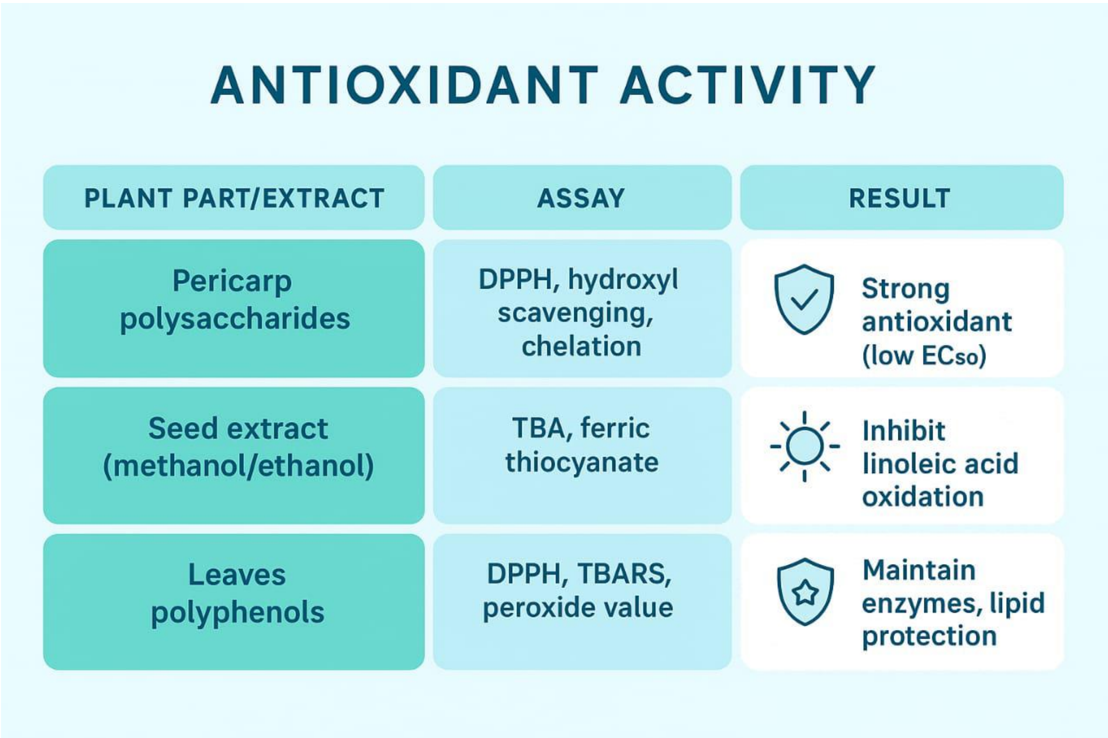

Figure 4: Antioxidant properties of zanthoxylum bungeanum extracts.

Antibacterial and Antiviral Potential

Research shows that Sichuan pepper and its active compounds are capable of reducing the formation of hazardous heterocyclic amines (HAs) produced during the grilling of beef.[20] Both powdered Sichuan pepper and hydroxyl-β-sanshool extracts were shown to decrease HA production at various concentrations, implying that the spice may help reduce long-term health risks linked to regular consumption of charred or grilled meats (Zeng et al., 2018).Beyond this, Zanthoxylum bungeanum essential oil has been incorporated into maize starch-based films, where it not only improved the films' physical properties but also enhanced their antimicrobial activity.[21] The oils appeared to act directly on the viral particles, with MNV-1 being more sensitive, pointing to their potential as natural agents for controlling viral contamination in food. On a broader medical note, infections caused by human rhinoviruses and enteroviruses remain widespread and lack effective treatments. In this context, Choi (2016) tested extracts from several Zanthoxylum species against picornaviruses and found that Z.[22] piperitum leaf extracts had broad-spectrum antiviral activity, reducing viral damage to host cells. This highlights the promise of Zanthoxylum plants as sources of natural compounds for developing new antiviral therapies.

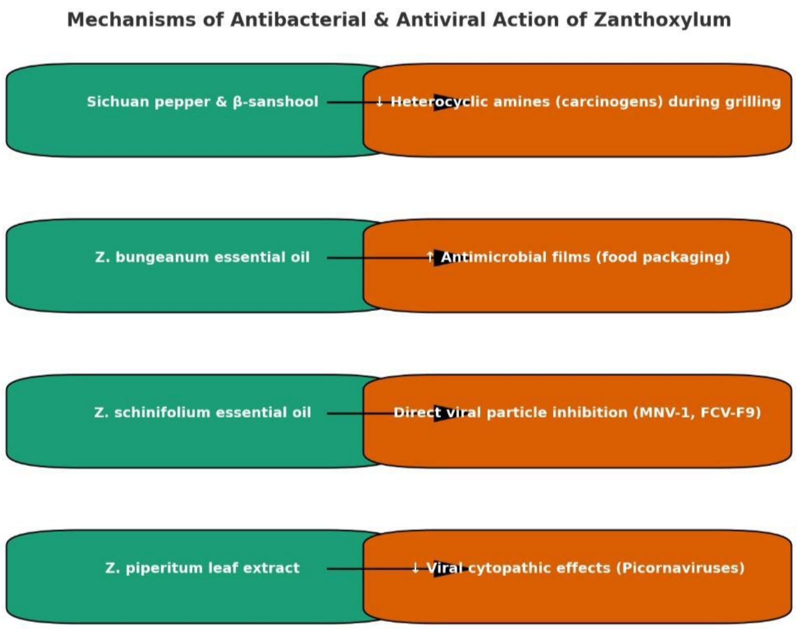

Figure 5: Mechanism of antibacterial & antibacterial action of zanthoxylum.

Application

Flavor Adjustment

Chemesthetic compounds in Sichuan pepper, such as sanshools and hydroxyl-sanshools, have been suggested for use in formulations that combine cooling agents and isothiocyanates to create a unique warming and tingling sensation, enhancing perceived pungency These formulations are intended for use in flavors and fragrances to provide novel sensory experiences.[23,24] Sanshools have also been added to fruit juice products to boost flavor, often together with cooling compounds, helping the beverages remain acceptable in taste even after long periods of warm storage.

Traditional Uses

Cultivation and utilization of Z. bungeanum date back over two millennia in China.[25] The earliest record appears in the Shijing, where its red fruits were prized and symbolically significant. During the pre-Qin era, its pericarps were already used as a distinctive spice for ceremonial dishes.In traditional Chinese medicine, the pericarps are the principal medicinal part, often processed by stir-frying or soaking in vinegar or salt water. Historical medical texts such as Shennong Ben Cao Jing described it as beneficial for strengthening teeth, enhancing eyesight, and dispelling cold and dampness. Later works including Mingyi Bielu and Zhenglei Bencao credited it with promoting blood circulation, easing joint pain, and treating disorders like throat blockage, vomiting, and postpartum abdominal discomfort. Bencao Gangmu.[26,27] documented its effectiveness against toothache, diarrhea, parasitic infections, and swelling. Modern clinical practice continues to employ Z. bungeanum for pain relief, digestive ailments, and itching-related conditions. Over 30 official formulations available as pills, tinctures, powders, and oral liquids include this herb. In Western herbal traditions, plants from the Zanthoxylum genus are referred to as “toothache trees,” valued for their numbing and analgesic properties.Beyond its medicinal value, Z. bungeanum remains a cornerstone of Chinese cuisine as one of the “eight essential condiments.” Its leaves, described in Bencao Gangmu, are also used medicinally to alleviate indigestion and itching. Fresh young leaves serve as garnishes or condiments, and seed oil is extracted for medicinal use, biodiesel production, and industrial purposes, with annual yields exceeding one million metric tons in China. The roots are used in traditional remedies for bruises, epigastric pain, eczema, and snake bites.[28,29]

Procedure

Basics of Fresh Sichuan Pepper Quality Check

The proposed quality evaluation system for fresh Sichuan pepper operates through a three-step workflow, as shown in the corresponding figures. In the initial step (Figure 1b), photographs of mature and semi-mature peppercorns are obtained and then annotated (Figure 1a).In the second stage (Figure 1d), images of pepper clusters are captured from both front & back perspectives. Using the predicted bounding information, individual peppercorns are cropped from the cluster images.The third step (Figure 1f) involves feeding the segmented peppercorn images into the MultiDomain-YOLOv8-cls classifier, which differentiates between mature and semi-mature fruits. For mature samples, the system evaluates color consistency by computing the average variation in local pixel values. Additional metrics—such as the proportion of dark pixels and pixel sparsity—are analyzed to determine the overall quality of the peppercorns.[30]

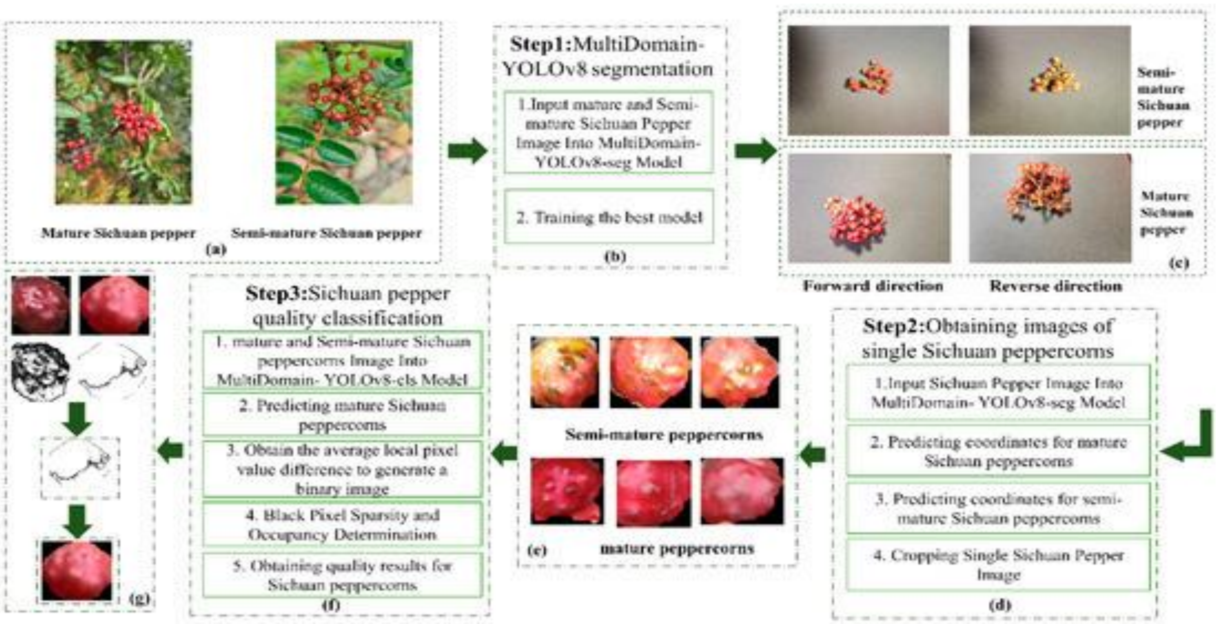

Figure 6: Pepper ripeness detection pipeline.

Sample Collection and Annotation Process

To build an effective training set, a diverse collection of Sichuan pepper samples at various ripeness stages was gathered from Hanyuan County in Sichuan Province, China. The dataset mainly included semi-mature and mature fresh peppercorns to match the classification criteria. Each sample was annotated in accordance with segmentation task requirements. Image collection was completed within a single day, during both morning and afternoon sessions. Since factors such as elevation and temperature influence ripening, photographs were taken from both the mountaintop and lower-elevation areas of the Hanyuan pepper fields. All images were taken using a standard smartphone camera. A total of 1,942 images were generated and annotated, and these were divided into training, validation and testing sets according to a 9:1 ratio for evaluating segmentation performance. Each peppercorn was labeled individually, and Figure X presents examples of the original and annotated images. To further assess the effectiveness of the high-quality pepper classification model, an additional dataset of 520 images of harvested pepper clusters was collected, consisting of 246 semi-mature and 274 mature clusters. Since environmental conditions—such as illumination, rainfall, and temperature—can produce noticeable ripeness differences between the front and back of the clusters, both views were photographed. Capturing these discrepancies allowed the model to learn features from different perspectives, enhancing ripeness and quality prediction accuracy. This multi-angle data acquisition approach expanded the dataset, improved the model's classification precision and generalization capability, and supported more reliable detection of high-quality Sichuan pepper. All images were taken under controlled, consistent lighting conditions, with representative samples shown in Figure X.

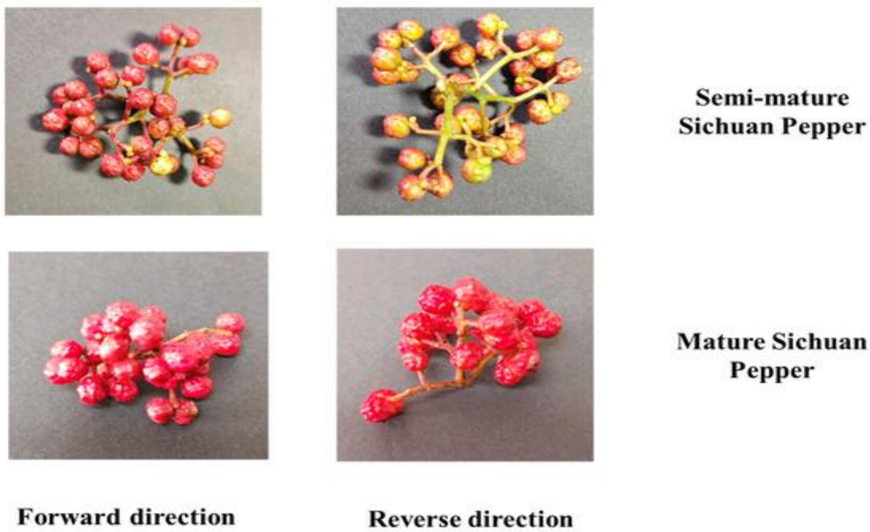

Figure 7: Semi-mature &mature Sichuan pepper samples.

Proposed Instance Segmentation Framework for Sichuan Pepper

YOLOv8 was chosen as the base framework because of its strong adaptability, ease of integration, and high performance in both segmentation and classification tasks, offering an effective balance between accuracy and inference speed.[31] The proposed model expands the standard YOLOv8 architecture by incorporating two new modules. Together, these modules combine information from frequency, spatial, and channel domains at multiple scales, enhancing feature representation and improving model robustness. The full architecture includes attention mechanisms, multi-scale fusion layers, and up-sampling components supported by programmable gradient optimization, forming a lightweight yet precise deep learning network.[32] Within the backbone, two YOLOv9 components—RepNCSPELAN4 and Adown—are integrated. As shown in Figure 4, RepNCSPELAN4 reduces the number of parameters while maintaining strong accuracy. In the shallow layers, where receptive fields are small, this module efficiently captures fine details such as edges, color shifts, and textural patterns by aggregating low-level features across different levels and scales. As the network progresses deeper and semantic information increases, computational demands grow. To handle this, the C2f module enhanced with SE attention is used, allowing the model to prioritize important features and accelerate inference. In addition, the traditional SPPF module from YOLOv8 is replaced with the SPPELAN module, which combines the strengths of SPP and ELAN. This substitution promotes more efficient feature aggregation and further improves overall performance. In the neck of the network, conventional spatial up-sampling typically focuses only on local pixel neighborhoods, limiting access to broader contextual information. The MS-D2F2M module is also incorporated, integrating multi-scale feature information from spatial and channel domains. This allows the network to utilize both detailed local features and global structural patterns. By integrating multi-scale information across spatial, frequency, and channel domains, the enhanced architecture generates a more comprehensive and expressive feature representation. Combined with attention mechanisms and lightweight components, the model achieves improved segmentation accuracy, faster inference, and lower computational cost.[33]

Health Benefits

Strengthens Immunity

High in zinc, this spice supports a healthy immune system. Zinc deficiency can be hard to detect, making regular intake important. Including Sichuan pepper in your diet can help your body better fight infections and stay resilient.[34]

Stimulates Appetite

During recovery from illness, it can be hard to regain appetite. Sichuan pepper contains compounds that enhance metabolism and stimulate hunger, helping your body absorb nutrients more effectively and recover faster.[35,36]

Acts as a Natural Pain Reliever

Sichuan pepper has mild analgesic properties. Certain compounds within it interact with pain receptors to reduce the perception of discomfort. Although not a permanent cure, it can provide temporary relief when applied topically or consumed moderately.[37]

Reduces Inflammation

Rich in antioxidants such as phytosterols and terpenes, Sichuan pepper helps neutralize free radicals that cause oxidative stress and inflammation. Its natural anti-inflammatory effect supports overall wellness.[38]

Improves Bone Health

Packed with essential minerals like phosphorus, manganese, copper, and iron, Sichuan pepper aids in maintaining strong bones and may help prevent age-related conditions like osteoporosis.[39]

Promotes Digestive Health

This spice supports digestion by stimulating gastric activity, reducing bloating, and easing constipation. It also helps prevent inflammation in the stomach lining, keeping your digestive system balanced.[40]

Supports Heart Health

Sichuan pepper contains potassium, which helps relax blood vessels, regulate blood pressure, and reduce cholesterol's harmful effects. Consistent consumption may enhance cardiovascular function and reduce the likelihood of heart attacks and strokes.[41]

Pharmacokinetics

At present, only small number of pharmacokinetic studies have investigated Zanthoxylum bungeanum and its major active constituents. Most available research has centered on the plant's alkylamides, particularly sanshool derivatives such as hydroxy-α-sanshool (HAS), hydroxy-β-sanshool (HBS), and hydroxy-γ-sanshool (HRS). The elimination half-life (t½) was approximately 79.26 minutes, and the area under the concentration–time curve was calculated as 102.015 g·h/kg).[42] In another investigation, Fang et al. (2014) assessed the absorption of alkylamides across different regions of the rat intestine. The half-life (t½) values were 179.33 minutes in the duodenum, 118.03 minutes in the jejunum, 134.01 minutes in the ileum, and 241.51 minutes in the colon, with the jejunum showing the most efficient absorption. A rapid and reliable UHPLC–MS/MS method was later developed to quantify plasma concentrations of HAS, HBS, and HRS in rats. It was detectable in brain tissue within 5 minutes of dosing and was almost completely eliminated within approximately 4 hours.[43]

Toxicology of Sichuan Pepper

For centuries, Zanthoxylum bungeanum has been regarded as a traditional Chinese medicinal herb with minimal toxicity. However, modern research on its toxicological properties remains limited, with most studies focusing on the evaluation of its extract. Early work by Tong et al. (1995) determined lethal dose of water extract of Z. bungeanum in mice was about 45 g/kg following intragastric administration, calculated on the basis of crude herb mass.[16] A subsequent investigation in 2010 reported a slightly higher LD_{50} of 51.14 g/kg with the authors suggesting that variations in plant genetics, growing conditions, and post-harvest processing could explain the differences in toxicity outcomes produced only minor hepatic alterations—such as slight ballooning degeneration, cytoplasmic vacuolization, and occasional necrotic foci—indicating minimal liver toxicity. Complementary in vitro assays using J774.1 macrophage cells revealed no detectable cytotoxic effects at WEZB concentrations of 100, 200, or 400 μg/mL.

More recently, the essential oil of Z. bungeanum (EOZB) has been assessed for its toxic effects. The LD_{50} values for EOZB varied depending on the route of administration—2.27 g/kg for oral (i.g.), 2.03 g/kg for intraperitoneal (i.p.), 4.64 g/kg for intramuscular (i.m.), and 5.32 g/kg for subcutaneous (i.h.) injections. Mice exposed to lethal doses exhibited symptoms such as lethargy, diarrhea, irregular heartbeat, limb twitching, and in some cases, death.[44]

Future perspective of Sichuan Pepper

Zanthoxylum bungeanum Maxim has been utilized across Asia for centuries as both a valued medicinal herb and a flavorful culinary ingredient. Extensive research has led to the isolation and identification of numerous chemical constituents from this plant, confirming its significance as an effective and versatile traditional remedy. Over the past decade, remarkable advancements have been achieved in understanding its pharmacological and chemical properties. Nonetheless, several scientific and practical challenges remain that require deeper exploration to support its broader clinical application. First, most pharmacological investigations have concentrated on crude extracts and formulations, with limited studies elucidating the precise mechanisms behind its therapeutic effects. Further research should therefore focus on identifying specific bioactive molecules, clarifying their mechanisms of action, and establishing detailed structure–activity relationships. Second, data on the pharmacokinetics and clinical evaluation of Z. bungeanum remain scarce. Toxicological assessments at the molecular and cellular levels are also limited.[45] Future studies should expand pharmacokinetic analyses to compounds beyond alkylamides and conduct more rigorous toxicity evaluations to ensure safety in clinical use. Third, hydroxyl-α-sanshool (HAS) has been recognized as a key active compound responsible for both the characteristic tingling sensation and several biological activities. However, its chemical instability—especially its sensitivity to oxygen due to a conjugated triene structure—poses a major challenge. Developing more stable analogs or derivatives of HAS and related sanshools through structural modification would improve their potential for pharmaceutical and industrial applications. Fourth, the number of traditional formulations and processed products containing Z. bungeanum has declined over time. To revitalize its clinical relevance, it is essential to design new medicinal preparations and modern product forms that meet contemporary therapeutic needs. Fifth, research has so far emphasized the pericarps, while other plant parts—such as leaves, seeds, stems, and roots—have received far less attention. Comprehensive investigation into the chemical composition and pharmacological potential of each plant part would promote the full utilization of this species. Sixth, due to the plant's rich biodiversity and its morphological similarity to other Zanthoxylum species, correct identification and quality control remain challenging. Hence, developing standardized authentication techniques and establishing a unified international quality evaluation system are critical for ensuring consistency and safety in its use. Finally, considering its broad geographical distribution and large-scale cultivation, improving harvesting efficiency and maintaining high product quality should be prioritized. In summary, the literature provides detailed information on the traditional uses, plant traits, chemical makeup, pharmacology, pharmacokinetics, and safety of Z. bungeanum. Continued research addressing the outlined challenges will enhance our comprehensive understanding of this plant and support its future development as both a medicinal and functional food resource.

CONCLUSION

Sichuan pepper (Zanthoxylum bungeanum) is a valuable spice with rich phytochemical diversity and significant medicinal potential. Its active compounds contribute to antioxidant, anti-inflammatory, antibacterial, and analgesic effects, making it useful in food, pharmaceutical, and cosmetic industries. Modern techniques, such as AI-based quality classification, further enhance its commercial value. However, more research on its pharmacokinetics, toxicity, and compound stability is needed to ensure safe and standardized applications. Overall, it represents a promising natural resource with broad scientific and industrial prospects**.**

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