

Review

Jiawa (ཇཡ་བ་) in Tibetan Medicine: A Review of Multi-Origin Use, Shared and Differential Chemical Constituents, and Pharmacological Relevance to Huangshui-Associated Joint Disorders

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Abstract

Jiawa (Wylie: lca ba) is a multi-origin Tibetan medicinal material used in classical prescriptions for Huangshui (Wylie: chu ser) disorders. This review summarizes traditional, phytochemical, and pharmacological evidence to discuss how the traditional use of Jiawa-related materials in Huangshui-associated joint disorders may be interpreted. Classical *materia medica* records, official standards, regional medicinal-use reports, and biomedical literature were integrated, with emphasis on three representative Jiawa-related sources: *Vicatia tibetica* de Boiss., *Sphallerocarpus gracilis* (Bess.) K.-Pol., and *Pleurospermum hookeri* C. B. Clarke var. *thomsonii* C. B. Clarke. The currently available phytochemical evidence indicates that these three sources differ in their reported chemical profiles, while several constituents have been documented in more than one source. Among the constituents reported from at least two representative sources, β -sitosterol, bergapten, ferulic acid, 3,5-dicaffeoylquinic acid, ligustilide, daucosterol, and isoimperatorin have been studied in arthritis-related experimental models involving inflammation, oxidative stress, immune regulation, angiogenesis, cartilage or bone damage, and pain signaling. In addition, constituents reported from individual sources are discussed according to the available constituent-level evidence. These studies mainly involve inflammation, oxidative stress, synovial hyperplasia, and bone metabolism for *V. tibetica*; inflammatory-pathway modulation for *S. gracilis*; and immune regulation, antioxidant protection, and cartilage or matrix preservation for *P. hookeri* var. *thomsonii*. Taken together, the available evidence provides preliminary chemical and pharmacological clues for understanding the traditional use of Jiawa-related materials in Huangshui-associated joint disorders. However, these observations are based mainly on phytochemical reports and constituent-level pharmacological studies. The relevance of these findings to authenticated Jiawa-related medicinal materials and Huangshui-associated disorders therefore requires further verification through direct comparative studies.

Keywords: Jiawa; Sowa Rigpa; Huangshui; Tibetan medicine; phytochemistry

1. Introduction

Jiawa (Wylie: lca ba) is an important medicinal material in Tibetan medicine and is traditionally used in classical Tibetan prescriptions for Huangshui-related disorders. According to the *Crystal Pearl Materia Medica*, Jiawa is traditionally classified into three types based on its distribution, flower color, and morphological characteristics: mountain-growing Jiaguo, field-growing Jiayong, and forest-associated Walang Jiawa [1]. Jiaguo is mainly recorded for snakebite poisoning and is regarded as the principal medicinal material in the “five roots” group; Jiayong is recorded for Huangshui-related disorders, particularly those involving cold-type bad-kan and gastric disease patterns; and Walang Jiawa is recorded as non-medicinal [2]. Although Jiaguo and Jiayong differ in their recorded traditional indications, both are traditionally associated with Huangshui-related disorders [2]. These records suggest that Jiawa was historically understood as a heterogeneous medicinal category rather than as a medicinal material with a single fixed botanical origin.

More recent literature indicates that the botanical-source attribution of Jiawa-related medicinal materials remains complex [3]. Several Apiaceae taxa have been recorded or used under Jiawa-related names, with botanical-source descriptions differing among classical texts, Tibetan medicinal standards, and regional clinical practice [3]. In modern Tibetan medicinal standards and clinical-use records, *V. tibetica* is recorded as a representative Jiawa-related source in Tibet, *S. gracilis* in Aba and Chamdo, and *P. hookeri* var. *thomsonii* in Qinghai (Supplementary Table 1). However, their correspondence with the botanical origins described in classical Tibetan *materia medica* has not been established through systematic textual research. Therefore, these taxa should not be regarded as confirmed botanical origins of classical Jiawa.

The possible relevance of Jiawa-related medicinal materials to modern arthritis research may be considered in relation to the traditional Tibetan medical concept of Huangshui, particularly when Huangshui affects the bones and joints [4]. In Tibetan medicine, Huangshui involving the



bones and joints may present as bone pain, arthralgia, restricted movement, and joint swelling [4]. These manifestations partially overlap with joint pain, swelling, functional limitation, synovial inflammation, cartilage destruction, and bone erosion observed in rheumatoid arthritis (RA) and other inflammatory joint disorders [4,5,6]. Therefore, contemporary pharmacological evidence from RA and other inflammatory joint disease models may provide a useful reference framework for discussing the bioactive constituents and possible mechanisms of Jiawa-related medicinal materials in Huangshui-associated bone and joint disorders. However, Huangshui-associated disorders should not be equated with RA; rather, their connection is based primarily on similarities in selected clinical manifestations and pathological processes.

In recent years, research on the phytochemistry and pharmacological activities of Jiawa-related medicinal materials have gradually increased [7]. The available evidence indicates that different Jiawa-related medicinal materials have different reported chemical profiles, and several constituents have been reported from more than one source [8]. However, the existing studies are somewhat fragmented and mainly focused on individual Jiawa-related materials, isolated compounds, and specific pharmacological models. Integrated analyses linking traditional use, botanical origin, reported chemical constituents, and pharmacological evidence in the context of multi-origin use and regional medicinal substitution remain limited.

This review focuses on three representative Jiawa-related medicinal materials: *Vicatia tibetica* de Boiss., *Sphallerocarpus gracilis* (Bess.) K.-Pol., and *Pleurospermum hookeri* C. B. Clarke var. *thomsonii* C. B. Clarke [8]. By integrating traditional records, botanical-source information, reported phytochemical data, and arthritis-related pharmacological evidence, this review discusses the multi-origin use of Jiawa-related materials in the context of Huangshui-associated joint disorders.

2. Literature Search and Evidence Organization

This review was designed to integrate traditional records, botanical-source information, phytochemical data, quality-control evidence, and pharmacological studies related to Jiawa-related medicinal materials. Targeted searches were conducted in classical Tibetan materia medica texts, official standards for Tibetan medicines, regional medicinal-use records, and electronic databases, including PubMed (<https://pubmed.ncbi.nlm.nih.gov/>), Web of Science (<https://www.webofscience.com/>), CNKI (<https://www.cnki.net/>), and WanFang Data (<https://www.wanfangdata.com.cn/>) for literature published up to May 13, 2026. The English search terms included (“Jiawa” OR “lca ba” OR “Huangshui” OR “chu ser”) AND (“Tibetan medicine” OR “Sowa Rigpa” OR “traditional use”), as well as (“*Vicatia tibetica*” OR “*Sphallerocarpus gracilis*” OR “*Pleurospermum hookeri* var. *thomsonii*”) AND (“phytochem-

istry” OR “chemical constituents” OR “quality control” OR “pharmacology” OR “anti-inflammatory” OR “anti-arthritis” OR “rheumatoid arthritis” OR “osteoarthritis”). Equivalent Chinese-language search terms corresponding to Jiawa, Huangshui, Tibetan medicine, the three representative botanical sources, phytochemistry, quality control, pharmacology, anti-arthritis activity, RA, and osteoarthritis (OA) were used in CNKI and WanFang Data.

Records were included if they addressed at least one of the following: classical or traditional records of Jiawa-related names, functions, indications, or prescriptions; official or regional records of medicinal sources and use; botanical information on Jiawa-related source plants; phytochemical, fingerprinting, or quality control studies of Jiawa-related medicinal materials; and pharmacological studies of Jiawa-related source plants, extracts, or reported constituents.

Records were excluded if they were unrelated to Jiawa-related medicinal materials, did not provide identifiable traditional, botanical, chemical, or pharmacological information, were duplicative, or fell outside the scope of this review regarding the traditional use, phytochemistry, or pharmacology of Jiawa. For compound-level evidence, studies were considered only when the investigated constituent had been reported from at least one Jiawa-related source plant, and the experimental evidence was relevant to the pharmacological discussion in this review.

Information on traditional names, botanical sources, medicinal use, prescriptions, reported constituents, source plants, experimental models, pharmacological effects, and reported or proposed mechanisms was extracted and synthesized. Because this review combines classical *materia medica* records, official standards, regional medicinal-use documents, phytochemical and quality-control studies, and experimental pharmacological evidence, it does not address a single, predefined clinical or intervention question suitable for PRISMA-based systematic screening. Accordingly, the evidence was organized according to source type and relevance to the topic, and synthesized narratively. Classical Tibetan medical texts, *materia medica* works, official standards, and regional records were used to summarize traditional names, source information, functions, indications, and prescription details, whereas pharmacological interpretations were based on experimental studies cited in the corresponding sections and tables. After applying these criteria, the final evidence synthesis included approximately 9 classical or Tibetan materia medica texts, 7 official or regional standards or medicinal-use records, 10 phytochemical reports, 3 quality-control or source-authentication studies, and 44 pharmacological studies.

3. Traditional Records, Botanical Origins and Clinical Applications

Jiaguo typically grows on shaded, moist mountain slopes and is characterized by finely divided leaves, red umbellate flowers, and surfaces covered with spines or coarse

hairs. Jiayong is commonly found along field margins, and its stems, leaves, and fruits resemble those of caraway. Jiayong has purple stems and white flowers. Walang Jiawa mainly grows in rocky mountain areas or forested sites and is morphologically similar to Jiayong [2]. These descriptions provide historical criteria for distinguishing different Jiawa types in classical Tibetan *materia medica*.

Classical Tibetan medical texts and regional *materia medica* records document the traditional indications and clinical use of Jiawa-related medicinal materials. These records indicate that Jiawa is traditionally used mainly within the indication spectrum of Huangshui-related disorders. Its recorded functions include clearing Huangshui, dispelling cold, tonifying deficiency, warming and strengthening the kidney and lumbar region, regulating gastric function, and relieving wind-dampness-related symptoms. In clinical-use records, Jiawa is applied to Huangshui-related conditions characterized by lumbar pain, gastric coldness, physical weakness, bad-kan-related patterns, and joint-related symptoms, especially when Huangshui affects the bones and joints [7,9]. Detailed source-specific records are summarized in **Supplementary Table 1**.

Later Tibetan *materia medica* texts further supplemented the recorded medicinal properties and traditional indications of Jiawa. The *Revised Crystal Pearl Materia Medica* describes Jiawa as pungent and astringent in taste, with warming properties, and records its use for cold-type Huangshui disorders and joint-related conditions, including joint swelling and swelling with pain [1]. Other relevant sources have also reported properties such as clearing heat, resolving toxicity, activating blood circulation, draining dampness, and dispelling cold, with applications in poisoning disorders, chronic heat diseases, insect and snake bites, dyspepsia, and wind-cold-dampness arthralgia. The traditional functions, recorded indications, medicinal parts, regional-use contexts, botanical-source records, and documentary basis for botanical-source attribution of Jiawa-related medicinal materials are summarized in **Supplementary Table 1**.

In clinical practice, Jiawa is commonly used in traditional compound formulations, such as the Twenty-five-Ingredient Catechu Pill, Pomegranate Sun-Wheel Pill, and Five-Root Powder. These formulations are mainly indicated for rheumatic arthralgia, joint swelling and pain, cold pain of the lumbar region and legs, and kidney deficiency with cold-type features. They are also indicated for Tibetan medical disease categories, such as Huangshui disease, white-channel disease (rtsa dkar), and Gangba disease. The compositions and traditional indications of representative Jiawa-related prescriptions are summarized in **Supplementary Table 2**.

Overall, classical *materia medica* records and traditional clinical-use records suggest that different Jiawa types are not identical in distribution, morphology, medic-

inal properties, or recorded traditional indications. However, their recorded traditional indications partly overlap within the broader context of Huangshui-related conditions, especially manifestations involving cold-type kidney and lumbar patterns and joint-associated symptoms such as swelling, pain, and impaired movement (**Supplementary Tables 1,2**). This traditional indication pattern provides a historical and medical context for the phytochemical and pharmacological discussion below. At the same time, the multi-origin use of Jiawa-related medicinal materials raises practical concerns, because different regions, standards, and traditional names may correspond to different botanical sources. This may lead to taxonomic ambiguity, difficulties in source authentication, regional medicinal substitution, mixed use or adulteration, and challenges in quality control, standardized clinical use, and the establishment of quality standards.

4. Comparative Phytochemistry of Representative Jiawa-Related Materials

Phytochemical investigations of Jiawa-related medicinal materials remain limited, and the overall phytochemical features of the three representative sources have not been fully characterized. In the studies reviewed here, 34 compounds have been reported from *V. thibetica*, 23 from *S. gracilis*, and 24 from *P. hookeri* var. *thomsonii* (**Supplementary Tables 3,4,5** and **Supplementary Figs. 1,2,3**). Because these studies vary in extraction procedures, analytical platforms, detection sensitivity, and depth of reporting, the summarized constituents should be regarded as literature-reported data rather than as complete phytochemical profiles. The available evidence is therefore not sufficient to define source-specific chemical markers for the three medicinal materials.

For comparative purposes, constituents reported in at least two of the three representative Jiawa-related medicinal materials were grouped as shared reported constituents (Fig. 1), whereas selected constituents reported only from individual materials and supported by available arthritis-related pharmacological evidence are presented as other reported constituents (Fig. 2). The remaining reported constituents are listed in **Supplementary Tables 3,4,5**. This arrangement was used to compare the reported phytochemical overlap and current patterns of compound-class reporting among the three materials.

Existing studies on *V. thibetica* have mainly reported phenolic acids and their derivatives, particularly caffeoylquinic and feruloylquinic acid derivatives, as well as flavonoids, coumarins, phthalides, and isoquinoline alkaloids [7,10,11]. Studies on *S. gracilis* have mainly reported coumarin derivatives, including simple coumarins, furanocoumarins, and pyranocoumarins, as well as polyacetylenes [12]. Studies on *P. hookeri* var. *thomsonii* have mainly reported fatty acids and their derivatives, flavonoids, chalcones, coumarins, and phenolic acids. Detailed constituent records and the corresponding primary

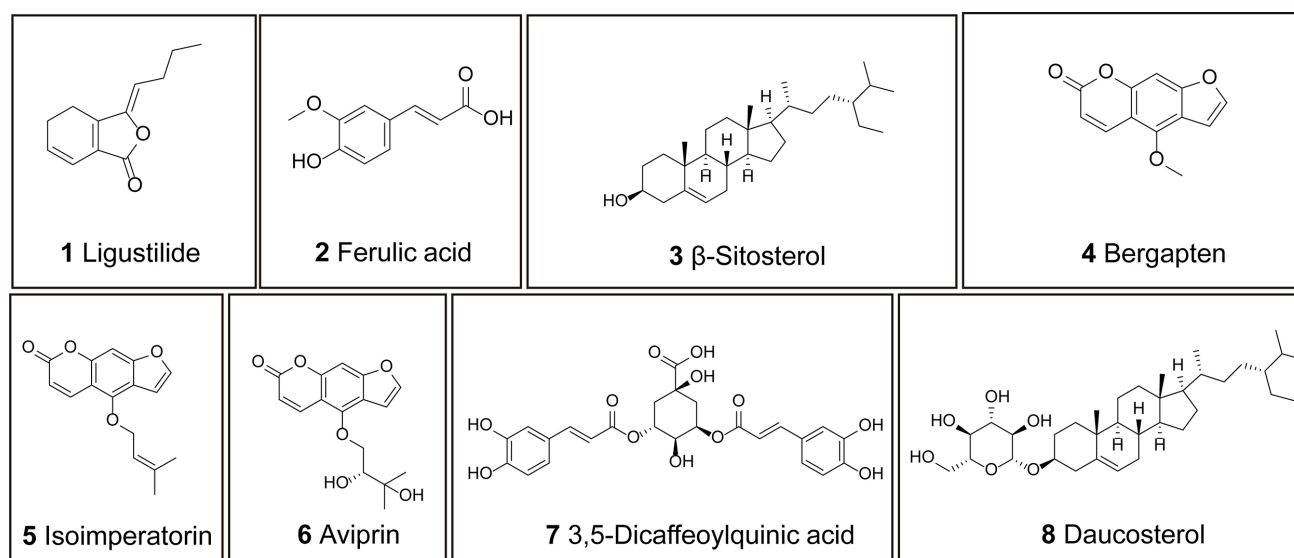


Fig. 1. Chemical structures of shared reported constituents in representative Jiawa-related medicinal materials. The compounds shown include ligustilide, ferulic acid, β -sitosterol, bergapten, isoimperatorin, aviprin, 3,5-dicaffeoylquinic acid, and daucosterol. These constituents have been reported from at least two representative Jiawa-related medicinal materials and are grouped here as shared reported constituents.

sources for the three materials are provided in **Supplementary Tables 3,4,5**.

Taken together, the available phytochemical literature indicates both partial overlap and different reporting emphases among the three representative Jiawa-related medicinal materials. The overlap is reflected by the shared constituents shown in Fig. 1 and by recurring compound classes such as phenolic acids, flavonoids, coumarins, sterols, and phthalides. The differences in reporting emphasis are mainly reflected by phenolic acid derivatives, phthalides, and isoquinoline alkaloids in reports on *V. tibetica*; coumarin derivatives and polyacetylenes in reports on *S. gracilis*; and fatty acid derivatives, flavonoids, chalcones, coumarins, and phenolic acids in reports on *P. hookeri* var. *thomsonii* (**Supplementary Tables 3,4,5**). This comparison provides a concise overview of the currently reported phytochemical data for the three Jiawa-related medicinal materials.

5. Arthritis-Related Pharmacological Evidence

Based on the traditional indications and comparative phytochemical findings summarized above, this section reviews the available pharmacological evidence concerning constituents reported from Jiawa-related medicinal materials in the context of arthritis and joint-related disorders. In Tibetan medicine, Huangshui involving the bones and joints may manifest as joint-related symptoms or disorders. Therefore, studies involving rheumatoid arthritis (RA), osteoarthritis (OA), and other inflammatory joint-disease models were used as the main pharmacological reference. Evidence from non-joint disease models, such as gastritis, dermatitis, or chronic pruritus, was

included only when it was relevant to other traditional Huangshui-associated manifestations. Such evidence was considered supplementary symptom-related information rather than direct evidence for Huangshui-associated joint disorders. To clarify the evidence hierarchy, Table 1 (Ref. [13,14,15,16,17,18,19,20]), Table 2 (Ref. [21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56]) classify the cited studies into four categories: I, direct evidence from Jiawa-related medicinal materials or extracts; II, isolated-compound evidence from arthritis or joint-disease models; III, isolated-compound evidence from non-joint inflammatory models; and IV, supplementary evidence indirectly linked to Huangshui-related manifestations.

5.1 Shared Reported Constituents and Arthritis-Related Pharmacological Relevance

Among the constituents reported from at least two representative Jiawa-related medicinal materials, β -sitosterol, bergapten, ferulic acid, 3,5-dicaffeoylquinic acid, ligustilide, daucosterol, and isoimperatorin have been associated with arthritis-related pharmacological activities. Although aviprin was also identified as a shared reported constituent, no eligible arthritis- or joint-related pharmacological studies were identified; therefore, it was not included in Table 1 or the subsequent pharmacological discussion. These shared reported constituents have been reported to influence pathological processes relevant to inflammatory joint disorders, including inflammatory cytokine production, oxidative stress, immune imbalance, synovial angiogenesis, cartilage degradation, bone resorption, and pain signaling (Table 1).

Table 1. Reported arthritis-related pharmacological effects and mechanisms of shared constituents from representative Jiawa-related medicinal materials.

Constituent	Compound class	Model/evidence	Reported arthritis-related pharmacological effects	Reported pathway/mechanism	Evidence group (I–IV)	Ref.
β -Sitosterol	Sterol	AIA	Reduced paw edema and arthritis index; increased body weight; decreased MDA and increased SOD, GSH and CAT; reduced TNF- α , IL-1 β , IL-2, IL-6, IL-16 and IL-17, and increased IL-10 and TGF- β ; decreased COX-2, PGE2, VEGF, NF- κ B, RANKL and STAT3	NF- κ B inhibition; HO-1/Nrf2 activation	Group II	[13]
Bergapten	Furanocoumarin	AIA	Reduced paw swelling, arthritis score and pain; increased body weight; decreased mRNA expression of IL-6, COX-2, TNF- α and NF- κ B; increased IL-4; alleviated pathological injury of the ankle joint and sciatic nerve	STAT3 inhibition; NF- κ B inhibition	Group II	[14,20]
Ferulic acid	Phenolic acid	AIA	Reduced paw volume and arthritis index; increased body weight, A/G ratio and Hb; decreased ESR, lymphocyte percentage, CRP, RF, TNF- α , JAK2 and TGF- β	JAK/STAT inhibition	Group II	[15]
3,5-Dicaffeoylquinic acid (Isochlorogenic acid A)	Phenolic acid	Osteoclast differentiation model	Inhibited osteoclast differentiation and bone resorption; decreased MMP13, IL-1 β , IL-23 and IL-17; reduced p-ERK, p-JNK and p-p38	IL-17/MAPK inhibition	Group II	[16]
Ligustilide	Phthalide	RANKL-induced osteoclastogenesis and bone resorption models	Inhibited RANKL-induced osteoclastogenesis and bone resorption; reduced RANK expression and osteoclast-related marker expression	RANK expression inhibition	Group II	[17]
Daucosterol	Sterol glycoside	OA model; chondrocyte senescence model	Alleviated osteoarthritis development; reduced chondrocyte senescence and ROS; restored mitochondrial function	JNK signaling inhibition	Group II	[18]
Isoimperatorin	Furanocoumarin	KOA rats; synovial cells	Reduced synovial inflammation and fibrosis in knee osteoarthritis; improved inflammation and fibrosis-related changes in synovial cells	cAMP signaling pathway regulation	Group II	[19]

Note: The following abbreviations are used: CIA, collagen-induced arthritis; AIA, adjuvant-induced arthritis; A/G, albumin/globulin ratio; Hb, hemoglobin; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; RF, rheumatoid factor; OA, osteoarthritis; KOA, knee osteoarthritis; RANKL, receptor activator of nuclear factor κ B ligand; MDA, malondialdehyde; SOD, superoxide dismutase; GSH, glutathione; CAT, catalase; ADAMTS, a disintegrin and metalloproteinase with thrombospondin motifs. Evidence group (I–IV) indicates the relationship between the cited pharmacological model and Huangshui-associated joint disorders. The four evidence groups used in this review are: I, direct evidence on Jiawa-related materials or extracts; II, isolated compound evidence in arthritis or joint-disease models; III, isolated compound evidence in non-joint inflammatory models; and IV, supplementary evidence indirectly linked to Huangshui-related manifestations. The entries in this table are classified as Group II because they are based on isolated constituents studied in arthritis, osteoarthritis, osteoclastogenesis, synoviocyte, chondrocyte, or other joint-related models. No entry in this table provides group I direct evidence on authenticated Jiawa-related materials or extracts. This classification reflects model relevance rather than the formal risk of bias or evidence-quality grading.

Table 2. Reported pharmacological relevance and potential mechanisms of source-associated reported constituents in representative Jiawa-related medicinal materials.

Source	Constituent	Compound class	Model/evidence	Reported pharmacological relevance	Reported pathway/mechanism	Evidence group (I–IV)	Ref.
VT	Quinic acid	Organic acid	AIA rats	Improved HDL and antioxidant enzyme levels; increased DDAH and cortistatin; reduced lipid-related indices, ADMA, homocysteine, MDA, nitrite, and mRNA expression of IL-6, IL-1 β and TNF- α .	Reduced inflammation and oxidative stress	Group II	[35]
VT	Umbelliferone	Coumarin	MH7A cells; AIA rats	Inhibited MH7A cell migration and invasion; suppressed F-actin remodeling; reduced IL-1 β , IL-6, IL-8, MMP-2 and MMP-9; alleviated joint damage and synovial inflammation.	Wnt/ β -catenin inhibition	Group II	[36]
VT	8-Methoxypsoralen	Furanocoumarin	OA rats; chondrocytes	Reduced Bax and caspase-3, increased Bcl-2, decreased IL-6, TNF- α and IL-1 β , reduced MDA, increased SOD and GSH-PX, and alleviated pain-related responses.	Sirt1 (sirtuin1) /AMPK activation; NF- κ B inhibition	Group II	[37]
VT	Caffeic acid	Phenolic acid	AIA rats	Reduced paw edema, inflammatory cell infiltration, pannus formation, cartilage and bone destruction, NF- κ B, CHI3L1, IL-1 β , MMP-9 and VEGF; decreased lipid peroxidation and NO; increased GSH and reduced caspase-3.	NF- κ B/CHI3L1/IL-1 β inhibition	Group II	[38]
VT	Rhein	Anthraquinone	AIA rats; RA-FLS cells	Reduced JUN, PTGS2 and TNF- α expression; inhibited abnormal RA-FLS proliferation.	p-JUN/JUN inhibition	Group II	[39]
VT	Apigenin	Flavonoid	CIA mice; FLS cells	Reduced arthritis index, synovial hyperplasia, inflammatory cell infiltration, pannus formation, FLS proliferation, angiogenic factors and osteoclast-related signaling; promoted FLS apoptosis and regulated cell-cycle progression.	Regulation of RANKL/RANK/OPG signaling	Group II	[23]
VT	Quercetin	Flavonoid	CIA rats; MH7A cells	Reduced arthritis score, ankle bone destruction, serum IL-1 β , IL-6, IL-17 and TNF- α ; inhibited MH7A proliferation, migration, invasion and glycolytic metabolism; promoted apoptosis.	JAK1/STAT3/HIF-1 α inhibition	Group II	[40]

Table 2. Continued.

Source	Constituent	Compound class	Model/evidence	Reported pharmacological relevance	Reported pathway/mechanism	Evidence group (I–IV)	Ref.
VT	Chlorogenic acid	Phenolic acid	CIA mice; MH7A cells	Reduced joint swelling, arthritis index, paw thickness, histological injury, bone erosion, TNF- α , BAFF and MH7A proliferation; promoted apoptosis.	NF- κ B and BAFF inhibition	Group II	[22]
VT	Neochlorogenic acid	Phenolic acid	A549 inflammatory cell model	Reduced TNF- α , IL-6, NO, iNOS, COX-2, NF- κ B activation and MAPK phosphorylation; increased HO-1 expression.	AMPK/Nrf2 activation	Group III	[21]
VT	4-Caffeoylquinic acid	Phenolic acid	RAW264.7 cells	Reduced NO, IL-6, TNF- α , iNOS, COX-2, TLR4, NF- κ B activation, MAPK phosphorylation, MDA and ROS; increased GSH, SOD and HO-1.	NF- κ B/MAPK inhibition; Nrf2/HO-1 activation	Group III	[41]
VT	3-Feruloylquinic acid	Phenolic acid	RAW264.7 cells	Enhanced antioxidant capacity and reduced NO, IL-1 β , IL-6, iNOS, COX-2 and NF- κ B expression.	NF- κ B inhibition	Group III	[42]
VT	4-Feruloylquinic acid	Phenolic acid	RAW264.7 cells	Reduced NO release.	NO suppression	Group III	[42]
VT	5-Feruloylquinic acid	Phenolic acid	RAW264.7 cells	Reduced NO release.	NO suppression	Group III	[42]
VT	Isochlorogenic acid B	Phenolic acid	HEK293 cells; dermatitis/chronic itch models	Reduced TRPV3 current and channel opening probability; alleviated ear swelling and chronic itch; reduced keratinocyte death.	TRPV3 inhibition	Group IV	[43]
VT	Isochlorogenic acid C	Phenolic acid	Acute gastritis mice; AGS cells	Protected gastric mucosa; increased PGE ₂ , Ptg1 and Muc6; reduced inflammatory mediators and mitochondrial ROS; preserved mitochondrial membrane potential.	PTGS1 activation; inflammatory pathway inhibition	Group IV	[26]
VT	(+)-Ursolic acid	Triterpenoid	RANKL-induced osteoclastogenesis; titanium particle-induced calvarial osteolysis	Inhibited osteoclast differentiation and bone resorption; attenuated titanium particle-induced osteolysis and reduced TRAP-positive osteoclasts.	NF- κ B and JNK inhibition; NFATc1/c-Fos-related osteoclastogenesis regulation	Group II	[44]
VT	Senkyunolide I	Phthalide	Chondrocytes	Reduced P16, P21, MMP13, ADAMTS5, mitochondrial dysfunction and ROS; increased COL2A1 and ACAN.	Nrf2/HO-1 activation	Group II	[25]
VT	Jatrorrhizine	Isoquinoline alkaloid	CAG rats	Improved gastric function; reduced gastric mucosal injury, inflammatory infiltration, H. pylori colonization, bacterial burden and inflammatory cytokines; increased gastric mucosal protective factors.	NF- κ B/NLRP3 inhibition	Group IV	[45]

Table 2. Continued.

Source	Constituent	Compound class	Model/evidence	Reported pharmacological relevance	Reported pathway/mechanism	Evidence group (I–IV)	Ref.
VT	Palmitine	Isoquinoline alkaloid	RAW264.7 cells; gouty arthritis mice	Reduced IL-1 β , IL-6, IL-18, TNF- α , MDA, NLRP3, ASC, caspase-1, joint swelling and synovial neutrophil infiltration; increased SOD and GSH.	NF- κ B/NLRP3 inhibition; Nrf2 activation	Group II	[46]
VT	Genistein	Isoflavone	CIA mice; FLS cells	Reduced paw swelling, joint structural damage, MMP-9, TNF- α , IL-1 β , IL-6, Rab27a, nSMase2, Mfge8, exosome secretion, β -catenin signaling and FLS migration; promoted osteogenic differentiation and mineralization.	Rab27/nSMase2/Mfge8 inhibition	Group II	[47]
VT	Formononetin	Isoflavone	OA rat model	Reduced osteoclast-related proteins, inflammatory proteins, osteoclast formation and differentiation, cartilage degradation, serum inflammatory factors, bone turnover markers, RAGE and ROS.	RAGE-RAS and NF- κ B/MAPK inhibition	Group II	[24,54]
SG	Esculetin	Coumarin	Yeast-induced pyrexia; acetic acid-induced writhing	Reduced fever, pain, inflammatory responses, COX-2, PGE2, IL-1 β , IL-12 and TNF- α ; increased HSC70 binding and decreased HSC70 protein level/activity, p-p38, ERK, Akt and AMPK.	HSC70/p38-MAPK inhibition	Group IV	[27]
SG	4'-O- β -D-glucosyl-5-O-methylvisamminol (5-O-methylvisammioside)	Chromone glycoside	RAW264.7 macrophages; RA-FLSs	Reduced inflammatory factors and abnormal proliferation; promoted apoptosis.	NF- κ B inhibition	Group II	[28]
SG	Falcarinol (Panaxynol)	Polyacetylene	CIA rats; RA-FLSs	Alleviated joint inflammation and pathological changes; inhibited RA-FLS proliferation, migration and invasion; promoted apoptosis.	TLR4/NF- κ B pathway inhibition	Group II	[55]
PH	Scopoletin	Coumarin	HFLS-RA cells	Inhibited abnormal RA-FLS proliferation, migration and invasion; reduced p-p65 and p-I κ B- α .	NF- κ B inhibition	Group II	[48]
PH	Chalcone	Chalcone	CFA-induced arthritis rats	Reduced paw edema and arthritis index; alleviated joint inflammation; decreased TNF- α , IL-1 β , IL-6 and IL-17 expression; showed analgesic properties.	Downregulation of TNF- α , IL-1 β , IL-6 and IL-17	Group II	[49]

Table 2. Continued.

Source	Constituent	Compound class	Model/evidence	Reported pharmacological relevance	Reported pathway/mechanism	Evidence group (I–IV)	Ref.
PH	Isoliquiritigenin	Chalcone	C20A4 chondrocytes; AIA rats	Increased cell viability; reduced ROS, Bax, cleaved caspase-3, iNOS, MMP13, arthritis index, paw swelling, cartilage damage and serum MMP13; increased Bcl-2, PGC-1 α , Sirt1, Nrf2 and HO-1.	Sirt1/PGC-1 α –Nrf2/HO-1 activation	Group II	[34]
PH	Licochalcone A	Chalcone	CIA/CAIA mice; RASFs	Inhibited RASF proliferation; promoted cell-cycle arrest and apoptosis; reduced IL-1 β , IL-6, ROS, paw swelling, arthritis index, inflammatory infiltration, synovial hyperplasia, pannus formation, bone destruction, TNF- α , IL-1 β and IL-6; increased HO-1 and NQO1.	NF- κ B inhibition; antioxidant response regulation	Group II	[29,50]
PH	Cynaroside	Flavonoid glycoside	Cartilage explants	Reduced NO $_2^-$ /iNOS, ROS, PGE2/COX-2, MMP-1/3/13, ADAMTS-4, proteoglycan loss, NF- κ B p65 nuclear translocation and MAPK phosphorylation; increased COL2 and ACAN.	NF- κ B/MAPK inhibition	Group II	[30]
PH	3,5-Dicaffeoylquinic acid	Phenolic acid	SW1353 chondrocytes	Reduced mRNA expression of IL6, PTGS2/COX-2, MMP1 and MMP13.	Reduced inflammation and matrix degradation	Group II	[51]
PH	Nobiletin	Polymethoxyflavone	OA chondrocytes; DMM mouse OA model	Reduced iNOS, COX-2, NO, PGE2, IL-6, TNF- α , MMP-13, ADAMTS-5, cartilage degeneration, synovial inflammation and subchondral bone abnormalities; increased aggrecan and collagen II.	PI3K/AKT/NF- κ B inhibition	Group II	[31]
PH	Luteolin	Flavonoid	CFA-induced paw inflammation model	Reduced O $_2^{\bullet-}$, ROS, elastase release, CD11b, chemotactic migration, NET formation, Raf1/MEK1/ERK phosphorylation, Raf1 kinase activity, paw swelling, inflammatory cell infiltration, Ly6G $^+$ cells and MPO.	Raf1/MEK1/ERK inhibition	Group II	[33,52]
PH	Falcarindiol [(3R,8S,9Z)-1,9-heptadecadiene-4,6-diyne-3,8-diol]	Polyacetylene	RAW264.7 cells	Reduced NO, iNOS, TNF- α , IL-6, IL-1 β , JNK, ERK, STAT1 and STAT3.	MAPK/JAK/STAT inhibition	Group II	[32]

Table 2. Continued.

Source	Constituent	Compound class	Model/evidence	Reported pharmacological relevance	Reported pathway/mechanism	Evidence group (I–IV)	Ref.
PH	Azelaic acid	Dicarboxylic acid	AIA	Reduced arthritis score, paw swelling, NF- κ B, COX-2, TNF- α , IL-17, IL-1 β , IL-6, PGE2, 5-LOX, anti-CCP, ESR, CRP, WBC, PLT and MDA; increased body weight, IL-4, IL-10, SOD, CAT and GSH.	NF- κ B and COX-2 inhibition	Group II	[53]
PH	Palmitic acid	Saturated fatty acid	Human OA chondrocytes; cartilage explants under inflammatory conditions	Reduced MMP1 gene expression in OA chondrocytes and glycosaminoglycan release from cartilage explants.	Attenuation of cartilage matrix degradation-related processes	Group II	[56]

Note: The following abbreviations are used: VT, *Vicatia thibetica*; SG, *Sphallerocarpus gracilis*; PH, *Pleurospermum hookeri* var. *thomsonii*; AA, adjuvant arthritis; AIA, adjuvant-induced arthritis; CIA, collagen-induced arthritis; CAIA, collagen antibody-induced arthritis; CFA, complete Freund's adjuvant; DMM, destabilization of the medial meniscus; OA, osteoarthritis; RA-FLS, rheumatoid arthritis fibroblast-like synoviocyte; HFLS-RA, human fibroblast-like synoviocytes from rheumatoid arthritis; RASF, rheumatoid arthritis synovial fibroblast; CAG, chronic atrophic gastritis; ADMA, asymmetric dimethylarginine; DDAH, dimethylarginine dimethylaminohydrolase; HDL, high-density lipoprotein; MDA, malondialdehyde; SOD, superoxide dismutase; GSH-PX, glutathione peroxidase; GSH, glutathione; CAT, catalase; anti-CCP, anti-cyclic citrullinated peptide antibody; MPO, myeloperoxidase; NETs, neutrophil extracellular traps; WBC, white blood cell count; PLT, platelet count; 5-LOX, 5-lipoxygenase. Evidence group (I–IV) indicates the relationship between the cited pharmacological model and Huangshui-associated joint disorders. The four evidence groups used in this review are: I, direct evidence on Jiawa-related materials or extracts; II, isolated compound evidence in arthritis or joint-disease models; III, isolated compound evidence in non-joint inflammatory models; and IV, supplementary evidence indirectly linked to Huangshui-related manifestations. In this table, Group II refers to isolated compounds studied in arthritis or joint-disease models, Group III refers to isolated compounds studied in non-joint inflammatory models, and Group IV refers to evidence linked only indirectly to Huangshui-related manifestations, such as pain, fever, dermatitis/itch, or gastrointestinal inflammation. No entry in this table provides group I direct evidence on authenticated Jiawa-related materials or extracts. This classification reflects model relevance rather than the formal risk of bias or evidence-quality grading.

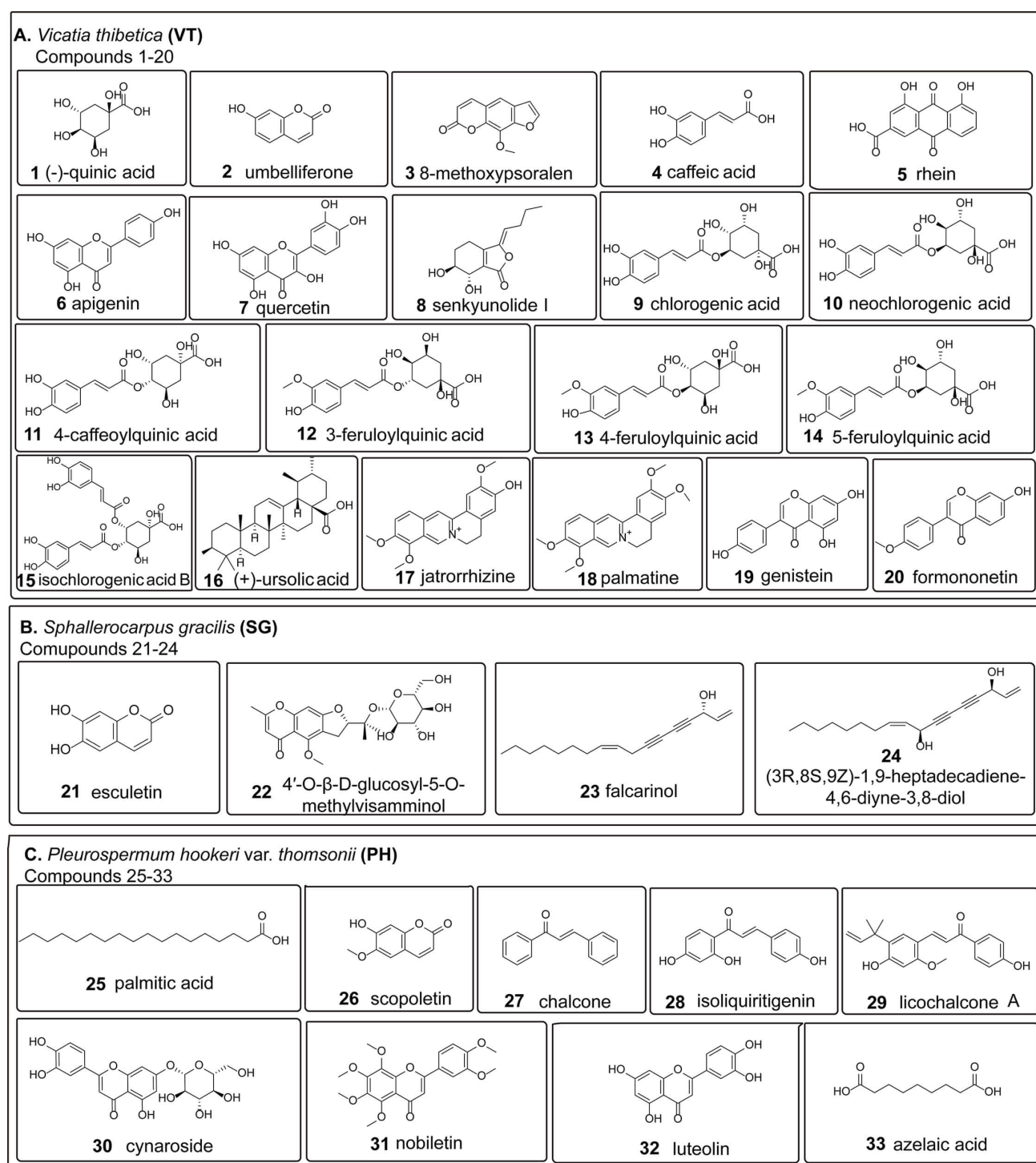


Fig. 2. Other reported constituents in the three representative Jiawa-related medicinal materials. (A) Compounds 1–20 reported from *Vicatia thibetica* de Boiss.; (B) Compounds 21–24 reported from *Sphallerocarpus gracilis* (Bess.) K.-Pol.; and (C) Compounds 25–33 reported from *Pleurospermum hookeri* C. B. Clarke var. *thomsonii* C. B. Clarke. The compounds shown in Fig. 2 represent selected other reported constituents from individual materials for which arthritis-related pharmacological evidence was identified, after excluding the shared reported constituents shown in Fig. 1.

β-Sitosterol has been reported to alleviate experimental arthritis by reducing paw edema and the arthritis index, regulating inflammatory cytokines and oxidative stress markers, and modulating NF-κB and HO-1/Nrf2-related signaling [13]. Bergapten has been reported to exert anti-

arthritic and analgesic effects in adjuvant-induced arthritis, accompanied by suppression of NF-κB activation [14] and STAT3-related inflammatory signaling [20]. Ferulic acid has been associated with improvement of arthritis-related indicators and inhibition of JAK/STAT signaling [15]. 3,5-

Dicaffeoylquinic acid has been reported to inhibit osteoclast differentiation, bone resorption, and IL-17/MAPK-related inflammatory responses [16]. Ligustilide has been reported to suppress RANKL-induced osteoclastogenesis and bone resorption by inhibiting RANK expression [17]. Daucosterol has been reported to alleviate OA by targeting chondrocyte senescence and suppressing JNK signaling [18]. Isoimperatorin has been reported to reduce synovial inflammation and fibrosis in knee OA by regulating the cAMP signaling pathway [19].

The reported activities of these isolated constituents mainly involve inflammation control, immune regulation, antioxidant protection, angiogenesis inhibition, pain modulation, and protection against cartilage and bone destruction. However, these compounds have not been established as characteristic constituents of the corresponding Jiawa-related medicinal materials, and the available evidence is derived mainly from constituent-level pharmacological studies. Therefore, these findings should be interpreted as a preliminary chemical-basis reference for understanding the possible pharmacological relevance of shared reported constituents in Huangshui-associated joint disorders, rather than as evidence establishing the therapeutic effects of Jiawa-related medicinal materials.

5.2 Other Reported Constituents and Their Pharmacological Relevance

In addition to the shared reported constituents discussed above, each representative Jiawa-related medicinal material contains other constituents reported in the available literature (Table 2). For *V. thibetica*, these constituents mainly include phenolic acids and related derivatives, as well as flavonoids, coumarins, phthalides, and isoquinoline alkaloids. Constituent-level studies have associated these compounds with anti-inflammatory and antioxidant effects, inhibition of abnormal synoviocyte behavior, and regulation of cartilage or bone metabolism. The reported mechanisms and related pathological processes include AMPK/Nrf2 [21], NF- κ B [22], synovial hyperplasia, angiogenesis and osteoclastogenesis [23], NF- κ B/MAPK [24], and Nrf2/HO-1 signaling [25]. Some evidence, such as that for isochlorogenic acid C, is derived from non-joint inflammatory models and was therefore considered supplementary [26]. Overall, constituent-level studies on the reported constituents of *V. thibetica* mainly involve inflammation, oxidative stress, synovial hyperplasia, cartilage protection, and bone metabolism.

For *S. gracilis*, the other reported constituents include coumarins, furanocoumarins, pyranocoumarins, polyacetyles, and related compounds. Available constituent-level pharmacological studies mainly associate these compounds with regulation of inflammatory pathways. Esculetin has been reported to inhibit HSC70/p38 MAPK-related inflammatory responses [27], while 4'-O- β -D-glucosyl-5-O-methylvisamminol (5-O-methylvisammioside) has been reported to target

inflammatory macrophages and RA-FLSs and suppress NF- κ B signaling [28]. Falcarinol (also known as panaxynol) has been reported to alleviate experimental arthritis in collagen-induced arthritis rats and inhibit abnormal proliferation, migration, and invasion of RA-FLSs while promoting apoptosis, with involvement of the TLR4/NF- κ B signaling pathway [55]. Falcarindiol has been reported to attenuate LPS-induced inflammatory responses in RAW264.7 macrophages through modulation of MAPK and JAK-STAT signaling [32]. These findings suggest that some reported constituents of *S. gracilis* have been investigated primarily in relation to inflammatory-pathway regulation.

The currently reported constituents of *P. hookeri* var. *thomsonii* mainly include flavonoids, chalcones, coumarins, phenolic acids, and fatty acid derivatives. These constituents have been associated with regulation of the NF- κ B [29], MAPK [30], PI3K/AKT [31], JAK/STAT [32], Raf1/MEK1/ERK [52], and Sirt1/PGC-1 α -Nrf2/HO-1 signaling pathways [34]. Representative constituents, including isoliquiritigenin, licochalcone A, cynaroside, nobiletin, and luteolin, have been associated with cytokine regulation, antioxidant protection, cartilage matrix preservation, and inhibition of inflammatory cell activation. Other constituents, such as scopoletin, falcarindiol, and azelaic acid, have also been reported in relation to anti-inflammatory, antioxidant, or cartilage-protective effects. Palmitic acid has been reported to reduce MMP1 gene expression in human OA chondrocytes and glycosaminoglycan release from cartilage explants under inflammatory conditions, suggesting a potential protective effect against cartilage matrix degradation in the experimental models studied [56]. Overall, constituent-level studies on the reported constituents of *P. hookeri* var. *thomsonii* mainly involve immune regulation, oxidative stress, inflammatory signaling, and cartilage or matrix protection.

Taken together, the other reported constituents summarized in Table 2 broaden the constituent-level pharmacological information beyond the shared reported constituents. Their reported activities mainly involve inflammation, oxidative stress, immune regulation, cartilage protection, and bone metabolism, and may provide preliminary clues for understanding possible differences in pharmacological emphasis among the three Jiawa-related medicinal materials. However, this evidence is derived mainly from isolated constituents, *in vitro* systems, animal models, and modern arthritis-related or inflammatory disease models. Individual compounds cannot represent the pharmacological effects of whole medicinal materials, and modern joint-disease models are not equivalent to the clinical and pathological contexts of Huangshui-associated disorders in Tibetan medicine. Therefore, the findings summarized in this section should be interpreted as indirect pharmacological evidence for understanding the traditional use and chemical relevance of Jiawa-related medicinal materials, rather than as direct evidence for the clinical efficacy of authenticated

Jiawa-related medicinal materials in Huangshui-associated disorders. Direct comparative studies using authenticated Jiawa-related medicinal materials are required to further evaluate the relationship among traditional use, chemical overlap, and pharmacological relevance.

6. Conclusions and Future Perspectives

This review integrates traditional records, botanical-source information, reported phytochemical data, and arthritis-related pharmacological evidence for representative Jiawa-related medicinal materials. The available literature indicates that *V. thibetica*, *S. gracilis*, and *P. hookeri* var. *thomsonii* differ in botanical origin, regional medicinal use, and currently reported phytochemical profiles. Traditional records and clinical-use reports indicate that Jiawa-related materials are used within the broader indication spectrum of Huangshui-associated disorders, including joint-related manifestations and other traditional indications. Taken together, Jiawa-related medicinal materials may be understood as a multi-origin traditional Tibetan medicinal category. Within this category, different regional or botanical-source materials may share overlapping traditional indications while differing in medicinal properties, functions, and clinical-use characteristics.

The comparative phytochemical findings show that the three representative Jiawa-related medicinal materials contain both shared reported constituents and constituents reported from individual materials. These data provide a useful framework for interpreting possible chemical overlap and differences in currently reported compound-class emphases among the three materials. From a pharmacological perspective, the shared reported constituents may provide preliminary clues regarding the chemical basis for common constituent-level activities related to inflammation, oxidative stress, immune regulation, cartilage protection, and bone metabolism. Meanwhile, the other reported constituents may help explain potential differences in pharmacological emphasis among the three representative materials. Based on the current constituent-level evidence, the reported constituents of *V. thibetica* are mainly associated with inflammation, oxidative stress, synovial hyperplasia, and bone metabolism; those of *S. gracilis* mainly with inflammatory-pathway modulation; and those of *P. hookeri* var. *thomsonii* mainly with immune regulation, antioxidant protection, and cartilage or matrix preservation.

At the present stage, the relationship among traditional use, chemical overlap, and pharmacological relevance should be interpreted as an evidence-based hypothesis rather than as a confirmed therapeutic-mechanistic explanation. The current evidence is valuable for generating mechanistic clues, but it remains insufficient to demonstrate the direct clinical efficacy of Jiawa-related medicinal materials or to clarify how the reported constituents contribute to the effects of whole medicinal materials after traditional preparation and administration. This distinction is particularly important because the pharmacological studies sum-

marized in this review mainly concern isolated constituents and experimental models, whereas Jiawa-related medicinal materials are traditionally used as whole medicinal materials, often within prescription contexts.

Future research should therefore move from constituent-level evidence toward direct studies of authenticated Jiawa-related medicinal materials. Priority should be given to reliable source authentication, standardized extraction procedures, comparable analytical platforms, quantitative phytochemical profiling, and harmonized pharmacological models. Direct comparative studies among authenticated *V. thibetica*, *S. gracilis*, and *P. hookeri* var. *thomsonii* will be essential for clarifying their shared and differential chemical characteristics and pharmacological properties. In addition, pharmacokinetic, metabolic, and prescription-based studies are needed to determine whether the reported constituents can reach biologically relevant exposure levels and how they may contribute to the traditional use of Jiawa-related materials. Such work will help clarify the material basis of Jiawa-related medicinal materials, improve quality control, and support their rational and standardized use in Tibetan medicine.

Abbreviations

AIA, adjuvant-induced arthritis; BAFF, B-cell activating factor; CAIA, collagen antibody-induced arthritis; CFA, complete Freund's adjuvant; CIA, collagen-induced arthritis; DMM, destabilization of the medial meniscus; FLS, fibroblast-like synoviocyte; HPLC, high-performance liquid chromatography; HUVEC, human umbilical vein endothelial cell; MAPK, mitogen-activated protein kinase; NF- κ B, nuclear factor-kappa B; OA, osteoarthritis; RA, rheumatoid arthritis; RA-FLS, rheumatoid arthritis fibroblast-like synoviocyte; RASF, rheumatoid arthritis synovial fibroblast; ROS, reactive oxygen species; Wylie, Wylie transliteration system. Abbreviations used only in tables are defined in the corresponding table notes.

Author Contributions

MZLA collected the literature, organized data and drafted the manuscript. RW screened the literature, verified data, contributed to the study design and supervision, and critically revised the manuscript. GZ conceptualized the review, designed the overall study, provided academic guidance and supervision, and critically revised the manuscript. All authors read and approved the final manuscript. All authors contributed to the editorial changes in the manuscript. All authors participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.31083/Pharmazie54026>.

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