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Psoralea corylifolia and *Curcuma longa*: An unexplored synergy for acne treatment: A review

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ABSTRACT

The use of herbal medicines and dietary supplements has grown by a significant margin in recent decades. This reflects the need to have safer and more effective therapeutic alternatives. The trend has been encouraged by increased antimicrobial resistance and adverse effects of synthetic drugs. This has revived interest in traditional medical systems such as Ayurveda, Unani, Siddha, and traditional Chinese medicine. These are relevant sources of bioactive compounds with clinical use. There is very little research on mixtures of plant extracts. There is, however, emerging evidence that some mixtures exert synergistic effects greater than those of individual extracts. Mixtures complement each other by targeting several pathophysiological pathways. There are still important gaps in terms of their safety, standardization, and mechanisms of action. This highlights the necessity of conducting additional research. In this regard, *Psoralea corylifolia* and *Curcuma longa* have received considerable attention. The two plants exhibit multiple pharmacological properties, such as antioxidant, anti-inflammatory, antimicrobial, and tissue-regenerative effects. These effects could be improved when they are used together, especially in the treatment of skin disorders like acne vulgaris. Acne is a multifactorial disorder which is not entirely dependent on the microbial load. It is also accompanied by changes in taxonomic structure and functional signature of the skin microbiota. This involves various lineages of *Cutibacterium acnes*, which correlate with the severity of the disease and response to treatment. Therapeutic interventions that simultaneously target inflammation, sebum production, bacterial virulence factors, and microbial balance are of special interest. This review critically analyzes the evidence that is available regarding the bioactive compounds, the mechanisms of action, as well as the possible synergistic interactions of *P. corylifolia* and *C. longa*. It highlights their suitability as candidates for topical or combination agents in acne and other inflammatory skin diseases.

Keywords: *Psoralea corylifolia*, *Curcuma longa*, Acne, Skin Disorders, Phytochemical Synergism, Plant Metabolites.

INTRODUCTION

Herbal medicines and supplements have become popular over the last decades. The use of medicinal plants as a source of healthcare is estimated to involve up to 80% of the world population, due to their widely reported therapeutic benefits in various diseases^[1-3]. This indicates a need to search for safer, more accessible and more culturally acceptable treatments^[4].

The main driver of this increasing interest in the use of herbal therapies is the expansion of antimicrobial resistance. In the case of *Staphylococcus epidermidis*, especially the clinical isolates, high percentages of resistance to penicillin and amoxicillin (60.9%) and cephalexin (52.2%) are demonstrated. Also, clindamycin resistance is demonstrated in up to 95% of cases and is observed in around 25% of cases against *Cutibacterium acnes*^[5,6]. Likewise, synthetic medications administered in dermatology, e.g. tretinoin, can have severe adverse effects including teratogenesis, cheilitis, dermatitis, xerophthalmia, and lipid abnormalities. This has prompted efforts to seek alternative treatment options that have a better safety profile^[7,8].

In this context, natural products that are based on the ancient medical traditions such as Unani, Ayurveda, Siddha, and traditional Chinese medicine have become more scientifically relevant since they are useful sources of bioactive agents that have multiple mechanisms of action. The systems are of key interest in the fields of medical anthropology and applied pharmacognosy, as they combine traditional

knowledge and modern medical research [9,10].

From a translational standpoint, the applicability of these traditional medical systems is enhanced in light of modern-day acne pathophysiology. Acne is perceived as a process that is multifactorial, characterized by changes in follicular keratinization and alterations in the amount and the composition of sebum. It also entails inflammatory reactions modulated by other immune pathways, including interleukin 1 beta (IL-1 β), interleukin 17 (IL-17), and interleukin 23 (IL-23). Another important constituent is cutaneous dysbiosis, which is linked with *Cutibacterium acnes*. In such circumstances, it is especially appealing that natural compounds have several biological targets since they can also alter these processes at the same time and do not result in the high level of selective pressure that is typical of traditional antibiotics [11].

Not many studies determine the therapeutic effects of herbal extract combinations. There is growing evidence that the synergistic response of various phytoconstituents can be used to increase clinical impact. This is the case with complex conditions, including diabetes, chronic inflammation, and skin disorders [1,12]. It is hoped that the creation of phytoactive mixtures will exploit alternative mechanisms of action. This increases their action and causes an enhanced therapeutic effect. However, there are also other side effects caused by such treatments, which highlight the importance of carrying out robust research in this area [13].

Extracts of *P. corylifolia* (usually referred to as babchi or babchi seeds) and *C. longa* (usually referred to as turmeric) on an individual basis have shown various biological properties such as wound-healing, antioxidant, anti-inflammatory, antimicrobial, antiviral, antitumor, and antimutagenic activities. These extracts have also been said to stimulate the immune, vascular, respiratory, skeletal, and cardiovascular systems [14-16]. The combination of *P. corylifolia* and *C. longa* may thus be able to yield better antimicrobial and anti-inflammatory effects.

Components of these extracts have been tested in clinical studies in dermatological treatment. Bakuchiol is the main meroterpenes of *P. corylifolia* and it has been evaluated in an open pilot study as a topical formulation in acne treatment. It was also tested as an adjuvant in a controlled trial in combination with adapalene. The clinical outcomes analyzed were reductions in inflammatory and non-inflammatory lesions and tolerability of the treatment. This therapeutic plausibility of individual phytocomponents is supported by the availability of this clinical evidence. It also explains the interest in the investigation of the formulations based on plant extracts and polyherbal mixtures [17,18].

In this context, the present review aims to critically report and tabulate the scientific evidence that is available concerning the individual biological properties of extracts of *P. corylifolia* and *C. longa*. It is concerned with how they are used to treat dermatological diseases, and how their still understudied potential synergistic effects are to be utilized in the management of acne. The review is limited to the dermatological sphere and does not involve metabolic and immunological conditions.

P. corylifolia

Babchi, a common medicinal plant called *P. corylifolia*, is utilized in traditional Ayurvedic and Chinese medicine. The genus name is based on the Greek word *psoraleos*, which means "affected by itching" or "leprosy." This is a species of the family Leguminosae. It is indigenous to China, India, and other parts of Asia. The level of phytochemical constituents can also change depending on the environmental and climatic factors. However, the seeds have been reported to have the highest amount of these compounds. The most interesting aspect of its pharmacological uses is in the treatment of skin ailments like acne, psoriasis, and vitiligo [19,20].

P. corylifolia has been studied for its phytochemical components. More than 100 bioactive compounds have been identified, including coumarins, flavonoids, quinones, phenols, and terpenoids. The seeds also contain furanocoumarins, flavonoids, and meroterpenes in high amounts. Bakuchiol is the most prominent constituent among these [21-23]. These secondary metabolites are responsible for the diverse pharmacological effects of the plant, including anti-inflammatory, antibacterial, antimycobacterial, antiviral, antifungal, antidermatophytic, antifilarial, anticancer, retinol-like, estrogen-like, antioxidant, photoprotective, antiosteoporotic, osteoblastic, cardioprotective, neuroprotective, immunomodulatory, antidepressant, antidiabetic, hepatoprotective, antiasthmatic, antihypercholesterolemic, anti-obesity, cytotoxic, antiulcer, antiplatelet, hepatotoxic, and pesticidal activities [19,20,22].

Some of the major active compounds are psoralen, isopsoralen, psoralidin, corylifolin, neobavaisoflavones, bavachalcone, and bakuchiol. They are found in the seeds and fruits of the plant [24]. Bakuchiol is a phenolic meroterpenes with low solubility and low bioavailability. It has retinol-like activity and various advantageous characteristics, including antioxidant, antifungal, antibacterial, anti-inflammatory, anti-aging, depigmenting, photoprotective, and anticancer properties [25].

Bakuchiol is not associated with any major adverse effects and is less irritating than retinol, which makes it a promising alternative [25,26]. Clinical research on the relevance of some phytocomponents of *P. corylifolia* in the dermatological sphere has been conducted. These experiments were directed towards topical application. Particularly, bakuchiol was tested in a prospective, randomized, and blinded trial on facial photoaging. It showed similar efficacy to retinol in the enhancement of wrinkles and hyperpigmentation. It also demonstrated a more positive cutaneous tolerability profile, less desquamation, burning, and stinging. Although this research did not target acne, the results of this study are clinically useful since they support the safety, tolerance, and viability of chronic topical application of extracts from *P. corylifolia*, which are the main points to be taken into account as to their possible use in other inflammatory dermatological disorders [27].

Corylin is another compound that can be used to protect the skin. It has been reported to reduce UV-induced photoaging in murine models. It achieves this by reducing oxidative stress and activating the nuclear factor erythroid 2-related factor 2 (Nrf2) [28].

Antimicrobial Activity of *P. corylifolia*

Flavonoids can inhibit the growth of *Cutibacterium acnes*, which plays an important role in the pathogenesis of acne. These compounds decrease the development of acne lesions by lowering the bacterial load on the skin. They share a chemical structure based on a phenylbenzopyran skeleton [11,22,29]. Flavonoids are a key group of compounds obtained from *P. corylifolia*. Some of these include flavonols, dihydroflavones, isoflavones, and chalcones, which have been isolated mainly from the seeds and fruits of the plant [30]. In another study, psoralidin, psoralen, bakuchicin, and angelicin were isolated from *P. corylifolia* seeds and showed antibacterial properties against Gram-positive and Gram-negative bacteria [31].

Anti-inflammatory Activity of *P. corylifolia*

Acne is often related to inflammatory processes that can cause the development of cysts, pustules, and papules. Many flavonoids have anti-inflammatory effects. These include bavachin [32], isobavachin [33], neobavaisoflavone [34], and isobavachalcone [35], which could prevent inflammation in acne and other inflammatory diseases, such as atherosclerosis [29,36,37]. Seo *et al.* noted that the *P. corylifolia* seed extract was effective in preventing dexamethasone-induced muscle atrophy in male C57BL/6 mice, which was attributed to the inhibition of oxidative stress and the inflammatory response [38]. Similarly, Pai *et al.* (2021) showed the anti-arthritis effect of *P. corylifolia* by

inhibiting inflammation and increasing the myeloid-derived suppressor cells in DBA/1J mice with collagen-induced arthritis [39].

Antioxidant Activity of *P. corylifolia*

Oxidative stress is part of the pathogenesis of acne. Flavonoids, which have antioxidant activity, are able to neutralize free radicals and prevent oxidative damage to the skin, thereby helping to decrease the severity of acne [29,40]. Bakuchiol is a phenolic meroterpene that is obtained from *P. corylifolia*, and it has antioxidant, free radical scavenging, anti-aging, and skin-whitening properties [41]. Experimental research has revealed that it has broad-spectrum antioxidant activity. It is effective in quenching superoxide, hydroxyl, peroxy, peroxynitrite, and singlet oxygen radicals. It also suppresses the process of lipid peroxidation [42]. Psoralidin, a coumarin of *P. corylifolia*, is also an isolated compound that exhibits high antioxidant activity with a half-maximal inhibitory concentration (IC₅₀) of 1.32 mg/L [22]. Other reports have revealed that the *P. corylifolia* root callus cultures yield more daidzein. The genistein concentration in the leaf callus cultures is higher. The latter has been linked to enhanced antioxidant activity [19,22].

Sebum Regulation by *P. corylifolia*

Some flavonoids regulate sebum production. Acne-prone skin is characterized by an increased content of sebum. These compounds could prevent follicular obstruction by lowering the sebaceous secretion, thereby preventing the formation of acne lesions [36]. Gidwani *et al.* (2010) examined the effectiveness of a semisolid formulation of a hexane extract of *P. corylifolia* and found it to be effective in the management of eczema among patients diagnosed with this condition [43].

P. corylifolia and its Synergy with Other Plants

P. corylifolia has been used in traditional Chinese medicine, Ayurveda, and modern herbal preparations in other countries over the centuries to enhance therapeutic effects through synergy. Table 1 is a summary of the studies that have examined the use of *P. corylifolia* with other medicinal plants to determine their composition, synergistic activity, and, in some instances, adverse effects or toxicity of combining them.

Collectively, the available scientific evidence suggests that *P. corylifolia* possesses a wide range of biological actions with respect to the pathophysiology of acne, such as antimicrobial, anti-inflammatory, antioxidant, and sebum-modulating effects. Additionally, its previous application in multifaceted herbal preparations and the research that has assessed its interactions with other medicinal herbs make it clear that it can cause synergistic interactions that improve therapeutic effects and alter adverse effects. *C. longa*, a medicinal plant commonly known for its anti-inflammatory and antioxidant effects, is also considered in order to evaluate how the combination of the two represents a complementary and promising approach to the treatment of acne.

In terms of safety, experimental evidence suggests that the co-administration of *P. corylifolia* with other plant extracts is unlikely to reduce toxicological risk. Studies in mice have demonstrated that combinations of certain plant extracts can change the bioavailability of active constituents and, under specific conditions, enhance hepatic exposure. Even though such results have been obtained only in animal models, they highlight the necessity of standardizing and toxicologically testing combined herbal preparations, as opposed to the analysis of individual extracts [30].

C. longa

C. longa, referred to as turmeric, has been widely used in traditional medicine, especially in Asian societies, due to its broad pharmacological activities. Its primary bioactive component,

curcumin, a polyphenolic compound derived from the rhizome of *C. longa*, has gained interest because of its anti-inflammatory, antimicrobial, and antioxidant properties. These properties make curcumin a prospective natural compound in the treatment of different skin diseases, such as acne and other dermatological disorders. In addition, there is evidence of the use of natural ingredients locally available to prevent skin aging in the Anak Dalam tribe in Indonesia. Among the 64 species, *Toona sinensis*, *Curcuma heyneana*, *C. longa*, and *Kaempferia rotunda* showed anti-aging effects in both *in vivo* and *in vitro* experiments [61].

Anti-inflammatory Properties of *C. longa*

Anti-inflammatory properties of curcumin are exerted by the interplay of curcumin with various molecular targets and signaling pathways. Curcumin reduces pro-inflammatory cytokines and transcription factors and thus suppresses the inflammatory response. This modulatory ability has endowed curcumin with potential therapeutic use in different inflammatory disorders [62,63].

Curcumin is the primary compound of *C. longa* that has anti-inflammatory effects, and it has been widely researched regarding its capacity to regulate inflammatory pathways. Specifically, curcumin suppresses several of the enzymes that play a role in inflammation, e.g., cyclooxygenase 2, lipoxygenase, and inducible nitric oxide synthase [14,63]. This inhibition lowers the synthesis of pro-inflammatory mediators, particularly prostaglandins and leukotrienes, which are frequently above normal levels in inflammatory skin diseases, namely acne and psoriasis [64].

Moreover, curcumin regulates the action of nuclear factor kappa B (NF-κB), which is a key transcription factor that controls pro-inflammatory genes [65]. Curcumin lowers the concentrations of pro-inflammatory cytokines, such as tumor necrosis factor alpha and interleukin 6, which are usually involved in chronic inflammatory skin diseases by inhibiting NF-κB activation [66]. The anti-inflammatory effect of curcumin can be used in the context of acne to reduce the erythema and inflammation of acne lesions. It also has the potential to control the inflammatory response and therefore prevent the development of mild acne into severe forms of acne, like nodular or cystic acne [67].

Antimicrobial Properties of *C. longa*

Another important characteristic related to the possible efficacy of *C. longa* against acne and other skin infections is its antimicrobial activity. Acne has often been linked with excess growth of *Cutibacterium acnes* (previously *Propionibacterium acnes*), a bacterium that grows in the pilosebaceous unit. Curcumin has a strong antibacterial effect against *Cutibacterium acnes*, as it can inhibit its growth and even minimize the acne lesions [67,68].

Also, the antimicrobial properties of curcumin are applicable to other pathogens, such as fungi and viruses; thus, it can be used as a general agent in the treatment of a wide range of skin infections. Curcumin is also reported to prevent the growth of *Candida albicans* [69,70]. It is believed that the antimicrobial effect of curcumin is primarily related to its capacity to impair the integrity of the pathogen cell membrane and interrupt basic metabolic functions. These processes support considering curcumin as a natural supplement or substitute for traditional antibiotics, especially in the context of antimicrobial resistance [71,72].

Antioxidant Activity of *C. longa*

Oxidative stress has been involved in the pathogenesis of several skin disorders, such as acne, psoriasis, and photoaging. Curcumin, the primary bioactive component of *C. longa*, is a well-known antioxidant that can neutralize free radicals and restore skin barrier function [14,65]. Neutralization of reactive oxygen species and promotion of endogenous antioxidant enzymes, including superoxide dismutase,

catalase, and glutathione peroxidase, are the main mechanisms of antioxidant activity of curcumin [14,66].

Curcumin also inhibits oxidative stress and subsequent damage to the skin caused by ultraviolet radiation and other environmental stressors by activating the Keap1-Nrf2 pathway, which is one of the major cellular defenses against oxidative stress [73,74]. This effect results in the upregulation of phase II detoxifying enzymes and therefore increases the ability of the skin to counter oxidative damage. When *C. longa* is used in combination with other medicinal plants, this antioxidant potential may enhance the therapeutic effect against different diseases, including skin disorders [74]. Table 2 is a summary of research articles comparing herbal formulations of *C. longa* in preclinical and clinical studies and their therapeutic and biological activities.

Flavonoids and their Role in Acne Treatment

The flavonoids in *P. corylifolia* represent a significant category of polyphenolic compounds, which are commonly known to have antioxidant, anti-inflammatory, and antimicrobial properties and are therefore potential agents in the management of acne. Daidzein, genistein, daidzin, and astragalin are some of the flavonoids found in *P. corylifolia* [23,29].

Acne vulgaris is a chronic skin condition marked by inflammation, bacterial proliferation, and oxidative stress. In this regard, curcumin, the primary bioactive component of *C. longa*, helps reduce erythema and swelling caused by acne lesions due to its anti-inflammatory effects, while its antimicrobial effects prevent the growth of *Cutibacterium acnes*, which is a major contributor to acne pathogenesis [67,68]. Also, curcumin's antioxidant activity can be used to reduce the effects of oxidative stress, which is widely associated with the development of acne [14,73]. In order to enhance its stability and bioavailability, different topical curcumin preparations, including gels and hydrogels, have been designed to treat acne, with encouraging outcomes in decreasing the severity of the disease and preventing relapse [67].

Curcumin can suppress the development of *Cutibacterium acnes*. Its photoactive effect has been tested *in vitro* in models of human keratinocyte inflammation caused by *Cutibacterium acnes* biofilms and has shown a notable decrease in the inflammatory reaction and bacterial survival [24]. Furthermore, the healing of cutaneous wounds of Wistar rats using turmeric (*C. longa*) and ginger (*Zingiber officinale*) phenolic compounds has been assessed. The findings revealed that these phenolic compounds, especially curcumin, stimulate cell proliferation, collagen synthesis, and tissue healing [75].

Synergistic Effect of *P. corylifolia* and *C. longa*

Chemical defenses are the most common means of surviving in unfavorable conditions for plants that do not have an adaptive immune system and are mediated by the production of a wide range of bioactive compounds that can disrupt critical processes in predators and pathogens [89,90]. Evolutionary interactions between plants and their antagonistic species have driven the development of high phytochemical diversity, with pathogens tending to develop resistance to particular plant defenses [79].

Such chemical complexity enhances the probability of effectiveness against various biological threats. Unlike the pharmaceutical model of a single active constituent, plants do not generate one active component but rather produce multiple components with various mechanisms of action [91]. Since many processes in animal parasites rely on enzymes and receptors similar to those of plant pathogens, such secondary metabolites can also be active in human diseases, including malaria [79].

The synergy between plant-derived compounds can be pharmacodynamic, where they interact with different molecular

targets and thus increase the therapeutic effect, or pharmacokinetic, where they alter the bioavailability of the active component or decrease its metabolism [91]. In addition, beneficial effects can occur, including immunomodulation, reversal of drug resistance, and reduced adverse effects. Such synergies are well documented in antimalarial activity, as well as in other pharmacological uses [92].

The results of the combination of *C. longa* with *P. corylifolia* have not been studied widely, yet the underlying mechanisms of action of the two plants separately indicate there is a feasible foundation for synergistic effects [65]. The anti-inflammatory nature of curcumin may be used in conjunction with the phototherapeutic nature of *P. corylifolia*, and the two species could be used together to enhance antioxidant defenses and inhibit microbial colonization in skin disorders such as acne and eczema [93]. In this respect, Monga *et al.* (2024) applied psoralen and curcumin in a TE formulation containing both active ingredients to test it against psoriasis. The *in vivo* experiment showed that there was positive synergism in a 5:0.2 proportion (5 µM TE curcumin and 10 µM TE psoralen), but this synergism was not supported by the levels of IL-17 and IL-23 found in the tissues of psoriatic animals [13].

Safety Considerations and Future Directions

Although the bioactive compounds of *P. corylifolia*, including psoralen and other flavonoids, have proven to be relevant in terms of therapeutic applications when applied to the treatment of acne, their clinical use should be evaluated with close consideration of the potential risks. The main aspects that should be properly addressed are safety, extract standardization, and clinical validation to ensure their consideration in dermatology. Psoralen is a photosensitizer whose reaction with ultraviolet light may cause phototoxic effects [94]. In clinical terms, these reactions can present as skin irritation, erythema, hyperpigmentation, or changes in cutaneous pigmentation [95]. Due to these effects, psoralen is contraindicated, especially when administered as a topical agent on sun-exposed areas or when administered alongside UV-based treatments [96,97]. From this perspective, safe concentrations, controlled conditions of use, and proper photoprotection strategies still need to be defined [98].

P. corylifolia extracts can be therapeutically effective and safe, with their performance directly linked to purity, chemical composition, and the level of standardization of the active constituents [99,100]. The consistency of the phytochemical content may also vary based on the source, growth conditions, and method of extraction, which can significantly affect the reproducibility of the registered biological effects [101]. Thus, well-controlled isolation, characterization, and purification techniques should be adopted to guarantee the quality, consistency, and safety of the final product, especially when used in dermatological applications [54].

Although *in vitro* and *in vivo* research on psoralen and flavonoids has shown promising initial results, the absence of controlled clinical trials limits the generalization of such results to clinical practice. Therefore, further clinical research is needed to conduct a systematic assessment of the effectiveness, safety, tolerance, and effective dosage of such compounds in humans with special reference to therapy against acne. In addition, future studies should focus on elaborating optimized topical preparations that have the greatest therapeutic effect but minimal side effects [22,40].

Table 1: Review of studies on *P. corylifolia* and its synergy with other plants

Country	Plant combination	Study objective	Type of study	Reference
China	Coumarin and bakuchiol from <i>P. corylifolia</i>	To evaluate whether co-administration of coumarin and bakuchiol under immune-stress conditions exacerbates hepatotoxicity in rats	<i>In vivo</i>	[44]
China	<i>Dipsacus asper</i> saponin components, coumarin components from <i>P. corylifolia</i> , and flavonoid polyglycoside components from <i>Epimedium</i> (Xian-Ling-Gu-Bao capsule)	To elucidate the pharmacodynamic material basis of the Xian-Ling-Gu-Bao capsule by testing <i>Dipsacus asper</i> , <i>P. corylifolia</i> , and <i>Epimedium</i> components against osteoporosis in zebrafish	<i>In vivo</i>	[45]
China	<i>Herba Epimedii</i> (70%), <i>Radix Dipsaci</i> (10%), <i>Fructus Psoraleae</i> (5%), <i>Rhizoma Anemarrhenae</i> (5%), <i>Radix Salviae miltiorrhizae</i> (5%) and <i>Radix Rehmanniae</i> (5%)	To assess estrogen-sulfation inhibitors in a multi-herb formula containing <i>Epimedium</i> , <i>Dipsacus</i> , <i>Psoralea</i> , <i>Anemarrhena</i> , <i>Salvia miltiorrhiza</i> , and <i>Rehmannia</i> in ovariectomized rats	<i>In vivo</i>	[46]
China	<i>Rhizoma Drynariae</i> (Gusuibu), <i>Herba Epimedii brevicornus</i> (Yinyanghuo), yam, <i>Radix Salviae miltiorrhizae</i> (Danshen), <i>Rehmannia glutinosa</i> (Sheng Di-Huang), and <i>P. corylifolia</i> fruit (Buguzhi)	To evaluate the mechanisms of Yigu Decoction in knee osteoarthritis using network pharmacology and molecular docking	<i>In silico</i>	[47]
China	<i>Trigonella foenum-graecum</i> L. and <i>P. corylifolia</i> L. (Hu-Lu-Ba-Wan formulation)	To evaluate whether Hu-Lu-Ba-Wan improves diabetes-induced erectile dysfunction in streptozotocin-induced diabetic rats by suppressing oxidative stress	<i>In vivo</i>	[48]
Korea	<i>Cornus officinalis</i> Sieb. et Zucc. and <i>P. corylifolia</i> L. (HBX-6 herbal formula)	To evaluate the therapeutic effects of HBX-6, a <i>Cornus officinalis</i> – <i>P. corylifolia</i> extract, in a testosterone-induced benign prostatic hyperplasia model in mice	<i>In vivo</i>	[49]
India	<i>Trigonella foenum-graecum</i> L. (fenugreek) and <i>P. corylifolia</i> (Somraji) seed aqueous extracts (administered separately and as a composite extract)	To compare the antidiabetic efficacy of aqueous seed extracts of <i>P. corylifolia</i> and <i>Trigonella foenum-graecum</i> , administered alone or in combination, in streptozotocin-induced diabetic rats	<i>In vivo</i>	[50]
India	Ethanol extracts of <i>Epimedium brevicornu</i> and <i>Drynaria fortune</i> (minimal base traditional Chinese medicine formula), with or without a third extract: <i>Salvia miltiorrhiza</i> (Danshen), <i>Lycium barbarum</i> root bark, or <i>Angelica sinensis</i>	To develop a minimal traditional Chinese medicine formula and evaluate its bone-specific biological activity <i>in vitro</i> and its ability to maintain bone mineral density in an ovariectomized rat model	<i>In vitro</i> and <i>In vivo</i>	[51]
USA	<i>Herba Epimedium brevicornum</i> Maxim (stem and leaves), <i>Radix morindae officinalis</i> (root), <i>Fructus Rosa laevigatae</i> Michx (fruit), <i>Rubus chingii</i> Hu (fruit), <i>Schisandra chinensis</i> (Turcz.) Baill (fruit), <i>Ligustrum lucidum</i> Ait (fruit), <i>Cuscuta chinensis</i> Lam (seed), <i>P. corylifolia</i> L. (fruit), and <i>Astragalus membranaceus</i> (Fisch.) Bge (root)	To examine the effects and mechanisms of a multi-herb preparation on cell growth, apoptosis, androgen receptor and prostate-specific antigen expression, and clonogenic capacity in androgen-dependent and androgen-independent prostate carcinoma cell lines	<i>In vitro</i>	[52]
China	<i>Viscum coloratum</i> 15 g, <i>P. corylifolia</i> 15 g, <i>Eucommia ulmoides</i> 15 g, <i>Lycium chinense</i> 9 g, <i>Tussilago farfara</i> 15 g, <i>Artemisia capillaris</i> 9 g, and <i>Pogostemon cablin</i> 9 g	To evaluate maximal expiratory flow–volume parameters in patients with asthma during the convalescent stage and to assess changes in airway obstruction after treatment with a kidney-invigorating Chinese herbal decoction	Clinical	[53]
China	Serum containing <i>Fructus Cnidii</i> (Shechuanzi) and <i>P. corylifolia</i> (Buguzhi) in different proportions (4:0, 3:1, 1:1, 1:3, 0:4)	To explore the effects of different proportions of <i>Fructus Cnidii</i> and <i>P. corylifolia</i> on a highly metastatic human breast cancer cell line and a bone marrow stromal cell line <i>in vitro</i> , assessing cell proliferation, migration, alkaline phosphatase activity, and mineralized nodule formation	<i>In vitro</i> (drug-containing serum prepared in rats)	[54]

Korea	<i>Xanthium stramarium</i> and <i>P. corylifolia</i> seed extracts	To evaluate whether highly purified <i>Xanthium stramarium</i> and <i>P. corylifolia</i> extracts, combined with UVA1 irradiation, can suppress cell proliferation, induce apoptosis, and reduce transforming growth factor- β 1 and collagen I expression in keloid fibroblasts	<i>In vitro</i>	[55]
Korea	<i>Xanthium stramarium</i> and <i>P. corylifolia</i>	To review natural products, including <i>Xanthium stramarium</i> and <i>P. corylifolia</i> extracts, used as adjuvants to other therapies with potential to improve keloid management and induce apoptosis	Review	[56]
Iran	<i>Glycyrrhiza uralensis</i> ; <i>Rosmarinus officinalis</i> ; curcumin from <i>C. longa</i> ; <i>Sida tiagii</i> and <i>Aloysia gratissima</i> ; <i>Aconitum carmichaeli</i> ; <i>Paeonia lactiflora</i> ; <i>Polygala tenuifolia</i> and <i>P. corylifolia</i>	To present a comprehensive overview of the neurological mechanisms of action underlying the antidepressant effects of medicinal plants	Review	[57]
England	<i>Centella asiatica</i> and <i>Psoralea corylifolia</i>	To use a rapid in vitro bioassay in SVK 14 keratinocytes to evaluate whether aqueous extracts of <i>Centella asiatica</i> and <i>Psoralea corylifolia</i> , as well as the triterpenoid glycosides madecassoside and asiaticoside, inhibit keratinocyte proliferation and may act as potential anti psoriatic agents	<i>In vitro</i>	[58]
India	Curcumin from <i>Curcuma longa</i> , methoxyphenols from Indian spices, dehydrogingerdione from ginger, and bakuchiol from <i>Psoralea corylifolia</i>	Overview of physico chemical methods (mainly pulse radiolysis and kinetic spectroscopy) used to assess the antioxidant activity and reaction mechanisms of selected Indian herbal extracts and active principles, including curcumin, methoxyphenols, dehydrogingerdione, and bakuchiol, studied both individually and in combination	Review	[59]
Japan	70% aqueous ethanol extracts of <i>Curcuma amada</i> Roxb. (rhizome), <i>Mallotus philippinensis</i> (Lam) Muell. (fruit glandular powder), <i>Myristica fragrans</i> Houtt. aril, and <i>Psoralea corylifolia</i> L. seeds	To evaluate the bactericidal activity of 50 Unani medicinal plants, including <i>Curcuma amada</i> , <i>Mallotus philippinensis</i> , <i>Myristica fragrans</i> , and <i>Psoralea corylifolia</i> , against <i>Helicobacter pylori</i> and to determine their minimum bactericidal concentrations	<i>In vitro</i>	[60]

Table 2: Review of studies on *C. longa* and its synergy with other plants

Country	Plant Combination	Study objective	Type of study	Reference
Morocco	<i>C. longa</i> L. and <i>Zingiber officinale</i>	To evaluate the anti-inflammatory activity and cutaneous wound-healing effects of topical creams containing phenolic extracts from turmeric (<i>C. longa</i> L.) and ginger (<i>Zingiber officinale</i>) in Wistar rats	Preclinical	[75]
India	<i>C. longa</i> and <i>Piper nigrum</i>	To assess the effect of piperine from <i>Piper nigrum</i> on the oral bioavailability and pharmacokinetics of curcumin from <i>C. longa</i> in rats and healthy human volunteers	Preclinical and clinical	[76]
Indonesia	<i>Toona sinensis</i> , <i>Curcuma heyneana</i> , <i>Curcuma zedoaria</i> , <i>C. longa</i> and <i>Kaempferia rotunda</i>	To summarize the anti-aging and antioxidant potential of traditional Indonesian medicinal plants used by the Anak Dalam Tribe	Review	[61]
India	<i>Mucuna pruriens</i> L. (DC.) and <i>Withania somnifera</i> L. (Dunal) and <i>C. longa</i> L.	To review Ayurvedic medicinal plants and treatment regimens for the management of idiopathic Parkinson's disease, including motor and non-motor symptoms	Review	[77]

Australia	<i>C. longa</i> , <i>Astragalus membranaceus</i> , <i>Glycyrrhiza glabra</i> , <i>Althaea officinalis</i> , <i>Echinacea purpurea</i> , <i>Sanguinaria canadensis</i> , <i>Codonopsis pilosula</i> , <i>Hydrastis canadensis</i> , <i>Lobelia inflata</i> , <i>Scutellaria baicalensis</i> and <i>Zingiber officinale</i>	To synthesize evidence on phytoconstituents that modulate signaling pathways in lung and colorectal cancer	Review	[78]
Madagascar	<i>Quassia amar</i> , <i>Artemisa annua</i> , <i>C. longa</i> , <i>Piper nigrum</i> , <i>Picrorhiza kurroa</i> , <i>Andrographis paniculata</i> , <i>Bidens pilosa</i> and <i>Hedyotis corymbosa</i>	To describe the synergistic potential of medicinal plants and phytochemicals for malaria treatment	Review	[79]
India	<i>C. longa</i> and <i>Andrographis paniculata</i>	To explore the docking interactions of phytochemical constituents from <i>C. longa</i> and <i>Andrographis paniculata</i> with the severe acute respiratory syndrome coronavirus (2 SARS-CoV-2) main protease	<i>In silico</i>	[80]
India	<i>P. corylifolia</i> and <i>C. longa</i>	To assess the synergistic anti-psoriatic effects of a combined transthesosomal (TE) curcumin–psoralen formulation	<i>In vitro</i> and <i>in vivo</i>	[13]
Thailand	<i>C. longa</i> and <i>Aloe vera</i>	To investigate the efficacy of <i>C. longa</i> and <i>Aloe vera</i> extracts incorporated into polyvinyl alcohol-based microfibers for <i>in vitro</i> wound healing	<i>In vitro</i>	[8]
Thailand	<i>C. longa</i> L. and <i>Centella asiatica</i>	To evaluate the antioxidant and antidiabetic effects of single and combined extracts of <i>C. longa</i> and <i>Centella asiatica</i> in diabetes management	<i>In vivo</i>	[81]
Thailand	<i>C. longa</i> and <i>Boswellia serrata</i>	To review and summarize the evidence on the efficacy and safety of <i>C. longa</i> and <i>Boswellia serrata</i> , alone and in combination, for knee osteoarthritis	Systematic review	[82]
Korea	<i>C. longa</i> and <i>Glycyrrhiza uralensis</i>	To assess the antiviral efficacy of a combined natural extract of turmeric (<i>C. longa</i>) and liquorice (<i>Glycyrrhiza uralensis</i>) against viral haemorrhagic septicaemia virus in olive flounder	<i>In vitro</i> and <i>in vivo</i>	[83]
Algeria	<i>C. longa</i> and <i>Moringa oleifera</i>	To evaluate the effects of combined aqueous extracts of <i>Moringa oleifera</i> and <i>C. longa</i> on lipid regulation, antioxidant capacity, and cardiovascular structure in hypercholesterolemic Wistar rats	<i>In vivo</i>	[84]
Indonesia	<i>C. longa</i> and <i>Centella asiatica</i>	To determine whether a combined extract of <i>Centella asiatica</i> and <i>C. longa</i> improves arterial stiffness and blood pressure in a hypertensive rat model	<i>In vivo</i>	[85]
Canada	<i>C. longa</i> and <i>Tamarindus indica</i>	To compare turmeric alone with a 2:1 tamarind–turmeric blend on cartilage explant responses to inflammatory stimuli and tissue homeostasis	<i>In vitro</i>	[86]
Vietnam	<i>Ampelopsis cantoniensis</i> , <i>C. longa</i> and <i>Taraxacum officinale</i>	To evaluate the acute toxicity and antibacterial activity of an aqueous extract of <i>Ampelopsis cantoniensis</i> combined with <i>C. longa</i> and <i>Taraxacum officinale</i> , and to enhance its performance through nanoformulation	<i>In vivo</i>	[87]
Turkey	<i>C. longa</i> , <i>Nigella sativa</i> , <i>Prunus mahaleb</i> and <i>Vitis vinifera</i>	To evaluate a polyherbal formulation containing <i>C. longa</i> , <i>Nigella sativa</i> , <i>Prunus mahaleb</i> and <i>Vitis vinifera</i> as a therapeutic strategy against streptozotocin-induced hepatic and pancreatic injury in diabetic rats	<i>In vivo</i>	[88]

CONCLUSION

The data collected in this review suggest that *P. corylifolia* is a promising source of bioactive compounds, including bakuchiol and psoralen, which have antimicrobial, anti-inflammatory, and antioxidant effects of interest in the treatment of acne and its consequences, including cutaneous scarring. Moreover, its addition to combined preparations with other medicinal plants has demonstrated synergistic action in various therapeutic situations, along with a good safety profile in controlled cutaneous use.

In turn, *C. longa* is characterized by the high concentration of curcumin, a commonly researched bioactive compound that is used in acne vulgaris treatment, primarily because of its anti-inflammatory, antimicrobial, and antioxidant properties and the capacity to regulate various pathways that mediate the pathophysiology of skin diseases.

Although research has already been conducted regarding the individual effects of the two species, no research has been found that specifically and systematically assesses the putative synergism between *P. corylifolia* and *C. longa* extracts in the treatment of acne. In this respect, future studies, *in vivo* and *in vitro*, are required to determine this combination with standardized and chemically well-characterized extracts. Furthermore, their mechanisms of action, bioavailability, and safety can be better clarified with the help of more detailed research in order to better define their therapeutic value and their viability as a complementary method in the treatment of acne.

Author Contributions

YYLS was involved in the conception and design of the study, literature review, execution of the research work, and preparation of the original draft. AKC contributed to manuscript translation, reference verification and completion, citation cross-checking, and review and editing of the manuscript. NLA contributed to supervision, guidance, and critical review and editing of the manuscript. All authors have read and approved the final version of the manuscript.

Data Availability Statement

The data that support the findings of this study are available and will be made available upon request.

Use of AI in Drafting of Manuscript

The authors declare that they have not used any generative AI/AI-assisted technologies in the writing of this manuscript.

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