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# PROPOLIS SUPPLEMENTATION - EFFECTS ON PHYSICAL ACTIVITY, SKIN, BONE HEALTH, AND CARDIOVASCULAR FUNCTION: A SYSTEMATIC REVIEW

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**ABSTRACT**

**Introduction:** In recent years, many sports supplements have incorporated several natural ingredients. One notable example is propolis, a bee-derived substance rich in bioactive compounds such as flavonoids, phenolic acids, and vitamins. Research indicates that bee glue has several therapeutic properties, including anti-inflammatory, antioxidant, and immunomodulatory effects. These mechanisms support wound healing, strengthen the immune system, combat respiratory infections, improve both recovery and physical capacity, all of which may collectively lead to enhanced athletic performance.

**Aim of the study:** This study aims to provide a comprehensive analysis of propolis properties. Through a detailed discussion and review of the evidence supporting the beneficial effects of propolis supplementation on the skin, as well as the muscular, skeletal, and cardiovascular systems.

**Material and method:** This article presents the current state of knowledge about the effects of propolis supplementation. A literature review was gathered using PubMed, ScienceDirect, and Google Scholar platforms, with a focus on papers from the last five years. The search included the keywords 'propolis', 'antioxidant activity', 'anti-inflammatory', 'exercise', 'skin regeneration', and 'cardiovascular function'.

**Results:** Literature review revealed that propolis emerges as a multi-target phytocomplex that attenuates inflammation, augments antioxidant defenses, and favorably modulates vascular and musculoskeletal function across pre-clinical models. Synergistic effects with exercise, biomaterial carriers, and microbiota-directed strategies underscore opportunities for combination interventions.

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**KEYWORDS**

Propolis, Antioxidant Activity, Anti-Inflammatory, Exercise, Skin Regeneration, Cardiovascular Function

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**Introduction**

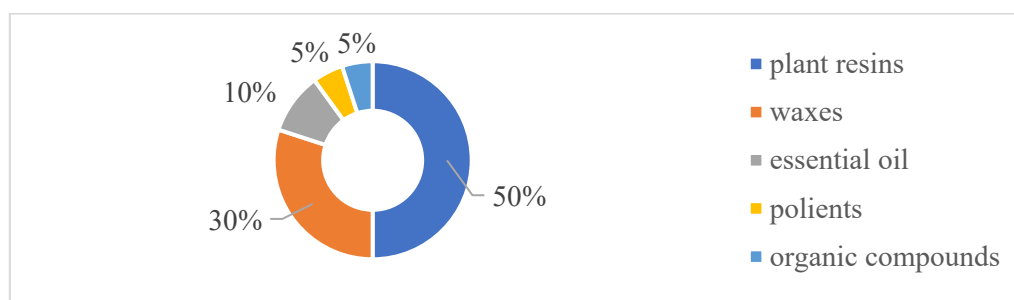
Propolis is a viscous, resin-rich material. The material is harvested by honeybees from the lipophilic secretions of buds, bark fissures, and other plant surfaces. It is subsequently mixed with salivary enzymes and beeswax and eventually forms a multifunctional biocement within the hive. Beyond its structural role, its complex assemblage of polyphenols, terpenoids, and aromatic compounds underpins a long-standing ethnopharmacological reputation for broad-spectrum antimicrobial activity, pronounced modulation of inflammatory cascades, and potent free-radical scavenging capacity, features that collectively justify its continued prominence in traditional and complementary medical practices (Bhatti et al., 2024; Jenny et al., 2024). Propolis constitutes a chemically heterogeneous matrix encompassing several hundred secondary metabolites. It comprises of flavonoids, phenolic acids, terpenoids, and assorted minor constituents. The specific qualitative and quantitative profile of these compounds is modulated by the botanical taxa exploited by bees, the geo-climatic context of the apiary, and seasonal fluctuations in plant phenology (Alanazi & Alenzi, 2024).

Since antiquity, propolis has served both preservative and medicinal roles. Egyptians embalmed bodies with it. Greeks (also Hippocrates) used it for wound treatment. Then, Incas employed it as an antipyretic (Anjum et al., 2019). Through successive centuries Arab, Persian, and European practitioners applied the resin to burns, oral lesions, and infections (Bankova et al., 2000). Subsequently, Soviet clinicians later exploited its antimicrobial effects against tuberculosis and wartime respiratory ailments (Bankova, 2005). Formal chemical study began in the early nineteenth century when Nicolas Vauquelin refined propolis extracts with alcohol and ether. By doing so, he laid the groundwork for its modern pharmacological investigation (Rojczyk et al., 2020).

Propolis is an exceptionally complex, plant-derived apicultural product. Its composition varies with the botanical sources frequented by bees, the prevailing environmental conditions, the species of bee, and the season of collection. Nonetheless, contemporary chromatographic and spectrometric surveys consistently show that it is

dominated by plant resins (50%), followed in abundance by waxes (30%), essential oils (10%), pollen (5%), and a diverse residue of low-molecular-mass organic constituents (5%) encompassing more than five hundred secondary metabolites – flavonoids, phenolic, and other polyphenolic compounds, terpenes and terpenoids, coumarins, steroids, amino acids, aromatic acids, and assorted alcohols (Ahangari et al., 2018) – see Figure 1. Moreover, propolis contains water- and fat-soluble vitamins, notably thiamine, riboflavin, pyridoxine, ascorbic acid, and tocopherol. It also contains physiologically significant electrolytes such as magnesium, calcium, potassium, sodium, copper, zinc, manganese, and iron, thereby endowing the matrix with both structural functions in the hive and a broad spectrum of bioactivities relevant to human health (Huang et al., 2014).

Propolis is a resinous, lipophilic bee secretion that is brittle at ambient temperature. Yet, it becomes viscid when warmed. Its colour ranges from yellow green to dark brown and most samples melt at 60–70°C, though exceptionally resin-rich varieties may approach 100°C (Toreti et al., 2013). Industry usually extracts propolis with solvents such as ethanol and turns the thick extract into many products – pills, skin creams, foods, antiseptics, and even meat preservatives (Anjum et al., 2019).



**Fig. 1.** Chemical structure of propolis

*Note.* Source: own elaboration based on Ahangari et al. (2018).

The therapeutic value of propolis depends largely on its polyphenols. These molecules are embedded in a matrix of high-molecular-mass lipids, waxes, and resins that limits gastrointestinal absorption (Pandareesh et al., 2015). Once ingested, polyphenols undergo extensive phase-I and phase-II transformations – hydroxylation, methylation, sulfation, glucuronidation. Then it must also be hydrolysed by gut microbiota before they can traverse the intestinal epithelium. However, the unabsorbed fractions are further cleaved into smaller phenolics that retain antioxidant activity. How much of a propolis compound the body can use depends on several things. Alcohol in a meal can help it get absorbed, while protein can slow it down (Pietta, Gardana & Pietta, 2002). The compounds are also broken down and removed from the body quite quickly. Their chemical makeup matters too: only the more fat-soluble ones, such as caffeic-acid phenethyl ester, can cross the blood–brain barrier and enter the brain (Majewska-Wierzbicka & Cieczot, 2012). What is more, inter-individual variation in urinary excretion suggests that age, renal function, and the specific propolis source likewise condition the overall systemic exposure to these bioactive metabolites (Alkhalidy et al., 2019).

### Material and methods of research

The literature search was carried out in PubMed, ScienceDirect, and Google Scholar for papers published from January 2019 to June 2025, with some exceptions. The search included the keywords ‘propolis’, ‘antioxidant activity’, ‘anti-inflammatory’, ‘exercise’, ‘skin regeneration’, and ‘cardiovascular function’. Only full-text studies written in English and presenting original data in humans, experimental animals or cell models were considered. Reviews, opinion pieces and conference abstracts without full articles were left out, as were reports that dealt solely with antimicrobial or neurological issues.

All titles and abstracts retrieved from the search were screened. If agreed that a record matched the topic, the full paper was read. From each eligible article there was noted the species or participant group, the type and dose of propolis preparation, how it was given, how long the treatment lasted, the comparison group, and the main findings on the skin, muscle, bone and cardiovascular system. Because the studies differed widely in design and outcome measures, the results were summarised in a descriptive way rather than pooled statistically.

## Results

### Propolis supplementation in physically active individuals

Across a range of sporting and clinical contexts, propolis has repeatedly attenuated oxidative and inflammatory stress, although its influence on conventional performance indices is less uniform. In physically active male military cadets ( $n = 54$ ), four weeks of high-dose Brazilian green propolis (450 mg twice daily) lowered plasma interleukin-6, shifted the IL-6 : IL-10 ratio, and increased total antioxidant capacity without altering maximal aerobic or anaerobic outputs (Soleimani et al., 2021). Comparable antioxidant preservation was reported in elite Japanese kendo athletes ( $n = 11$ ) undertaking a four-day training camp. Daily ingestion of 787.5 mg propolis maintained the fraction of reduced human serum albumin within physiological limits, whereas placebo recipients exhibited a pronounced oxidative shift (Imai et al., 2005). Moreover, central fatigue also appears modifiable. In resistance-trained young men ( $n = 18$ ), a one-week pre-load with high-dose propolis accelerated the recovery of maximal knee-extension torque within two minutes after a 100-repetition fatigue task and prevented the fall in voluntary activation and EMG amplitude seen under placebo, yet left peripheral twitch metrics unchanged (Tsuchiya et al., 2022).

Metabolic and endocrine outcomes are similarly sensitive to supplementation. Among male endurance runners ( $n = 44$ ), four weeks of 1 g day<sup>-1</sup> propolis elevated circulating betatrophin from ~331 to ~476 ng dL<sup>-1</sup> and produced a modest body-mass reduction, changes absent in a non-supplemented training comparator (Rashvand et al., 2022). Synergistic effects emerge when propolis is paired with structured exercise in metabolically challenged populations. In women with type-2 diabetes and dyslipidaemia ( $n = 60$ ), thrice-weekly combined aerobic–resistance sessions plus 500 mg propolis daily achieved concurrent reductions in malondialdehyde and interleukin-6, elevations in superoxide dismutase and total antioxidant capacity and favourable shifts in adiponectin, CTRP12, SFRP5, and the lipid profile. However, exercise or propolis alone yielded only partial benefits (Moayedi et al., 2023). A parallel interaction was documented in adults with non-alcoholic fatty liver disease ( $n = 32$ ): alanine- and aspartate-aminotransferase activities declined after eight weeks of high-intensity interval training, with the largest decrements occurring when each session was accompanied by thrice-daily 50 mg Iranian propolis tablets, whereas the supplement in isolation proved inert (Irandoost et al., 2024).

Ergogenic benefits have been most evident in pediatric and multi-component hive-product interventions. In young competitive gymnasts (ages 6–12 y,  $n = 24$ ), four weeks of honey-based blends enriched with bee-pollen, royal jelly and propolis improved grip strength, muscular endurance and anaerobic power. It was all without disturbing routine haematological variables (Saritaş et al., 2023). By contrast, adult cohorts show subtler functional gains. In another study, physically trained men ( $n = 7$ ) completing two 30-day crossover phases reported lower post-exercise pain and reduced lymphocyte counts during the artemipillin-C-rich propolis phase, despite unchanged training load and body composition (Caperuto et al., 2019).

Pre-clinical evidence suggests that these systemic adaptations may extend to structural preservation under extreme conditions. In male Wistar rats subjected to two weeks of hind-limb suspension, twice-daily gavage with 500 mg kg<sup>-1</sup> Brazilian propolis prevented soleus muscle capillary rarefaction by suppressing anti-angiogenic mediators p53 and thrombospondin-1 while up-regulating pro-angiogenic signals. On the other hand, ambulatory controls receiving propolis were unaffected (Tanaka et al., 2019).

### Systemic pathways of propolis action in neuromuscular regulation

Accumulating evidence from a spectrum of animal and cell-culture models indicates that propolis orchestrates a coordinated defence of skeletal muscle that engages metabolic, redox, inflammatory and even neurovascular axes. Ethanol-extracted propolis given to C57BL/6 mice for three weeks at 400 mg kg<sup>-1</sup> day<sup>-1</sup> prolonged exhaustive-swim time by nearly thirty percent. Simultaneously it expanded hepatic and intramuscular glycogen pools while blunting the rise in lactate, urea, lactate dehydrogenase, and multiple pro-inflammatory cytokines. Antioxidant enzyme activities rose in parallel, and untargeted metabolomics revealed a normalisation of six fatigue-linked metabolites, changes that were strongly associated with a shift in gut microbiota toward butyrate-producing genera (Huang et al., 2025). In rats trained for six weeks at seventy percent VO<sub>2max</sub>, a water-soluble propolis extract (50 mg kg<sup>-1</sup> day<sup>-1</sup>) acted synergistically with running to produce the greatest increases in muscle and liver glycogen, the highest activities of superoxide dismutase, glutathione peroxidase and catalase in gastrocnemius and the sharpest fall in malondialdehyde. On the other hand, propolis or training alone achieved only partial effects (Kwon et al., 2014). Overall, these animal studies show that propolis boosts metabolism and antioxidant defenses, which in turn improves physical performance.



Mechanistic work in cell culture reinforces this perspective. In the D-galactose premature-senescence model, ethanolic propolis extract restored C2C12 myoblast viability. Moreover, it halved the proportion of senescence-associated  $\beta$ -galactosidase-positive cells and re-established myogenic differentiation by mobilising nuclear factor-erythroid-2-related factor 2 (Nrf2) and haem oxygenase-1 while concurrently repressing p38 phosphorylation and p53 expression, thereby linking redox control with anti-apoptotic signalling (Tian et al., 2023). The relevance of these pathways in whole animals is underscored by two independent ageing or metabolic-disease models. In D-galactose-aged mice propolis restored myofibre cross-sectional area, enhanced Nrf2 nuclear translocation, elevated the Bcl-2 : Bax ratio and suppressed the ubiquitin ligases MuRF1 and MAFbx. It was indicated that there was a simultaneous control of oxidative stress, apoptosis and proteolysis (Tian et al., 2022). In leptin-receptor-deficient Db/Db mice modelling sarcopenic obesity, eight weeks of dietary Brazilian green propolis (0.08–2 % w/w) sharpened glucose tolerance, increased soleus and plantaris mass. It also lowered non-alcoholic-fatty-liver-disease activity scores. What is more, hepatic immune polarisation shifted toward M2 macrophages and ILC2s, muscle and liver saturated-lipid stores fell while faecal excretion rose and the intestinal microbiota acquired a more favourable Bacteroidetes : Firmicutes ratio with enrichment of butyrate-linked genera (Okamura et al., 2022). By contrast, in a twenty-week methyl-glyoxal model of chronic glycation stress, 0.1 % Brazilian propolis curtailed AGE accumulation, boosted glyoxalase-1 activity and suppressed Il-1 $\beta$ , Il-6 and Tlr4 in fast-twitch extensor digitorum longus yet did not fully rescue its mass, whereas the slow-twitch soleus displayed only marginal benefits (Egawa et al., 2019). Together these studies suggest that the magnitude of the anabolic response to propolis varies with fibre phenotype and the nature of the catabolic insult, but consistently involves antioxidant and inflammatory modulation reinforced by alterations in gut ecology.

A parallel line of investigation focuses on vasomodulatory constituents of propolis that could indirectly benefit working muscle (by optimising perfusion and blood-pressure control). The flavonoid 3,3'-O-dimethylquercetin, isolated from Caatinga propolis, acted on two types of ion channels in rat tail-artery muscle cells. It blocked CaV1.2 L-type calcium channels while activating large-conductance Ca<sup>2+</sup>-activated K<sup>+</sup> channels. Eventually, it led to a potassium-sensitive and concentration-dependent relaxation of depolarised arterial rings (Son et al., 2024). Chrysin, another abundant propolis flavonoid, reduced rat coronary arterial tone by inhibiting TMEM16A (ANO1) Ca<sup>2+</sup>-activated Cl<sup>-</sup> channels. The vasorelaxation was attenuated in Cl<sup>-</sup>-free medium and weakened by blockade of cAMP/PKA or NO/PKG signalling, indicating that CaCC inhibition is primary and is then amplified by cyclic-nucleotide cascades (Ma et al., 2020).

Beyond muscle and vasculature, propolis also appears to promote neuromuscular recovery. In a rat sciatic-nerve transection model, a propolis–gum-Arabic conduit spanning a critical gap yielded superior sciatic-function indices from day 30 onward. By day 90, it produced larger muscle-fibre diameters, thicker myelin and a higher density of myelinated axons than achieved with conventional autografting (Nosratiyan et al., 2021). Compared to the skeletal-muscle data, these findings suggest that propolis or propolis-derived biomaterials could deliver holistic support to the neuromuscular system.

### **Propolis as a biomaterial component supporting skin regeneration**

A substantial part of recent studies has recast propolis from a traditional antiseptic into a versatile building-block for advanced wound biomaterials. Propolis consistently accelerates closure of full-thickness skin defects when immobilised within structural protein scaffolds. A type-I-collagen hydrogel fortified with ethanolic propolis and eucalyptus extracts closed deep dorsal wounds in Sprague–Dawley rats by day 21, outperforming collagen–propolis or collagen–eucalyptus single-additive controls in both macroscopic contraction (~65 % by day 7) and histological maturity (Tahmasebi & Yazdanian, 2025). Comparable contraction indices were later reproduced with a polyvinyl-alcohol matrix containing Indian propolis (93–94 % in burn and excision models), whose physicochemical optimisation by design-of-experiments yielded pH-stable, viscosity-appropriate gels with sustained in-vitro release (Kapare et al., 2023). A complex ointment containing propolis, honey, apilarnil, collagen, chitosan, egg-white lyophilisate, and four medicinal-plant extracts cut wound size by 98 % by day 9 in Wistar rats with incisions, excisions, or burns. This rapid closure was linked to faster granulation and well-organised collagen remodelling (Andritoiu et al., 2025).

Nano-enabled formulations further extend this therapeutic range. Particularly in thermally injured tissue. A nano-emulsion made with ethanolic propolis, hyaluronic acid, and vitamin K shrank second-degree burns in rats by 98 % within 14 days. It also boosted new blood-vessel growth and thickened collagen (Elsamman et al., 2024). In parallel study the Punjabi propolis was used. Silver nanoparticles 50–60 nm across were synthesised with Punjabi propolis as both reducing and capping agent. These particles showed very low-

nanomolar antioxidant and anti-inflammatory  $IC_{50}$  values, inhibited *Staphylococcus aureus* and *Proteus mirabilis*. Moreover, when formulated in a polymer gel, these particles sped up burn-wound closure and collagen deposition in rabbits compared with a vehicle gel (Islam et al., 2024).

Mechanistic work shows that propolis acts through both immune and tissue-repair pathways. Network-pharmacology analysis identified twenty-eight proteins common to propolis compounds and UV-induced dermatitis, with TNF, NFKB1, MMP-9 and IL-2 emerging as key nodes. Follow-up tests in UVB-irradiated fibroblasts confirmed that propolis extract lowers MMP-9 and IL-2 in a dose-dependent way (Cheng et al., 2025). Complementary in-vitro study showed that red Brazilian propolis inhibits NF- $\kappa$ B transcription ( $IC_{50} < 10 \mu\text{g mL}^{-1}$  in keratinocytes) while stabilising HIF-1 $\alpha$  and up-regulating its target genes, behaviour only partly reproduced by green propolis and supporting chemotypic specificity in scar-minimising pathways (Magnavacca et al., 2022). In vivo, these molecular signatures manifest as coordinated matrix and cytokine changes: 1 % red-propolis paste enhanced collagen I : III balance, down-regulated MMP-9, and elevated TGF- $\beta_3$  and VEGF in rat excisional wounds (Conceição et al., 2022), whereas 10 % Chihuahua propolis shortened closure time and strengthened tensile load in murine incisions while favouring type-I-collagen deposition (Balderas-Cordero et al., 2023).

A well-designed formulation can strengthen propolis's natural effects. Using a Box–Behnken design, researchers prepared an emulgel containing 5 % propolis and *Passiflora edulis* seed oil. This emulgel penetrated the stratum corneum better and delivered more polyphenols to deeper skin layers than an equal-dose propolis suspension. As a result, wounds re-epithelialised faster, hydroxyproline content rose, and local TNF- $\alpha$ , IL-1 $\beta$ , and IL-6 levels fell more sharply (Gupta et al., 2022).

To sum up, the diverse methodologies, i.e., protein hydrogels, polymeric films, nano-emulsions, metal-nanoparticle gels and emulgels, arrive at a common outcome. Propolis, whether alone or co-formulated with synergistic botanicals or polymers, simultaneously curbs bioburden, dampens inflammation and augments antioxidant tone.

### **Modulatory role of propolis in maintaining bone and cartilage homeostasis**

Growing evidence from animal and cell studies shows that polyphenols in propolis act at key points in bone and cartilage balance. These polyphenols slow tissue breakdown and protect joint structure. In chondrocytes treated with IL-1 $\beta$ , the propolis compound caffeic-acid phenethyl ester inhibits NF- $\kappa$ B and activates the Nrf2/HO-1 pathway, which lowers iNOS and COX-2, preserves aggrecan and collagen II. Moreover, it was proved that in rat osteoarthritis, it delays cartilage damage (Sun et al., 2022). In another study it was showed that poly(p-coumaric-acid) nanoparticles offer a drug-free alternative that targets the same redox-inflammatory pathways. In a model of temporomandibular-joint osteoarthritis they outperformed standard hyaluronic-acid injections. By keeping oxidative stress, matrix breakdown and ferroptosis low over time, the particles promoted coordinated repair of cartilage and the underlying bone (Guo et al., 2024). Pinocembrin also shields the cartilage endplates of spinal discs from oxidative damage. It works by activating Nrf2-driven mitophagy and preventing ferroptosis. When given systemically, pinocembrin maintained disc height and reduced endplate calcification in vivo, but these benefits vanished if Nrf2 was knocked down (Wang et al., 2023).

Propolis flavonoids act on both sides of bone remodelling. Pinocembrin blocks RANKL and dampens NF- $\kappa$ B/ROS/NFATc1 signalling, which stops osteoclast formation and bone breakdown in cell studies and prevents trabecular bone loss in ovariectomised mice (Hong et al., 2024). In contrast, kaempferol corrects titanium-particle damage to osteoblast activity by restoring Runx2, Sp7, and osteocalcin expression and turning on Wnt/ $\beta$ -catenin signalling. By doing so, it led to a dose-dependent drop in periprosthetic bone loss in a mouse skull model (Qiu et al., 2023). Even exogenous toxins are tractable: CAPE ( $10 \mu\text{mol kg}^{-1}$ , i.p.) partially reverses the fracture-healing deficit imposed by chronic cigarette-smoke exposure, restoring woven-bone deposition and dampening osteoclastic resorption (Acikan et al., 2022).

Propolis compounds can also counter bone loss caused by hormones or lifestyle factors. In ovariectomised rats, oral quercetin stops trabecular bone loss. It does so by increasing beneficial gut bacteria (*Lactobacillales*, *Prevotellaceae*, *Blautia*), raising short-chain fatty acids in the gut, strengthening intestinal tight junctions, and lowering blood levels of LPS, IL-1 $\beta$ , and TNF- $\alpha$ . When the gut microbiota is wiped out with antibiotics, this bone protection disappears, but it returns after faecal microbiota transplantation (Feng et al., 2024). Another study showed that pairing exercise with ferulic acid adds benefits that exercise alone cannot provide. In ovariectomised rats, twelve weeks of tower-climbing combined with a ferulic-acid diet lowered blood triglycerides, protected femoral bone mineral density and repaired skin structure, whereas tower-

climbing without the polyphenol did not. This suggests ferulic acid supplies biochemical signals missing from mechanical loading on its own (Lee et al., 2025).

Taking into consideration studies described above, it reveals that propolis flavonoids dampen oxidative-inflammatory cascades, rebalance osteoblast-osteoclast activity and engage microbiota or mechanotransductive pathways to protect bone and cartilage.

### **Regulation of cardiovascular function by propolis constituents**

Recent studies show that different propolis fractions act at several critical points along the cardiovascular disease pathway. They influence endothelial inflammation, ion channel-linked redox balance, vasomotor tone and overall blood pressure control. In human gingival fibroblasts stimulated with lipopolysaccharide or interferon- $\alpha$ , Polish ethanolic propolis extract and its main component, caffeic-acid phenethyl ester, dampen pro-atherogenic signals. They lower interleukin-6, E-selectin, and endothelin-1. On the other hand they raise the anti-inflammatory cytokine interleukin-10 and shift the local cytokine and adhesion profile toward a state that is less likely to promote atherosclerosis (Kurek-Górecka et al., 2024). Another study revealed that in microvascular endothelial cells, very low (nanomolar) concentrations of CAPE open the heat-sensitive TRPV1 channel, causing a quick influx of  $\text{Ca}^{2+}$  and  $\text{Na}^{+}$ . Within seconds, this ion flow triggers an antioxidant response—seen as a rapid change in a HyPer redox sensor—which disappears if TRPV1 is blocked or silenced, directly linking TRPV1 activation to CAPE's protective effects (Hidalgo et al., 2025).

Propolis flavones relax blood vessels in multiple ways but do not always lower blood pressure over time. In rat aortas, chrysin works by boosting nitric-oxide signalling and opening  $\text{K}^{+}$  channels while blocking  $\text{Ca}^{2+}$  entry. Yet three weeks of oral chrysin did not reduce blood pressure in hypertensive rats. It suggests it may be poorly absorbed or counteracted in the whole organism (Tew et al., 2023). In coronary arteries, chrysin also reduces  $\text{Ca}^{2+}$ -activated  $\text{Cl}^{-}$  currents through TMEM16A/ANO1 channels. Blocking these channels or inhibiting cAMP/PKA and NO/PKG signalling reduces chrysin's relaxing effect. From this study, it is suggested that chrysin eases vasospasm partly by targeting CaCCs (Ma et al., 2020).

Conversely, multi-component or structurally distinct propolis preparations do improve haemodynamics in disease models driven by neuro-humoral and oxidative stress. In a specific study it was proved, that a tritherapeutic mixture of propolis, royal jelly and, bee venom normalises blood pressure and electrocardiographic indices in dexamethasone-loaded rats. On the other hand it was proved that it lowered circulating angiotensin II, endothelin-1, TGF- $\beta$  and NF- $\kappa\text{B}$  activity, performing comparably to losartan (Abd El-Hakam et al., 2022). In renovascular hypertension, galangin diminishes systemic ACE activity and angiotensin II, down-regulates myocardial  $\text{AT}_1$ -receptor, TGF- $\beta_1$  and collagen-I, and restores Nrf2/HO-1 signalling and antioxidant enzyme profiles in the stenotic kidney, cumulatively reversing cardiorenal remodelling to a degree equivalent to losartan (Chaihongsa et al., 2022). Finally, in salt-loaded rats Chinese water-soluble propolis dose-dependently rescues left-ventricular output, repairs vascular architecture and suppresses Nox2/Nox4-driven ROS. Thus, study confirmed that polyphenol-rich propolis can offset haemodynamic and oxidative sequelae of dietary sodium excess (Zhou et al., 2020).

Altogether, these findings show that propolis compounds protect the heart and vessels on several fronts (reducing endothelial inflammation, balancing calcium-driven redox signals, blocking vasoconstrictor ion channels, etc.).

### **Discussion and Conclusions**

Findings across skin, muscle, bone and cardiovascular models converge on a common mode of action. Propolis polyphenols suppress inflammation, activate antioxidant defences and secondarily adjust ion-channel or hormonal pathways. Furthermore, propolis can hasten wound closure, blunt muscle fatigue, preserve trabecular bone and ease vascular dysfunction. Benefits intensify when propolis is paired with complementary stimuli – exercise, hyaluronic-acid carriers, or gut-modulating prebiotics. Hence, results of studies point to clear opportunities for combination strategies.

Translation is limited mainly by two hurdles. First, chemical heterogeneity. Botanical source and extraction method shift the polyphenol profile, so standardised fingerprinting is essential. Second, uneven bioavailability, because lipophilic esters such as CAPE penetrate tissues, whereas larger polar constituents do not. Hence, nano-emulsions and encapsulation are therefore needed for consistent systemic exposure. Small human trials already echo the antioxidant and immunomodulatory effects seen in animals. These trials suggest mechanistic conservation.



To sum up, propolis is a multi-target phytocomplex with credible pre-clinical evidence for supporting tissue repair, metabolic resilience and vascular health. Future work should standardise preparations, optimise delivery and run larger, well-controlled clinical trials. By doing so it would be possible to confirm whether the broad benefits observed experimentally can be translated into routine preventive or therapeutic use.

#### Author's contribution:

Conceptualisation and project administration: Paula Folta

Methodology: Cezary Lubas and Anna Opalińska

Validation: Paula Folta, Kacper Szeląg and Małgorzata Zach;

Formal analysis and investigation: Karolina Błądzińska and Maciej Błądziński

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