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Propolis: Bioactivity, Therapeutic Applications, and Future Directions

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Abstract: Propolis is a resinous hive material with a chemically diverse composition that has traditionally been used in different communities and is now being investigated for oral care, wound treatment, antimicrobial formulations, metabolic support, and advanced delivery systems. Although studies have reported several biological activities, translating propolis into a therapeutic product remains difficult. Its chemical composition can vary according to plant source, location, season, bee species, harvesting practices, and extraction method. This review articles examines the steps needed to move propolis from collection to clinical use, with particular attention to Pakistan. These steps include beekeeper awareness, botanical and geographic traceability, hygienic harvesting, chemical characterization, quality control, product formulation, safety assessment, and clinical validation. Better coordination among farmers, researchers, clinicians, and industry may help convert locally produced propolis into reproducible and responsibly tested products. The central argument is that the therapeutic and commercial value of propolis will depend not simply on isolated bioactivity claims, but on consistent raw-material quality, traceability, analytical standardization, safety, and evidence-based translation.

Keywords: Propolis; therapeutic applications; antioxidant activity; antimicrobial activity; apiculture; bioactive compounds

1. Introduction

Bees of the genus Apis play a fundamental role in ecosystems. This has resulted in species diversifying and spreading across Asia, Africa, and Europe (Holzer et al., 2026). Honeybees are social insects in the family Apidae (Order: Hymenoptera), which includes all honey-producing species (Tsadila et al., 2023). Beekeeping is an important practice that benefits agriculture, the environment, and communities (Richardson, 2023). From early honey-hunting traditions to modern commercial pollination operations, Beekeeping has evolved into a complex agroecological sector that integrates biological, environmental, and economic processes. Honeybees are critical to crop productivity, biodiversity, and ecosystem stability across diverse landscapes.

The honeybee (A. mellifera) is a globally distributed insect, absent only from polar regions, and contributes more than US$200 billion annually to the global economy through pollination and hive products (Usman et al., 2022). Pakistan covers an area of 132,700 km2. It is the richest natural heritage of pollinator diversity due to its diverse geographical features. The climate is subtropical and semiarid with ten agroecological zones (Saeed, 2022). Pollinators like Honeybees of the Apis genus have a unique ecological niche among insect pollinators due to their eusocial structure and managed hives. It's defined by cooperative brood care, division of labor, and overlapping generations, enabling colonies to function as coordinated superorganisms capable of efficiently regulating thermoregulation, foraging, resource allocation, and disease defense. Apis mellifera is the most domesticated and commercially used pollinator among the more than 20,000 bee species (Saeed, 2022). It is native to Europe, Africa, and Western Asia, but has been selectively bred all over the world, producing subspecies adapted for honey production, gentleness, disease resistance, and climate tolerance (Meixner et al., 2010). These features position the bee keeping industry as a natural tool for poverty alleviation, livelihood diversification, and rural economic development (Amulen et al., 2017).

Beekeeping in Pakistan is practiced under stationary and migratory systems. Stationary beekeeping depends on local floral resources and is suitable only where nectar flows are consistent. Migratory beekeeping involves seasonal movement of colonies across agro-ecological zones, especially between Punjab and Khyber

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Pakhtunkhwa, to utilize successive blooms. Beekeeping in Pakistan faces multiple biotic and abiotic challenges, including excessive pesticide use, deforestation, climate variability, and a shortage of skilled personnel, contributing to declining honeybee populations. Despite these constraints, the country has strong apicultural potential due to its diverse agro-ecological zones. Pakistan produces approximately 16,000 metric tons of honey annually and exports nearly 4,000 tons (Gyawali, 2025), mainly to Middle Eastern markets, generating about US$23 million in foreign exchange (Usman et al., 2022).
Besides honey, honeybees produce several valuable by-products, including pollen, bee bread, royal jelly, beeswax, and propolis. Among these, propolis is particularly important as a rich source of bioactive compounds with antioxidant, antimicrobial, and anti-inflammatory properties, making it a promising but underutilized resource for nutraceutical, pharmaceutical, food, and cosmetic applications (Giampieri et al., 2022).

Propolis is a substance collected and processed by honeybees from various plant sources. Its chemical composition varies considerably with botanical origin, geographical location, season, climate, and honeybee species, resulting in differences in its biological activity. Propolis is rich in flavonoids, phenolic acids, terpenoids, and other bioactive compounds. Propolis has demonstrated antioxidants, antimicrobial, anti-inflammatory, immunomodulatory, and anticancer activities in experimental studies. These properties have generated interest in its therapeutic potential. Variations in composition, extraction methods, and limited clinical evidence remain important challenges for its translation into reliable therapeutic applications (Hossain et al., 2022).

2. Apiculture as the Foundation of Hive-Product Value

Apiculture begins with the managed rearing of bees, but its value is wider than honey alone. A healthy and well-managed colony can provide pollination services and several hive products, including honey, beeswax, pollen, bee bread, royal jelly, propolis, bee venom, queen bees, and live colonies for multiplication. These byproducts are often treated as secondary, especially in small farming systems, but they can become important raw materials for nutrition, cosmetics, dentistry, dermatology, wound care, and pharmaceutical formulation when they are collected and processed under controlled conditions (Ayad et al., 2025; Kapoor and Bhutani, 2026; Martinotti et al., 2025).

Propolis is particularly important because bees produce it mainly from plant resins and use it within the hive. Bees collect resins, buds, exudates, waxes, and other plant materials, mix them with salivary secretions, and use the resulting substance to seal cracks, strengthen hive surfaces, and reduce microbial pressure. This is why propolis is often called bee glue. For researchers, however, interest is not only its physical role in the hive.

Propolis contains plant-derived compounds that have been associated with antioxidant, anti-inflammatory, antimicrobial, immunomodulatory, and wound-supporting activities (Hernández-Martínez et al., 2024; Kapoor and Bhutani, 2026; Vind et al., 2026). Before propolis can be considered a credible therapeutic material, it must progress through a series of interconnected stages, beginning with farmer awareness and hygienic collection, followed by botanical and geographic traceability, chemical fingerprinting, biological evaluation, product formulation, quality assurance, safety assessment, clinical validation, and finally commercial translation. Each stage contributes to the quality, reproducibility, and scientific reliability of propolis-based products.

Failure to maintain traceability and standardization at any point may compromise chemical consistency, biological performance, regulatory acceptance, and the validity of subsequent research findings. The proposed translational framework (Figure 1) summarizes this stepwise pathway and provides a practical roadmap for the responsible development of standardized propolis products in Pakistan.

Propolis is collected by honeybees from plant resins and utilized within the hive for protection and structural maintenance. After harvesting, raw propolis is cleaned, processed, and standardized to obtain bioactive extracts, which can be developed into various therapeutic and healthcare products. This pathway highlights the translational potential of propolis from hive to therapeutic application.

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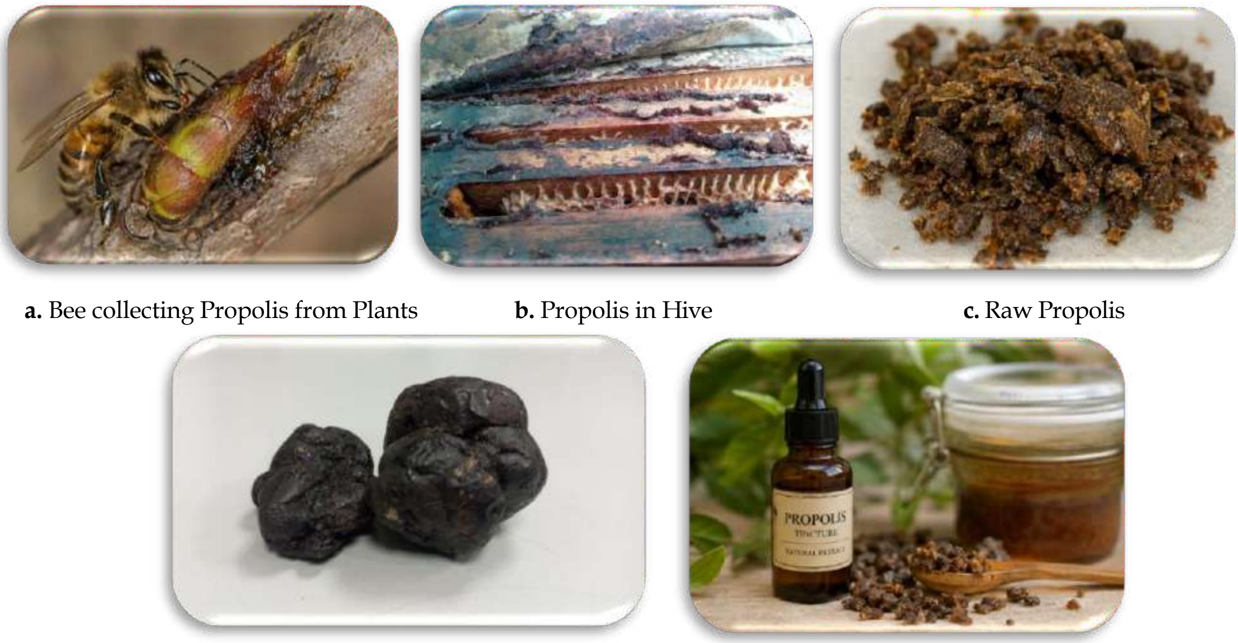

a. Bee collecting Propolis from Plants **b.** Propolis in Hive **c.** Raw Propolis

d. Processed/cleaned/Standardized **e.** Therapeutic Propolis Product

Figure 1. Propolis from hive to therapeutic product. The schematic illustrates the translational pathway of propolis from its natural plant-derived origin to potential therapeutic applications. Honeybees collect resinous materials from plant buds, bark, leaves, and other exudates and incorporate them into the hive, where propolis contributes to hive sealing, structural maintenance, and colony protection. Harvested propolis is subsequently separated from impurities such as wax and debris and processed to obtain cleaner raw material. The resulting propolis extracts can be incorporated into diverse pharmaceutical, nutraceutical, and healthcare formulations, including tinctures, capsules, creams, gels, and sprays.

2.1. Why Propolis Is Promising but Difficult

A major limitation in propolis research is the lack of a universally standardized composition. A sample from one region may contain high levels of phenolic acids, flavonoids, and aromatic compounds, while another may be richer in waxes, carbohydrates, terpenoids, or different plant markers. Quantitative 1H NMR work has shown clear separation between Scandinavian and Australian propolis, and studies of Moroccan and Australian stingless-bee propolis also show how strongly local vegetation can shape biological activity (Aboukhalaf et al., 2024; Ebner et al., 2025; Vind et al., 2026). This variability is scientifically valuable, but it is also the reason propolis cannot be translated responsibly without standardization. The therapeutic promise remains strong. A recent meta-analysis of randomized trials suggests that propolis supplementation can improve selected inflammatory and oxidative-stress biomarkers in adults (Bahari et al., 2025). Oral-health evidence is especially active, with studies and reviews examining plaque, gingivitis, periodontitis, recurrent aphthous stomatitis, oral mucositis, ventilator-associated pneumonia, and post-procedure wound healing (Assis et al., 2026; Ballouk et al., 2025; Çakmak & Nural, 2024; Darbanian et al., 2024; Etebarian et al., 2024; Pattnaik et al., 2026; Roberts et al., 2024; Sycińska-Dziarnowska et al., 2025; Takeuchi-Hatanaka et al., 2025; Waqar et al., 2024)Skin and wound-care research is also developing, including chronic ulcer treatment and activity against *Cutibacterium acnes* biofilm (Athanasopoulou et al., 2025; Rocha et al., 2024).

Extraction adds another layer of uncertainty. Natural deep eutectic solvents, ultrasound-assisted extraction, emulsions, and other newer methods can improve recovery of phenolic compounds, antioxidant activity, stability, and digestive behavior (González Montiel et al., 2024; Hernández-Martínez et al., 2024; Trusheva et al., 2024). These methods are useful, but they also mean that two laboratories may not be testing the same thing. A change in solvent, temperature, storage, or digestion model can change the extract enough to affect the result.

Table 1. Examples of Regional Propolis Types, Major Bioactive Constituents, Reported Biological Activities, and Representative References

Geographic origin / Propolis type	Dominant bioactive compounds	Reported biological activities	Representative reference
Brazilian Green	Artepillin C, p-coumaric acid	Anti-inflammatory, antioxidant, wound healing	Rocha et al., 2024
European Poplar	CAPE, Pinocembrin, Chrysin, Galangin	Antioxidant, antimicrobial, immunomodulatory	Martinotti et al., 2025
Moroccan	Phenolic acids, flavonoids	Antioxidant, antimicrobial	Aboukhalaf et al., 2024
Australian (Tetragonula)	Polyphenolic compounds	Radical scavenging activity	Ebner et al., 2025
Scandinavian	Phenolic acids and flavonoids (distinct metabolomic profile)	Antioxidant potential	Vind et al., 2026

Still, propolis should not be presented as a cure-all. Metabolic-health studies suggest possible benefits for fasting blood sugar, triglycerides, oxidative balance, and fatty-liver-related biomarkers, but these findings remain supportive rather than curative (Fazeli Moghadam et al., 2026; Gholami et al., 2024; Nazari-Bonab et al., 2024; Rab et al., 2026). Anticancer reviews describe interesting signaling pathways, although much of that evidence is still preclinical (Valivand et al., 2024).

Figure 2. Importance of propolis in various fields

Even antimicrobial work needs careful interpretation: one study found synergy between Polish propolis extract and amphotericin B against selected yeast pathogens, but it also reported antagonistic interactions with some antifungal agents (Bollin et al., 2026). Overall, the available findings support further controlled research and product development. They do not yet support unrestricted clinical use or self-medication.

2.2. Production and Awareness Begin at the Hive

Problems with propolis quality often begin during collection at the apiary. Many farmers and beekeepers know how to manage honey and wax because these products are visible, familiar, and easier to sell. Propolis is different. It may be scraped away as waste, mixed with old wax and debris, or collected without any record of location, season, or floral surroundings. If farmers do not know what propolis is, they cannot see it as a possible source of extra income. Good propolis production does not require complicated technology at the beginning, but it does require discipline. Beekeepers need to recognize resin-rich deposits, use clean propolis traps or safe scraping tools, avoid mixing propolis with wood chips, dead insects, soil, paint residues, or old wax, and store it in clean, dry, dark, labelled containers.

A useful batch record should include apiary location, date, season, bee stock, dominant nearby flora, harvesting method, and storage conditions. Without this information, researchers cannot reliably link laboratory findings to the location, season, or botanical source of the sample. Chemical use around hives is another concern. Unnecessary antibiotics, pesticides, acaricides, smoke contaminants, dirty tools, and poor storage can reduce propolis quality. Residues may damage consumer trust, interfere with chemical profiling, or make the material unsuitable for therapeutic development. Propolis training should therefore be linked with good beekeeping practice, integrated pest management, hygienic collection, and residue monitoring rather than taught as an isolated topic. Farmers also need a clear economic reason to change their practice. Propolis should be explained not only as research material, but as a possible additional income stream. That income is realistic only if the product is collected cleanly, graded properly, stored safely, and connected to buyers who value documentation. Without a market link, awareness campaigns will remain weak.

2.3 Pakistan: A High-Potential but Understudied Setting

Pakistan's varied climate, vegetation, and agricultural regions provide a useful setting for studying differences among local propolis samples. Plains, mountains, forests, arid zones, irrigated agriculture, and seasonal floral flows may produce propolis that differ in color, resin source, phenolic profile, antimicrobial activity, and safety markers. This possibility is important, but it should be tested rather than assumed. A coordinated region- and flora-specific map of Pakistani propolis is still missing, and a sample from one district should not be treated as representative of the whole country. A national program should begin with botanical and geographic traceability. Samples need to be collected across provinces, seasons, and floral zones, then studied through chromatographic, spectroscopic, metabolomic, and bioassay-based methods. Recent authentication research shows that chemical profiling and international standardization are central to propolis quality control (Pastor et al., 2025). Pakistan can build on this approach while still developing its own local evidence instead of borrowing assumptions from unrelated ecosystems. Notably, in Pakistan the use of propolis is very limited. Beekeepers do not have much awareness about its uses (Figure 2).

Local knowledge should be documented with care. Informal reports suggest that some farmers or community members use propolis for stomach discomfort, chew it in a way compared with *naswar*, or apply it to the upper surface of wounds. These reports should not be written as clinical proof. They are, however, useful starting points for field surveys because they show how people recognize, value, and use propolis outside formal research settings. Human capacity is just as important as biodiversity. Sustained propolis research will require collaboration among apiculturists, chemists, microbiologists, pharmacists, clinicians, extension workers, and industry partners. If senior scientists such as Dr. Kardar are willing to support propolis work, they need students, apiculturists, chemists, microbiologists, pharmacists, dentists, clinicians, extension workers, and industry partners around them. The weak linkage between farmers, academia, and industry is not a small administrative weakness; it is one reason promising hive products often remain laboratory topics instead of becoming reproducible products.

3. Proposed Perspective Study Design

The practical way forward is a staged prospective study. The first stage should be a field survey of beekeepers and farmers across different ecological zones of Pakistan. The survey should ask whether they recognize propolis, how they remove it from hives, whether they see it as waste or a saleable product, which chemicals are used around colonies, and what local uses are reported. Anecdotes about stomach discomfort, chewed as a resinous substance in a manner like the local smokeless tobacco product (naswar), and wound application should be recorded as community knowledge, not as proven treatment.

The second stage should collect propolis samples from the same surveyed areas. Each sample should be linked with province, district, season, dominant flora, hive type, bee stock, harvesting method, storage condition, and photographs of the raw material. Original propolis photographs can strengthen the paper if they are genuinely field-collected, clear, dated, owned by the authors or properly permitted, and used with consent where people or private apiaries are identifiable. The third stage should connect laboratories and industry partners. Universities can carry out chemical fingerprinting, antioxidant testing, antimicrobial screening, residue analysis, and microbial-quality testing. Industry partners can evaluate drying, storage, packaging, HACCP documentation, hygiene certification, QA/QC records, and production technology training needs. Farmers remain central because they control the first and most fragile step: clean production. Only after that chain is working should selected batches move toward product development. Early products should be realistic: oral-care preparations, topical wound-care formulations, dermatological products, or standardized supportive supplements. Any clinical testing should use traceable batches, defined doses, safety monitoring, and modest claims.

3.1. From Raw Material to Therapeutic Product

Clinical development depends on consistent quality control during harvesting, laboratory testing, formulation, storage, and product evaluation. At the farm level, the priorities are clean harvesting, batch separation, and traceable storage. At the laboratory level, they are authentication, marker compounds, solvent selection, microbial testing, contaminant screening, and batch-to-batch reproducibility. At the product level, the priorities become stability, delivery system, dose, packaging, labelling, allergy warnings, and intended use. Formulation science matters because raw propolis is not always easy to use. It can have poor water solubility, a strong taste, variable absorption, and inconsistent release.

Recent work on nanoparticles, liposomes, hydrogels, niosomes, self-microemulsifying systems, and related platforms shows how delivery systems may improve stability, bioavailability, mucosal retention, and controlled release (Kaspute et al., 2026). Food and digestion studies also show that emulsions and storage conditions can change measured phenolic content and antioxidant activity (González Montiel et al., 2024). These details determine whether a product is merely interesting on paper or usable in practice. Quality systems should be built early. Hazard Analysis and Critical Control Point (HACCP) thinking that hygiene certification, QA/QC documentation, storage protocols, production technology training (PTT), residue testing, microbial limits, and global propolis acceptance standards should be treated as part of the research design. These systems protect farmers, patients, researchers, and companies. They also make local products more acceptable to national and international markets. Safety should remain visible throughout the paper. Natural products are not automatically harmless. Propolis can irritate the skin or mouth, trigger allergic contact dermatitis, and interact with medicines or other products. People with allergies to bee products, plant resins, balsam of Peru, or related cosmetic ingredients should be cautious (de Groot et al., 2026). Pregnant people, patients with chronic disease, immuno-compromised patients, and people taking regular medication should use propolis only with professional guidance.

3.2. Recommendations for a Prospective Research Agenda

The biological activity of propolis is largely attributed to phenolic acids, flavonoids, and prenylated phenolic compounds. Among the best-characterized constituents are caffeic acid phenethyl ester (CAPE), pinocembrin, galangin, chrysin, and artepillin C, which have been associated with antioxidant, antimicrobial, anti-inflammatory, immunomodulatory, and wound-healing activities. Because the abundance of these compounds varies according to botanical origin, geographic location, bee species, and extraction methods, the biological effects of propolis also differ considerably among regions. A realistic propolis research agenda for Pakistan should begin with farmers and beekeepers rather than product claims.

Field surveys should assess awareness, local terminology, collection practices, willingness to harvest propolis, perceived economic value, and barriers to market access. The information generated should guide region-specific sampling strategies, beekeeper training, and the development of standardized protocols for propolis collection, traceability, and quality assurance. Researchers should then create a region- and flora-specific sample bank. Each sample should be linked with date, location, season, nearby vegetation, hive management practice, raw-material photographs, and storage conditions. Academia, industry, and farmers should work through shared protocols. Farmers can provide traceable samples, universities can perform chemical and biological testing, and industry can support scale-up, packaging, certification, and market development. This linkage is currently weak, but it is the only route by which propolis can move beyond small laboratory studies.

Training must be practical. Production technology training should cover clean collection, propolis-trap use, grading, drying, storage, labelling, residue avoidance, HACCP principles, hygiene certification, and basic business awareness. Farmers should leave the training with a clear message: quality is what turns sticky hive material into a saleable byproduct. Clinical research should also be focused. The most realistic early products are oral-care preparations, topical wound-care products, dermatological formulations, and standardized supplements tested for specific supportive outcomes. Trials should use chemically characterized propolis, clearly stated doses, safety monitoring, and realistic claims.

4. Conclusion

Propolis research combines beekeeping, plant chemistry, microbiology, product development, and clinical investigation. Recent research supports genuine biological activity in oral care, wound care, skin applications, inflammation, oxidative stress, antimicrobial research, and delivery-system development. The same research also explains why translation is difficult: propolis varies by region and flora, extraction changes composition, clinical evidence is uneven, and quality control is essential.

For Pakistan, this difficulty is also an opportunity. The country's biodiversity and climatic variation may produce distinctive propolis types, but that potential will remain hidden without field surveys, farmer training, regional mapping, chemical profiling, residue control, and industry-academia collaboration. Future work should thus focus on traceable production, farmer training, standardized laboratory testing, and carefully designed clinical studies. These measures are necessary before Pakistani propolis can be developed into reliable therapeutic products.

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Author Contributions: Conceptualization: Annas Awais and Zainab Shoaib; Methodology: Annas Awais, Zainab Shoaib, Umair Yasin, and Ahmed Waqas; Literature Search and Data Collection: Annas Awais and Zainab Shoaib; Investigation: Annas Awais, Zainab Shoaib, Umair Yasin, and Ahmed Waqas; Writing – Original Draft: Annas Awais and Zainab Shoaib; Writing – Review and Editing: Umair Yasin and Ahmed Waqas; Supervision: Umair Yasin. All authors have read and approved the final manuscript.

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