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Review Article

PROPOLIS: A NEW HOPE FOR BROAD SPECTRUM ANTI-MICROBIALS AND ANTI-VIRALS

Bijay Kumar and *Santosh Kumar Singh
Molecular Biology Unit, Institute of Medical Sciences, Banaras Hindu University
Varanasi – 221 005, India
Author for Correspondence: bhu.santosh@gmail.com

ABSTRACT
Pharmaceutical industries are always keen to utilize the natural products as a promising source of new drugs. Propolis (resinous bee product) is known for centuries for its variety of health benefits across the globe. It has been collected by honey bees from different parts of plants (bud, stem and exudates) in different geographical locations. Propolis has attracted the attention of scientific community for its variety of useful biological activities which are related to its chemical composition. Several in vitro and in vivo studies demonstrated its different activity like anti-microbials and anti-virals. However, there is lack of information in its clinical effectiveness. The aim of this review is to discuss the chemical composition and its potential for the development of novel anti- microbials and anti-virals.

Keywords: *Propolis, Bee Glue, Anti-Bacterials, Anti-Fungals, Anti-Virals*

INTRODUCTION

Nature always surprised us with the variety of natural products that can be promising source of novel drug development. The utilization of these natural products toward the development of new pharmaceutical agents is an urgent need to combat the current clinical problems (Newman & Cragg, 2007). Propolis, a complex compound which is popularly known as honey bee glue is a resinous product which honey bees collect from variety of plants and mixes with bee wax and salivary secretions (Silva-Carvalho *et al.,* 2015). Honey bees use propolis on their hives as protective agent against predators and microorganisms, to repair the damage of hives, as thermal protector and to create aseptic niche for their larvae. Propolis was used by humans since ancient time to fulfill the needs of food and health but only in recent years interest in this complex product has been increased due to its broad spectrum biological and pharmaceutical properties (Silva-Carvalho *et al.,* 2015). Propolis is hydrophobic and hard when in cold but is flexible and very sticky in hot conditions. Chemically, propolis is composed of resin (50 %), wax (30 %), essential oils (10 %), pollen (5 %) and other substances including minerals, other organic compounds like phenolic acids, flavonoids, terpens, aromatic aldehydes, alchohals, fatty acids, stilbenes, and β-steroids (5 %) (Silva-Carvalho *et al.,* 2015). Analysis of propolis from different geographical region indicated that the standardization of its chemical composition is difficult since it depends on different season, vegetation and other environmental conditions.

In recent years multiple in vitro and in vivo studies indicated wide variety of biological activities like anti-microbial, anti-viral, anti-inflammatory, anti-oxidant, anti-tumorigenic and immunomodulatory activities. In the current review article we will discuss the potential of propolis as a candidate to develop the anti-microbial and anti-virals.

Propolis in Ancient and Modern Times

Propolis is known since bee's domestication, the humankind always explored all the possible natural products for their own benefit and propolis (natural anti-microbial for healthy hive) is one of them. The use of propolis is stated back in 300 BC, where it was used in folk medicine (Khalil, 2006; Silva-Carvalho *et al.,* 2015). The priests of Egypt were familiar with the chemical and medicinal properties of propolis. They learned the embalming properties from honey bees and utilize this knowledge for mummification of corpus and prevent spread of infection. Greek and Roman physicians' also utilized propolis for wound treatment as antiseptic and cicatrizing agent. Persians used propolis for treatment of eczema, rheumatism and myalgia. Ancient South Americans used propolis for fever as antipyretic agent. During 17th and 20th century propolis was utilized for variety of human and vatenerian medicines

including tuberculosis in Europe. During World War II (1939-1945), propolis was used to treat wounds by the doctors. Japan considered propolis as very promising pharmacological agent in 1985 and nowadays uses successfully in alternative medicine (Khalil, 2006; Silva-Carvalho *et al.,* 2015). Propolis is one among those natural products that maintained the popularity since ancient time.

Origin and Composition

In 1960's, it was thought that besides the chemical complexity of propolis the composition of it is more or less constant irrespective of geographical locations. Later after analyzing very large samples across the globe, it became evident that the composition of propolis is highly variable and difficult to standerize due to different vegetation, season and other environmental conditions (Falcao *et al.,* 2013; Khalil, 2006; Silva-Carvalho *et al.,* 2015). More than 300 substances were reported in propolis and new studies reports the presence of novel compounds in it. Broadly, the main constituents of propolis are resin and volatiles (products obtained from different part of plants) (Falcao *et al.,* 2013; Falcao *et al.,* 2010; Sun *et al.,* 2012). Based on the resin types, propolis is classified as poplar, birch, green, red, pacific and canarians. The active chemical compounds in propolis ranges from methylated, esterified and hydroxilated forms of flavonoids, phenolic acid and their esters, diterpinoids, polyisoprenylated benzophenones, xanthorrhoeol, pterostilbene, sakuranetin and pinostrobins. Propolis from tropical region withdrawn significant attention due to its peculiar chemical profiles. Prenylated phenylpropanoids, prenylated coumaric acids, acetophenones, diterpenic acids and caffeoylquinic acids were shown common in Brazilian propolis. Significant amount of minerals and vitamins were also found in propolisviz. magnesium, calcium, iodine, sodium, potassium, manganese, zinc, copper, iron, Vitamin B1, B2, B6, C, D and E. additionally, propolis also contain multiple active enzymes like α-amylase, β-amylase, α-lactamase, β-lactamase, transhydrogenase, esterase and maltase. Polysaccharides like ribose, fructose, starch, glucose, talose, rhamnose, saccharose are also reported in propolis (Kurek-Gorecka *et al.,* 2013; Silva-Carvalho *et al.,* 2015).

Biological and Therapeutic Properties of Propolis

Despite being known since ancient times for its multiple therapeutic value, propolis has not been considered therapeutic agent in conventional medicine. The major cause may be the lack of in depth research on the standardization of its chemical composition as well as biological activity, which remain indispensable for acceptance in health system. Therefore, the characterization of propolis from different geographical origin and corresponding chemical composition is essential. These information may help in elucidating the underlying mechanism behind the different therapeutic properties of propolis and will be useful for development of potential drug candidates. In last decades, variety of pharmacological and therapeutic properties of propolis from different geographical locations were shown which ranges from its antibacterial, anti-fungal, anti-viral, anti-inflammatory, anti-oxidant, immunomodulatory and anti-tumoral activities. This vide variety of therapeutic property in one natural compound attracted the attention of researchers for considering it as potential drug candidates for multiple diseases (Amoros *et al.,* 1992; Kujumgiev *et al.,* 1999; Ordonez *et al.,* 2011; Scazzocchio *et al.,* 2006; Silva-Carvalho *et al.,* 2015; Silva *et al.,* 2012).

Antimicrobial Activity

It is one of the most studied and well-documented activity of propolis. This activity was investigated with rapt attention in recent years against multiple infectious diseases due to emergence of resistant strains against commonly used antibiotics.

1. Antibacterial Activity

Studies on propolis indicated that it is active against wide variety of bacterial pathogens and particularly, it is more efficient against gram-positives as compared to gram-negative bacteria. These data demonstrated that propolis inhibits bacterial motility, enzyme activity, exhibits bacteriostatic activity at low concentration, can be bactericidal at higher concentrations and affects the integrity/membrane potential of cytoplasmic membrane (Mirzoeva *et al.,* 1997; Silva-Carvalho *et al.,* 2015). Multiple investigations from different laboratories indicated that ethanol extract of propolis exhibits anti-bacterial activity against *E. coli, Bacillus subtilis, Rhodobacter sphaeroids, Helicobacter pylori, Staphilococcus*

aureus and pseudomonas aeruginosa (Monzote *et al.,* 2012; Silva-Carvalho *et al.,* 2015; Wojtyczka *et al.,* 2013).

2. Antifungal activity

Like anti-bacterial activity, propolis also exhibited broad range of anti-fungal activity against multiple fungal pathogen of clinical interest. Propolis ethanol extract (PEE), propolis water extract (PWE), propolis methanol extract, propolis dichloromethane extract and propolis n-hexane extract was used to investigate anti-fungal activity and found effective against *Candida ablicans, C. glabrata, C. tropicalis, C. krusei,Trichophyton rubrum and Aspergillus fumigates* (Boisard *et al.,* 2015; Ota *et al.,* 2001; Silva-Carvalho *et al.,* 2015).

Anti-viral activity

It was shown that propolis from different geographical regions displays significant anti-viral activity by acting at different levels and interfering with the replication of few viruses. It was demonstrated that PWE and PEE exhibits potent anti-HSV-1 activity when used prior to infection step. In this experiment galangin and chrysin were identified as the main antiviral ingredient of propolis. Similarly propolis were found effective against adenovirus type 2, vesicular somatitis virus (VSV), echovirus 30, coxsackie virus B3, B4 and A9, picornavirus and poliovirus type 2. In the recent past, propolis was tested against HIV-1 in cell culture system using $CD4^+$ lymphocytes and microglia. In this study inhibition of virus expression was observed in concentration dependent manner (Gekker *et al.,* 2005; Sartori *et al.,* 2012; Silva-Carvalho *et al.,* 2015). In general, the probable mechanism of antiviral activity of propolis is through the inhibition of viral entry and replication.

CONCLUSION

Since ancient times herbs and natural products has been utilized as medicinal agents initially in folk medicine and later based on several scientific evidences these compounds were developed as drugs. Propolis is one among the rare natural compounds which retains its popularity for its medicinal value since ancient time (Silva-Carvalho *et al.,* 2015). As discussed in this article, propolis contains wide spectrum of compounds that might be useful in treatment of variety of pathological conditions. Presence of spectrum of bioactivities, long history of propolis use, its safety profile and continuous discovery of new compounds in it make it very attractive candidate for novel drug development which may be very useful in different clinical conditions. However, it is essential to make serious efforts to standardize the propolis composition since it varies significantly across different geographical locations. Propolis extract may offer a economic solution for multiple disease conditions. To promote the use of propolis in modern medicine, the active ingredients for its all variety of activity needs to be identified. Towards the goal of achieving novel drugs from propolis several levels of clinical trials are also essential in addition to existing in vitro and in vivo studies.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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