A Review on Propolis - As a Novel Folk Medicine

Mathivanan V¹, Gh Nabi Shah², Mudasar Manzoor³, Mir GM⁴, Selvisabhanayakam⁵

1. Professor Dept. of Zoology, Annamalai Univ, Annamalainagar -608002, Tamil nadu, India
2. Research scholar, Dept. of Zoology Annamalai Univ, Annamalainagar -608002, Tamil nadu, India
3. Research scholar, Dept. of Zoology Annamalai Univ, Annamalainagar -608002, Tamil nadu, India
4. Professor Cum-chief Scientist, Division of Entomology, Sher-e-Kashmir Univ. of Agricultural Sci. And Tech., kashmir-191121, India
5. Professor and Head Department of Zoology, Annamalai University, Annamalainagar -608002, Tamil nadu, India

*Corresponding Author: Professor Dept. of Zoology, Annamalai Univ Annamalainagar – Tamil nadu, India, E-mail: mathivandanndr@gmail.com, Mobile No: 9345131523

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ABSTRACT

Propolis is a natural resinous mixture produced by honeybee Apis mellifera from substances collected from parts of plants, buds and exudates. Bees gather propolis from different plants, in the temperate climate zone mainly from poplar. Current biological applications of propolis include formulations for cold syndrome (upper respiratory tract infections, common cold, flu-like infections), wound healing, creams, eye treatments, Asthma, treatment of burns, acne, HPV (Human papilloma virus), Diabetes, mouthwashes and toothpastes to prevent caries and treat gingivitis and stomatitis. It also possesses the antifungal activities in ocular and vaginal infections. South Indian Propolis possesses antimicrobial, antifungal, antiviral, immunostimulatory, anti-inflammatory, anti-cancer and anti-oxidant activity. Worldwide propolis has a tremendous popularity; but in India, studies over propolis are not done extensively. The need of the hour is to explore its possible Pharmaceutical and Biological activities.

Key Words: Propolis, biological applications, Potential, South Indian Scenario.

1. INTRODUCTION

Propolis is very popular, because of its beneficial effect on human health. Propolis have been extensively employed by man since ancient times, especially in folk medicine to treat several maladies. Egyptians knew very well its anti-inflammatory properties and used bee glue to embalm their cadavers. Incas employed propolis as an anti-pyretic agent. Greek and Roman physicians used it as mouth disinfectant and as an astringent and healing product in wound healing treatment, prescribed for topical therapy of cutaneous and mucosal wounds (Bankova et al 2000).

In Folk Georgian medicine, they used ointments with propolis to cure some diseases. There was the custom of placing a propolis cake on the belly button of the new born baby and also they rubbed children’s toys with propolis. In folk medicine, the use of propolis is widely known especially for the treatment of burns. People inhale propolis in case of affections of respiratory tracts and of the lungs. It is also efficient for burns and angina. Propolis was used effectively on wounds by doctors during the Anglo-Boer war and during World War II. It was also used in hospitals from 1969 (Makashvili, 1975).

This product has, therefore, gained popularity as a traditional (folk) medicine for health amelioration and disease prevention (Teixeira et al, 2010). Some examples including its utilization for increasing the body’s natural resistance to infections and lowering blood pressure and cholesterol levels. It has been also used in mouth wash products and toothpastes to prevent Caries and treat Gingivitis and Stomatitis (Gomez et al, 2006), in Cough Syrups, Oral Pills, Lozenges, Ointments, Lotions, and Vitamins (Scheman et al, 2008). Therapists often use propolis for the relief of some inflammations, viral diseases, fungal infections, ulcers and superficial burns along with acupuncture. Ayurveda and homeopathy (Scheman et al, 2008).

Propolis is available in the world markets in different forms as capsules, lozenges, tincture and cream in Europe and America. It is already available in Russia as toothpaste. Further, research is being carried out at Oxford University, on the benefits of Propolis (Wander 1995). In ancient times, propolis has been widely used by different cultures for differing purposes; among which its use in medicine is included (Cañas 2002, Krell 1996 and Burdock 1998). Currently, research is being carried out on its activity, effects and possible uses in biology and medicine. The most prominent are its application as a dietary supplement, its use in the pharmaceutical industry and clinical applications in animal science (Krell, 1996; Burdock 1998, Banskota et al, 2001 and Bracho, 2003).

The aim of this review is to draw the attention of South Indian pharmaceutical and health care workers towards propolis as a folk, natural remedy and its plausible use in different diseases.

2. POTENTIAL USES OF PROPOLIS IN HUMAN HEALTH

2.1. Wound Healing

A study conducted by Magro-Filho and Carvalho, (Magro-Filho O, 1994) analyzed the effects of propolis mouth rinse on the repair of surgical wounds after sulcoplasty by the modified Kazanjian technique. Patients returned 7, 14, 30 and 45 days after surgery for cytological and clinical evaluation. It was concluded that: (a) the mouth rinse containing propolis in aqueous alcohol solution aided repair of intra-buccal surgical wounds and exerted a small pain killing and anti-inflammatory effect. (b) the vehicle employed had a minor irritant effect on intra-buccal surgical wounds and (c) exfoliative cytology showed epithelisation of infrabuccal Surgical wounds. They also examined histological the effects of propolis topical application to
dental sockets and skin wounds. It was concluded that topical application of propolis hydroalcoholic solution accelerated epithelial repair after tooth extraction but had no effect on socket wound healing (Magro Filho and Carvalho, 1990). Another study conducted by Adeyemi and Ogunjimi (2011) with fifty patients of septic wounds aged from 20-60 years. The wounds of the 80% of the patients showed remarkable signs of improvement at the end of 4th day: 60% had their wounds completely healed at the end of 10th day; the remaining 40% healed completely at the end of the 15th day. All healed wounds were without scars or blisters. It can be concluded that lotion of the propolis with honey has great potential for the treatment and healing of septic wounds. It is recommended, that, it should be incorporated in the treatment plans of septic wounds and other gangrenous wounds by hospitals in Nigeria.

2.2. Creams and Lotions
Propolis is used as cream or lotions for different cosmetic purposes. The propolis uses for cosmetics have been investigated (Lejeune et al., 1984, Lejeune et al., 1988). Its use is based on the antibacterial, antifungal, anti-viral anti-acne, anti-inflammatory, antioxidiant effects, epithelial, micro-circulation and topical anaesthetic effects. Low toxicity and good skin compatibility have been demonstrated, despite the risk for allergic reactions. For skin lotions and creams for cosmetic use 1-2 % propolis seems to be the appropriate amount (Jong-Sung and Kun-Suk, 1997). However, before use a test on a small skin surface should be made, if there is a propolis allergy problem. The possible allergising effects should be marked on the product.

2.3. Oral use as Mouth rinse
Koo et al. (2002) evaluated the effect of a mouth rinse containing propolis on 3-day dental plaque accumulation. Six volunteers took part in a double-blind crossover study performed in two phases of 3 days. During each phase, the volunteers refrained from all oral hygiene and rinsed with 20% sucrose solution 5 times a day to enhance dental plaque formation and with mouth rinse (placebo or experimental) twice a day. On the 4th day, the plaque index (PI) of the volunteers was scored and the supragingival dental plaque was analyzed for insoluble polysaccharide (IP). The plaque index for the experimental group was, significantly less than for the placebo group. The experimental mouth rinse reduced the insoluble polysaccharide concentration in dental plaque by 61.7% compared to placebo. An experimental mouth rinse containing propolis SNB-RS was thus efficient in reducing supragingival plaque formation and insoluble polysaccharide formation under conditions of high plaque accumulation.

Ozan et al. (2007) performed a study to compare the effects of four different mouthrinse containing propolis solutions and mouth rinse containing 0.2% chlorhexidine (CHX) on oral microorganisms and human gingival fibroblasts. Mouth rinse containing propolis was prepared at four different concentrations as 10, 5, 2.5 and 1%. Besides, CHX was used as control group. The antibacterial effects of five solutions on oral microorganisms were tested and their cytotoxic effects on human gingival fibroblasts were evaluated by agar diffusion test. At this concentrations, effectiveness of mouth rinse containing propolis samples on oral microorganisms were not found as effective as CHX. On the contrary, samples found less cytotoxic on human gingival fibroblasts than CHX.

Koru et al. (2007) collected propolis from four different regions in Turkey and from Brazil used against nine anaerobic strains. EEP (Ethanolic Extract of Propolis) determined minimum inhibitory concentrations (MIC) and minimum bactericidal concentrations (MBC) on the growth of test microorganisms by using agar dilution method. Death was observed within 4 h of incubation for Peptostreptococcus anaerobius and p.micors and Lactobacillus acidophilus and Actinomyces naeslundii, while 8 h for Prevotella oralis and Prevotella melaninogenica and Porphyromonas gingivalis, 12 h for Fusobacterium nucleatum, 16 h for Veillonella parvula. It was shown, that, propolis samples were more effective against Gram positive anaerobic bacteria than Gram negative ones.

2.4. Propolis in Dentistry
2.4.1. Root Canal
Treatment of root canal and periodontitis Kosenko and Kosrish (1990) suggested the addition of 4% alcohol solution of bee glue as filler for root-canal filling, besides the traditional treatment of the root-canal with bee glue solution. Clinical and radiographic examinations have demonstrated a high efficacy of such an esthetic and chronic forms of periodontitis. This filler is characterized by its anesthetizing effect. It is preserved in the root canal and does not stain the tooth crown, promotes regeneration of the bone structure and prolongs the effect of 0.4% water-alcohol bee glue emulsion.

Qatham et al. (2003), studied Sodium hypochlorite as an endodontic irrigant, possesses problems of toxicity, odor and discoloration of operator items. An equally effective, but safe irrigant is desirable. The purpose of this study was to compare the anti-microbial activity of propolis with that of sodium hypochlorite in a root canal system. Forty-nine extracted human teeth with large carious lesions reaching the pulp were instrumented using step-back technique. Propolis, sodium hypochlorite and saline were used as irrigants. Microbiological samples were taken from the teeth immediately after accessing the canal, and after instrumentation and irrigation. The results of this study indicated that the propolis has antimicrobial activity equal to that of sodium hypochlorite.

2.4.2. Application of Propolis to dental sockets and skin wounds
Magro-Filho and Carvalho (1990) examined cutaneous wound healing and socket wound after tooth extraction in rats with topical application of either a 10% hydro alcohol solution of Propolis or 10% hydro-alcohol solution alone. The animals were sacrificed at 3, 6, 9, 15 and 21 days after the operation. It was concluded that topical application of Propolis hydro-alcoholic solution accelerated oral epithelial repair after root extraction but had no effect on socket wound healing.

2.4.3. Dental pulp capping
With a view to extending the range of biologically active preparations for direct and indirect capping of the dental pulp, Lonita et al. (1990) used a paste made from an alcoholic solution of Propolis and zinc oxide. The study included 150 teeth with indirect pulp capping of deep cavities and 50 teeth with direct pulp capping. The evolution of the capping was followed clinically, radiologically and morphologically. The results obtained showed, that, the paste with Propolis exerted effects similar to those of zinc eugenol. The morphologic study of the indirect capping showed that secondary dentin developed shortly after the application of the paste, and that, it was followed by the development of pulpitis and sclerotic transformation of the pulp. In teeth with direct capping a protective film developed at the opening of the pulp chamber. In time, the pulp wound underwent cicatrization by fibrosis with a trend to remineralization. No areas of pulpal degeneration were found in the rest of the pulp tissue and this suggested that the pulp was more histophilic than the pastes based on calcium hydroxide, with which an area of necrosis occurred at the opening of the chamber, and calcium and fibrous degeneration occurred in the coronal pulp.

2.4.4. Dental hypersensitivity
At King Saud University, College of Dentistry, Riyadh. (Mehroud et al.2000) twenty-six female subjects with age range 16-40 years (mean 28 years) were included in the study. Propolis was applied twice daily on teeth with hypersensitivity. The
hypersensitivity was assessed on a visual scale 0- 10 and by slight, moderate and severe classification at baseline, after 1 and 4 weeks. Seventy per cent of the subjects had severe hypersensitivity at the baseline. At first recall, 50% reported moderate hypersensitivity, fifty per cent (50%) reported slight hypersensitivity at second recall and 30% had no hypersensitivity while only 10% had moderate hypersensitivity. It was concluded that Propolis had a positive effect in the control of dental hypersensitivity (Mahmoud et al., 2000). Mahmoud et al. (2000) concluded in his study that the effect of propolis on dental hypersensitivity, they reported that propolis has a positive effect in the control of dental hypersensitivity. Mahmoud et al. (1999) and Hidaka et al. (2011) have suggested that propolis may have potential as anti calculus agents in toothpaste and mouthwashes.

2.4.5. Dental caries
It is also known as tooth decay or a cavity, Hayacibara et al. (2005) reported in his recent studies that, propolis show potential effect on the dental caries. In this 12 distinct types of Brazilian propolis have been chemically characterized and classified from type-1 to -12 (Park, 2002), shown the anti-caries potential of propolis from the Southern (type-3) and Southeastern (type-12) regions of Brazil (Park et al., 1998; Koo et al., 1999,2002). Propolis samples lower the intensity of caries and dentalplaque accumulation in vivo (Koo et al., 2002). Propolis is associated with two mechanisms of action, i.e., anti-caries/anti-plaque properties: (1) It shows anti-microbial activity against cariogenic bacteria, and (2) it inhibites glucosyltransferases enzymes (GTFs) activity (Koo et al., 2000). However, all the studies were conducted by using raw propolis extract and a very little is known about the putative anti-caries compounds in the EEP. Considering that propolis fractionation is the first step in identifying the active compounds of this natural product, the study aims to evaluate the influence of isolated fractions of propolis type-3 and -12 on streptococcus mutans and GTF activity in vitro, and on caries development in vivo. At the end of the experiment they concluded that the EEP and H-fraction type-3 and 12 were equally effective in reducing dental caries in rats. The data suggest that the putative cariostatic compounds of propolis type-3 and 12 are mostly non-polar; and H-fraction should be the fraction of choice for identifying further potentially novel anti-caries agents.

2.4.6. Pulp therapy in primary and permanent teeth
Direct pulp capping with propolis in rats may delay dental pulp inflammation and stimulate reparative dentin. Partial dentin bridge formation was seen in these animals after application of propolis (Santos, 2005). Another study in Manipal College of Dental Sciences, Manipal, conducted on premolars for direct pulp capping also showed that propolis is equally efficacious as calcium hydroxide. It has been concluded in a study that propolis can be used along with calcium hydroxide as an intracanal medicament (Tandon, 2008).

2.5. Propolis in Gynecology
Zawadzki and Scheller, (1973) investigated 90 cases of therapeutic activity of 3% EEP in cases of vagina and uterus cervix inflammation caused by S. pyogenes. They observed that, more than 50% of the cases responded well to treatment with EEP. The action of propolis to treat, inflammatory and distrophic lesions of the female genital system caused by protozoan and fungi has studied. Some 137 cases of diffuse inflammations, ulcerations and ex-ulcerations of cervix uteri diseases were investigated by Roman et al. (1989). After 20-25 days of associated treatment (allopathic and apitherapeutic) very good results were obtained in 53 cases, good results in 24, and satisfactory in 28 cases. The results obtained by Roman et al. (1989) confirm that, propolis potentiates the antisepic, antifungal and antichromonas actions of specific chemical medicines. Stojko and Stojko (1993) also reported the use of propolis preparations for treatment of gynaecological disorders.

Dota et al. (2010) studied in vitro antifungal activity of propolis ethanol extract (PEE) and propolis micro particles (PMs) obtained from a sample of Brazilian propolis against clinical yeast isolates of importance in the vulvovaginal candidiasis (VVC). PEE was used to prepare the micro particles. Yeast isolates (n=89), obtained from vaginal exudates of patients with VVC, were exposed to the PEE and the PMs. Moreover, the main antifungal drugs used in the treatment of VVC (Fluconazole, Voriconazole, Itraconazole, Ketoconazole, Miconazole and Amphotericin B) were also tested. MIC was determined according to the standard broth micro dilution method. Some Candida albicans isolates showed resistance or dose-dependent susceptibility for the azol drugs and Amphotericin B. Non-Candida albicans isolates showed more resistance and dose-dependent susceptibility for the azolic drugs than Candida albicans. However, all of them were sensitive or dose-dependent susceptible for Amphotericin B. All yeasts were inhibited by PEE and PMs, with small variation, independent of the species of yeast.

2.6. Propolis in Diabetes
The administration of ethanolic extract of Brazilian green propolis (10 and 90 mg/kg) for 7 days to STZ-induced diabetic rats had no effect after diabetes establishment (Sartori et al., 2009). The long-term administration (28 days) of Brazilian green propolis (200 mg/kg) was also investigated, in order to explore its therapeutic potential in STZ-induced diabetic rats (Sufalo et al., 2009). Based on these findings from laboratory, propolis did not seem to counteract STZ effects, even when administered over a short (7 days) or long (28 days) term to animals, while data from literature revealed that propolis administration over a long-term could exert a positive effect in diabetic animals. Inflammatory cytokines and oxidative stress have a central role in the pathogenesis of acute pancreatitis, and the treatment with ethanolic extract of propolis (300 mg/kg) improved the biochemical and histopathological findings in a rat model of experimental pancreatitis (Buyukberber et al. 2009). As to isolated compounds (Okutan et al. 2005) reported that the eight-week treatment with CAPE (10_mol/kg) reduced the oxidative stress in STZ-induced diabetic rats. All these data indicate that, further research is still needed in order to investigate the optimal concentrations of propolis or its constituents, intake period and the type of extract, exploring its potential use for diabetes treatment in humans.

2.7. Ophthalmology
Propolis rich in antioxidants, prevents 70% of cases of cataract formation induced by exposure to selenites (Orhan et al., 1999). After inducing corneal lesions with sodium hydroxide or silver nitrate in a group of rabbits, topical treatments with propolis extracts or dexamethasone were applied. Similar results were obtained for both substances (Hepsen et al., 1999, Ozturk et al., 2000) in posterioric keratitis, the local application of thin propolis dressings for 10-15 days significantly accelerates corneal epithelisation, reduces by half recuperation, and doubles visual sharpness in control patients (Maichuk et al., 1995).

2.8. Anti Cancer Properties
Ethanol extracts of propolis have been found to transform human hepatic and uterine carcinoma cells in vitro, and to inhibit their growth (Matsumo, 1992). Propolis was also found to have a cytotoxic and cytostatic effect in vitro against hamster ovary cancer cells and sarcoma-type tumours in mice (Ross, 1990). A substance called Artepillin C has been isolated from propolis, and has been shown to have a cytotoxic effect on human gastric carcinoma cells, human lung cancer cells and mouse colon carcinoma cells in vitro (Kimoto, et al., 1998).
2.9. Human Papiloma Virus
One major threat for women is the human papiloma virus (HPV) infection which can lead to cervical cancer, which is the most frequent cancer in women, especially in underdeveloped countries. But, even in Western countries, there are many HPV-associated dysplasias which require surgery by means of cervical conisation or even hysterecomy. Two studies have shown that, propolis-containing local therapy can eradicate HPV infections within six months. In a randomised trial, HPV infections were present after three months of treatment in 28% of patients treated with propolis compared to 90% in the control group (Ilijazovic et al. 2006). Similarly, another study described an improvement in cytological PAP smears (Papanicolaou test) of 76% with the use of propolis (Imhof et al. 2005). Here, treatment with bee products offers an interesting approach which could avoid invasive surgery.

2.10. Rhinitis
Rhinitis is a symptomatic disorder of the nose, with nasal obstruction, secretion and sneezing, most commonly induced by allergen exposure, bacteria or virus. It is a global health problem, affecting social life, sleep, school and work performance, regardless of gender, age and ethnic background (Hellgren et al. 2010). Shimmei et al. (2009) studied the effect of Brazilian propolis on sneezing and nasal rubbing in experimental allergic rhinitis of mice, concluding that propolis may be effective in the relief of symptoms of allergic rhinitis through inhibition of histamine release.

2.11. Asthma
Asthma is a chronic inflammatory disorder of the pulmonary airways due to the hyperresponsiveness to inhaled allergens, leading to reversible airflow obstruction and airway inflammation, persistent airway hyperactivity and airway remodeling (Sy et al. 2008). Khayyal et al. (2003) administered an aqueous extract of propolis 13% daily for 2 months to patients with mild to moderate asthma. As a result, propolis-treated patients showed a reduced incidence and severity of nocturnal attacks and improvement of ventilator functions.

2.12. Hepatoprotective Action
The liver is perhaps the hardest working organ of the body. It has hundreds of tasks to perform, including detoxification of the blood. A sluggish liver means fatigue and ischemia and a high risk of having a hepatoprotective function. Hepatoprotective activity for different types of propolis has been reported, which correlated to the antioxidant activity (Banskota et al. 2001a, 2001b). Propolis counteracts hepatic effects of alcohol liver injury in mice (Lin et al. 1997, Remirez et al. 1997) and also of paracetamol induced liver damage of mice (Gonzalez et al. 1994) and carbon tetrachloride induced liver damages in rats (Gonzalez et al. 1995).

2.13. Other Diseases
Propolis can be used in paediatric diseases, radiculitis, polyradiculoneuritis and gastric ulcers (Ludyanski, 1994). In a monograph dedicated to the use of propolis in medicine, successful treatments of the following diseases were mentioned: tuberculosis, psoriasis, skin mycosis, and inflammations of the stomach and duodenum (but general use in these cases cannot be recommended) (Tichonov et al. 1998).

3. POTENTIAL USES OF PROPOLIS IN ANIMAL HEALTH
3.1. Antimicrobial Action in Chickens
In chickens, propolis is effective against S. aureus and S. epidermidis in vitro (Glinnik and Gapanovich, 1981). One hundred and six strains of S. aureus were tested, all of them were susceptible to 0.5-1.0 mg propolis/ml. Strains resistant to benzyl/penicillin, tetracycline, and erythromycin were sensitive to propolis. Propolis had a synergistic effect when combined with any of the three antibiotics used against the antibiotic resistant strains (Shub et al., 1981).

3.2. Liver Protective in Chicken
Giurgea et al. (1981) reported that daily administration of 20 mg/100 g b.wt. standard propolis extract (SPE) to chicken for 15 days increased plasma total protein and gamma-globulin content. They suggested that, also propolis has an anabolic effect and stimulated the immunologic processes. They also reported that daily administration of 20 mg propolis extract to chickens for 15 days changed the blood concentration of cholesterol, transaminase (ALT & AST), total proteins and amino acids. It also stimulated the immune system. In another study (Giurgea et al., 1982) the investigators reported that chicken fed on propolis extract showed a significant increase in serum total protein and a slight reduction in the glycogen level. Interaction of purifiedpropolis in vitro with serum albumin or human serum proteins caused conformational changes in the protein and increase ceruloplasmin activity (Olinescu et al., 1982). Giurgea et al. (1984) found that daily administration of propolis extract to chikens caused a marked increase in the myoglobin, protein fraction and muscle total protein when compared to corresponding control. They also stated that, propolis extract affects the levels of cholesterol, transaminase activity, total protein, gamma globulins and free amino acids. They found increases in gamma globulins and proteins and suggested that propolis had an anabolic effect, and it also stimulated the body’s immune response.

3.3. As Veterinary Medicine
Mastitis: Application of propolis linement (Mirolyubov and Barskov 1980; Meresta et al., 1989; Kegl et al.1995; Dudko & Kurpisz, 1996 and Teteren, 1998) Gynecological diseases: application of propolis candies (Teteren, 1998) Feeding of weak pigs, prophylactics of gastronenterological and respiration diseases of pigs: feeding with 0.5 % propolis in milk (Teteren, 1998) Improves weight gain and reduced diarrhoea in mild-fed calves with 5 ml of 20% ethanol extract (Gubicza and Molnar, 1987); Prophylactics of calf diarrhoea: To feeding 0.5 ml/kg of 10% ethanol extract (Teteren, 1998) Prophylactics against paratyphoid fever of ducks: feeding with 50 % propolis aqueous extract (Teteren, 1998). Wound healing: application of 5% propolis in fish oil or fat (Teteren, 1998). As a local anaesthetic in surgery: to 1 % TEP (Tzakoff, 1978) Against foot-and-mouth disease’ induced damages on the uterus of cows and pigs against enzootic pneumonia of pigs stimulant for the growth of underdeveloped lambs, pigs and calves (Tzakoff, 1978). Teteren describes several preparations for veterinarian use: Biogel 10, similar to Biogel 5 but contains 1 % propolis (Teteren, 1998). In veterinary medicine, it is used to heal wounds and in the treatment of many pathologies, such as diarrhoeas, abscesses, burns, dermatosis, mastitis, coccidiosis and eimeria in rabbits, etc. Additionally, it is used in weight gain programs for unweaned calves and egg-laying hens (Krell, 1996).

3.4. Cattle Dermatophytosis
It is known that propolis possesses antimicrobial, antioxidative, antiluier and antitumor activities. Therefore, propolis has attracted much attention in recent years as a useful or potential substance used in medicine and cosmetics products.
Furthermore, it is now extensively used in foods and beverages with the claim that it can maintain or improve human health (Khalil, 2006 and Syamsudin et al., 2009). Recently, propolis had gained popularity application in veterinary such as treatment of young cattle dermatophytosis (Cam et al., 2009).

3.5. Vaccine Adjuvant
Propolis can stimulate higher antibody production, suggesting its use in vaccines, as an adjuvant (Sforzin, 2007). Phenolic compounds such as artepillin C and the derivatives of cinnamic acid besides other flavonoid substances were abundant in the propolis extract, and they could be the main substances with adjuvant action (Fischer et al., 2007). In recent years, it has been used as an adjuvant for mammals, poultry and fish. Propolis could stimulate leukocyte activity and antibody titre in vaccinated fish and increased the survival rate following challenge (Chu, 2006). Because of unique ultrastructure, vaccines with propolis as adjuvant have many advantages such as high stability, slowly release in the body and long storage stage (Shen et al., 2002).

Most vaccines typically depend on the inclusion of substances known as adjuvants that stimulate an immune response. Researchers seeking to develop a vaccine against Suid herpesvirus type1 (SuHV-1), which causes an infectious disease among swine, combined green propolis with an ethanol extract and tested it on mice. The mice showed an increased cellular immune response and increased protection against SuHV-1. This response did not occur with propolis alone, but only when the antigen was absorbed in a particulate adjuvant, like aluminum hydroxide. Thus, when associated with auxiliary substances like aluminum hydroxide, green propolis extract may increase the potency of vaccines, especially those that depend on the cellular immune response for protection (Gelferson Fischer, 2007).

4. POTENTIAL USE OF PROPOLIS AS DIETARY SUPPLEMENT
In Argentina, the INAL (The National Food Institute) recognized propolis as a diet supplement in 1995 (file 2110-003755-4 in the Argentine Food Code) (Gonzalez et al., 2003). Dietary supplementation of laying hens exposed to heat stress with propolis (5 g/kg diet) can attenuate heat stress stress induced oxidative damage and increase growth performance and digestibility, improve eggshell thickness and egg weight (Tatti Seven, 2008, Tatti Seven et al., 2009). Propolis supplemenations as alternative to antibiotic in broilers in heat stress condition (Tatti Seven, 2008). Addition of propolis at 3g/kg in the laying hen’s diet resulted in significant increases in the serum IgG and IgM levels and erythrocyte count, significant decreases in the peripheral blood T-lymphocyte percentage. Hemoglobin and hematocrit values and total leucocyte and differential leucocytes counts were not influenced by propolis supplementation (Cetin, et al., 2010).

Supplementation of lambs with propolis improved weight gain, feed utilization, percentage of dressed meat, meat digestibility and tenderness (Bonomi et al., 2002). Weight gain and feed consumption of pregnant cows with propolis supplementation were improved (Bonomi, 2003). The live weight gain, feed utilization, carcass yield, meat digestibility and tenderness of young bulls fed with mixed feeds with propolis were improved (Bonomi and Bonomi, 2002). The addition of 30 ppm propolis to feed improved egg production in laying hens. Speed of growth and the use and digestibility of feed were enhanced by the inclusion of 40-60 ppm propolis in feed for hen, turkeys, and by 20-40 ppm in feed for guinea fowl, ducks, broilers and rabbits (Bonomi, 2002).

Table 1: Propolis: Geographic origin, activity, chemical compounds in South Indian scenario

<table>
<thead>
<tr>
<th>S.No</th>
<th>Geographic Region</th>
<th>Activity</th>
<th>Solvent used in extraction</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Karnataka</td>
<td>Antibacterial</td>
<td>Petroleum ether, chloroform, ethanol, methanol and 40% methanol</td>
<td>Selvan et al. 2011</td>
</tr>
<tr>
<td>2</td>
<td>West Bengal</td>
<td>Anti-oxidant</td>
<td>Ethanol and water</td>
<td>Laskar et al. 2010</td>
</tr>
<tr>
<td>3</td>
<td>Gujarat</td>
<td>Antioxidant, antmiocibial</td>
<td>Ethanol, water, petroleum ether, chloroform, ethanol, methanol and 40% methanol</td>
<td>Kumar, 2008</td>
</tr>
<tr>
<td>4</td>
<td>Madhya Pradesh</td>
<td>Anti-microbial, Hepatoprotective</td>
<td>Ethanol</td>
<td>Bhadouria, 2012</td>
</tr>
<tr>
<td>5</td>
<td>Maharashtra</td>
<td>Anti-microbial anti-bacterial</td>
<td>Ethanol, Methanol</td>
<td>Wagh et al. 2011, Borkar et al. 2012</td>
</tr>
</tbody>
</table>

5. PROPOLIS IN SOUTH INDIAN SCENARIO
The South Indian Propolis extract contains amino acids, phenolic acids, phenolic acid esters, flavonoids, cinnamic acid, terpenes and caffic acid and several constituents which varies due to different geographical region and climate. It possess several biological activities (Kujunjievik et al., 2009) such as antimicrobial, antifungal, antiviral, immunomodulator, anti-inflammatory, anti-cancer and anti-oxidant activity on the basis of their geographical region. In India the propolis sample shows the composition (Table 1). Wagh et al. (2011), studied HPLC identification and antibacterial and antifungal activity of ethanolic extract (80%) of Indian propolis in ophthalmic infections, obtained from Shirpur, Maharashtra region. Borkar et al. (2012) also have reported the anti-bacterial activity of Indian propolis collected from Shirpur, Maharashtra region.

5.1. South Indian Propolis in Cancer treatment
Propolis is widely used in Indian folk medicine for the treatment of stomach ulcers. The preventive and curative effects of Indian propolis (propolis samples from Mudvaiathanadal, Tamil Nadu) for ulcers were evaluated using models of acute gastric lesions induced by ethanol and indomethacin in rats. Moreover, the effects of ethanolic extract of propolis on gastric content volume, total acidity and pH, using the pylorus ligated model were also evaluated. Animals pretreated with propolis extract showed a significant reduction in lesion index in both ethanol and indomethacin induced ulcer models in a dose dependent manner when compared to the control group. Similarly, post-treatment with propolis (300 mg/kg body weight) for a period of 15 days revealed a statistically significant improvement in the ulcer healing process p < 0.05. In the pylorus ligated model, it was observed that the Indian propolis extract displayed an antisecretory activity, which led to a significant reduction in the gastric juice volume, total acidity and pH. These findings indicated that, Indian propolis displays both ulcer preventive and ulcer curative properties and provides a scientific rationale for the use of propolis in the traditional medicinal system (Iyam Pillai et al, 2010).

5.2. Biological activity of South Indian Propolis
Propolis, a natural product of honeybee, has been used for thousands of years in folk medicine for several purposes. Propolis collected from Gujarat, west zone of India shows antimicrobial and antioxidant activity. The antimicrobial activity was done by agar diffusion method against Staphylococcus aureus, Bacillus subtilis, Pseudomonas aeruginosa, Escherichia coli, Candida albicans and Aspergillus niger. Ethanolic extracts of sample showed high antibacterial activity against Gram-positive (B. subtilis) but least activity against Gram-negative bacteria (P. aeruginosa and E. coli). The yeast C. albicans showed the moderate zone of inhibition whereas A. niger did not show any activity. Pet. ether and chloroform extracts did not show any

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activity. The maximum zone of inhibition of the ethanolic extracts of propolis (EEP) was found against the B. subtilis at the conc. 200 mg/ml where as the least was in the 40% methanolic extracts. The free radical scavenging effect of propolis as well as of vitamin C in 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical system was determined. The free radical scavenging activity of EEP was 70.96% and 72.97% respectively in the concentration range of 100 mcg at the difference of 30 min and 1hr respectively. The result of free radical scavenging effect of vitamin C was 94.7% at 100 mcg and 93.4% at 10 mcg. The methanolic extracts showed the least free radical scavenging when compared to the 40% methanolic and ethanolic extract of the propolis (Nilesh kumar et al., 2008).

6. CONCLUSION

✓ Propolis is one of the few natural remedies that have maintained its popularity over a long period of time, propolis has been shown to lower blood pressure and cholesterol levels. However, clinical studies to substantiate these claims are required. Until this becomes available, physicians should weigh the benefits of propolis as an adjuvant therapy for the good of cancer patients.

✓ It is therefore comprehensible that we should now switch on to-back to nature approach where propolis seems a promising alternative medicine for the control of different diseases with good response and lower associated risks.

✓ This paper reviews various clinical implications of propolis to improve the human and animal health.

✓ Propolis can be used in the management of dental caries, endodontic as well as periodontal infections, vital pulp therapy, in the treatment of oral lesions and repair of surgical wounds. It helps in recovery of eye cataract, vagina- uterus cervix inflammation, chronic inflammatory disorder of the pulmonary airways and nasal obstruction in human.

✓ In animal health propolis had gained popularity application in treatment of young cattle dermatophytosis, foot-and-mouth disease, induced damages on the uterus of cows and pigs.

✓ Dietary supplementation of animal with propolis can increase growth performance and digestibility. Furthermore, propolis is useful substance used in veterinary medicine and acts as an excellent adjuvant and

✓ Pharmaceutical and health care workers of South Indian should pay attention towards propolis and its plausible use in different references.

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