

The Use of Propolis as Alternative Medicine in Treatment of the Toxicological Insults

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ABSTRACT

Propolis (bee glue) is a collected natural mixture from the flowers and leaf buds of the plant via the honeybees. The flavonoid content of propolis can exert an antioxidant effect through scavenging the free radicals protecting the body against the lipid peroxidation along with the activation of antioxidant enzymes. A number of researches have studied the efficacy of propolis in ameliorating the manifestations of some toxicological insults. Most of these studies showed that propolis could prevent and detoxify the serious toxicity of some drugs and chemicals depending on its antioxidant activity.

Keywords: Propolis, Antioxidant, Prevention, Treatment

INTRODUCTION

Propolis (bee glue) is a collected natural mixture from the flowers and leaf buds of the plant via the honeybees. It is an adhesive and resinous substance wherein it mixes with the salivary secretions and wax of honeybees to seal the holes of honeycombs¹. It is utilized in the foods to promote human health as well as a protective agent against some medical perturbations. It has several therapeutic effects such as anti-inflammatory, antifungal, antimicrobial, anticancer, and antioxidant².

Propolis contains more than 300 biochemical components such as flavonoid and amino acids besides some vitamins and minerals as well as a number of fatty acids and some enzymes such as glucose-6-phosphatase. The flavonoid content of propolis can exert an antioxidant effect through scavenging the free radicals protecting the body against the lipid peroxidation along with the activation of antioxidant enzymes such as catalase and superoxide dismutase³.

Propolis is used as an alternative medicine in the different parts of the world several years ago until now based on the above mentioned beneficial health effects⁴. Recently, more attention have been paid by the researchers to the propolis use as a natural antioxidant in the prevention and treatment of some toxicological problems depending on the toxicity mechanism

of the most of toxic agents that depends on the oxidative stress process generating the reactive oxygen species leading to a lipid peroxidation in the different organs⁵.

From this a point of view and depending on the available published data, this study will mention as possible as to the most of studies that were conducted on the use of propolis as a treatment in the poisoning cases.

Propolis and the Toxicity of Drugs

Treatment of chronic diseases usually requires a long and repeated course of the administration of the drugs. Some of these drugs have side toxic manifestations that are difficult to be avoidable. These toxic manifestations are a major challenge for the designer of treatment strategy, especially if there are not substitutes for these drugs. From this a point of view, some researches started to use an adjuvant or alternative medicine to lessen the risk of these drugs intoxications.

Cancer is considered one of the chronic diseases that its treatment needs a long, repeated and concurrent course of chemotherapeutic drugs that its common serious toxic side effects are known. Cyclophosphamide, doxorubicin, and Methotrexate are important members of the family of chemotherapeutic drugs that have toxic manifestations.

In last years, many studies were conducted on the chemotherapeutic drugs by using the propolis to ameliorate its toxicity on the body organs and systems. El-Naggar et al.,⁶ conducted their study on the toxicity of cyclophosphamide using the propolis as a potential natural product to protect the body against this drug toxicity. This study elucidated that propolis has an ability to ameliorate the most toxic manifestations of cyclophosphamide. Propolis can improve and normalize the hepatic and renal biochemical levels such as alanine aminotransferase, aspartate aminotransferase, urea and creatinine associated with an improvement in the count of white blood cells and platelets concomitant with an attenuation in the toxic hepatic and renal histopathological changes.

In the same context, Boutabet and his colleagues⁷ conducted their study on another anticancer drug that is doxorubicin and investigated the role of propolis in alleviating its toxicity. Those researchers carried out an analytical and pharmacological study of propolis using thin layer chromatography, gas chromatography, and ultraviolet high-performance liquid chromatography and showed that the total flavonoid concentration in the propolis is 370 mg. Therefore, The flavonoid content of propolis can reduce the toxic effect of doxorubicin restoring the renal functions based on its scavenging effect. Moreover, propolis can lessen the lipid peroxidation and malondialdehyde concomitant with an increase in the renal glutathione concentration preventing the renal oxidative stress that is induced by the toxic reactive metabolites of doxorubicin.

In the related context, Rizk et al.,⁸ provided evidence that the use propolis as an adjuvant agent with doxorubicin can alleviate its testicular toxicity without affecting its therapeutic efficiency wherein it protects the testis from the oxidative and apoptotic effects of doxorubicin. Furthermore, Risk and other colleagues showed that morphometric and histopathologic studies besides the biochemical findings support the observed antioxidant and anti-apoptotic effects of propolis in amelioration the toxic effect of doxorubicin on the testis.

Otherwise, the findings of Almansour study⁹ proved the weak ameliorative effect of propolis in modulating the hepatic and renal toxicity that are induced by methotrexate. Therefore, propolis can partially alleviate some of the toxic morphometric and biochemical alterations of

methotrexate without achievement any attenuating effect on the toxic hepatic alterations that are also induced via methotrexate.

In addition, there were many scientific trials to use the propolis in another field of drug toxicity such as the toxicity amelioration of the analgesics drugs. Non-steroidal anti-inflammatory drugs are considered a class of analgesic drugs that are used in the treatment of chronic pain and inflammation. Diclofenac sodium is a member of non-steroidal anti-inflammatory drugs that are commonly used in a long or repeated course in the treatment of rheumatoid illnesses such as rheumatoid arthritis, so diclofenac sodium has a high possibility of inducing nephrotoxicity. According to Amin and his colleagues¹⁰, propolis as a renoprotective agent has a promising positive effect on diclofenac sodium-induced nephrotoxicity based on assessing the renal function tests, and parameters of lipid peroxidation and antioxidant, which are significantly improved by the concurrent use of propolis.

In a similar context, propolis has also a hepatoprotective effect against the toxicity of another analgesic drug that is paracetamol. González et al.¹¹ studied the effects of propolis in a model of acute hepatotoxicity that is induced by a high oral dose of paracetamol; they concluded that propolis could nearly exert the same effect of N-acetylcysteine (paracetamol antidote). Propolis can significantly improve the serum levels of hepatic enzymes and increase the glutathione concentration in the liver tissues alleviating hepatotoxicity-induced by paracetamol.

It is known that gentamicin is a well-established nephrotoxic agent besides its adverse toxic effect on male reproduction according to the study of Fetouh and Azab¹². Aldahmasha et al.,¹³ can clearly prove the renoprotective role of propolis in alleviating the morphological and biochemical aspect of gentamicin-induced nephrotoxicity showing its ability to reduce the oxidative stress and apoptosis in the renal tissues. Regard to the study of Fetouh and Azab, the concurrent administration of propolis with gentamicin succeeded to ameliorate its toxic effect on the reproductive system, so they advise the patients to use the propolis during the treatment by gentamicin. Moreover, this study demonstrated that the propolis produces a significant improvement in all the parameters of seminiferous tubules and total numbers of

Sertoli cells, round spermatids, daily sperm production and Leydig cells besides the testosterone level.

Furthermore, propolis supplementation can nearly normalize all hematological parameters that result from the toxicity of anti-tuberculosis drugs (rifampicin and isoniazid). Therefore, propolis can restore the normal level of hemoglobin preventing the occurrence of anemia concomitant with maintaining the normal count of red blood cell and white blood cell depending on its ability to recover significantly the cellular membrane and organ functioning¹⁴.

Propolis and the Toxicity of Chemicals

Likewise, a number of studies proved the protective role of propolis in alleviating the toxicity of some chemicals and other toxic agents. Lead is one of the widespread toxic metals that is serious to human health because of its multifaceted physiological and biochemical harmful actions. Lead exposure stimulates the production of reactive oxygen species that destruct the polyunsaturated fatty acids of phospholipids in the cell membrane causing an impairment in the cellular function and gene mutation. Therefore, searching for new potent trends to ameliorate its toxicity has become an urgent necessity.

From this point of view, the study of El-Masry and his colleagues¹⁵ suggested that propolis may be used as a protective agent against lead-induced neurotoxicity wherein the low levels of lead exposure may lead deleterious effects on the central and peripheral nervous systems causing a learning impairment, a decrease in hearing, and cognitive functions impairment. Propolis can ameliorate the neurological toxicity of lead via normalization of AChE activity, inhibition of brain malondialdehyde. It protects also the mitochondrial NADH-cytochrome C reductase, SDH and cytochrome C activities that play a role in the lead-induced neurotoxicity. Moreover, propolis can increase the vitamins in the brain tissues such as vitamins C and E. From another aspect, propolis can maintain the number of spermatocytes, spermatid and the sertoli cell of testes against the cell damage induced by lead intoxication according to Widawati et al.,¹⁶.

Moreover, Talas et al.,¹⁷ investigated the antioxidant effects of propolis in modulating the arsenic toxicity based on assessing the biochemical parameters and histopathologic

findings. Propolis could improve catalase activities and decrease the levels of malondialdehyde in the various tissues alleviating the different aspects of arsenic intoxication.

Another study was undertaken by Bhadauria¹⁸ to assess the protective effect of propolis against the overall toxicity of aluminum in the different organs such as the liver, kidney, and brain. The result of this study revealed that propolis could modulate all toxic features of aluminum wherein it can mitigate the oxidative stress and preserve the histological structures improving the liver, kidney and brain functions. Furthermore, propolis restores the normal Biochemical levels of AST, ALT, uric acid, urea, cholesterol, and triglyceride concomitant with a decrease in the hepatic, renal, and neuronal lipid peroxidation besides an increase in the activity of hepatic, renal and neuronal of adenosine triphosphatase, superoxide dismutase, catalase, and glutathione. Propolis also improves AChE activity in forebrain, midbrain, and hindbrain that was inhibited by the aluminum toxicity.

Phenol intoxication is considered one of the occupational and public health hazards wherein it may cause nephrotoxicity, neurotoxicity, immunotoxicity, hematotoxicity, and cytotoxicity. The toxic manifestations of phenol are attributed to the phenoxy-type radical production that has the ability to impair the epithelial cell membrane. Elshama and his colleagues¹⁹ utilized the antioxidant properties of propolis to attenuate the toxic effect of phenol on the lymphatic and hematological system. Propolis can restore the normal count of the blood cells and the normal serum level of immunoglobulin along with a significant improvement in the histopathological alterations of the lymph nodes, thymus gland, and spleen.

In addition to, propolis was also proved its efficacy as a useful natural hepatoprotective agent with a wide therapeutic index wherein it can ameliorate acute, sub-chronic, and chronic liver injury. Bhadauria²⁰ validated the use of propolis against carbon tetrachloride intoxication that is a well-known hepatotoxicant and induces also the renal injury via the oxidative stress leading to the biochemical alterations. Moreover, propolis therapy succeeds to maintain the normal levels of catalase, adenosine triphosphatase, glucose-6-phosphatase, and alkaline phosphatase regulating the antioxidative defense activities. It preserves also the hepatic and renal structures

concomitant with restoring the normal serum levels of other biochemical parameters such as protein, albumin, bilirubin, creatinine, urea, triglycerides, and cholesterol.

On another hand, Liu and his colleagues²¹ concluded also that propolis has renoprotective properties wherein its renal protective mechanism is attributed to its potent superoxide scavenging; hence, it could indirectly protect the kidney from superoxide-induced renal damage in the cases of ethanol toxicity. In accordance with the study of Liu and his colleagues, pretreatment with propolis could prevent the ethanol induced-renal failure significantly based on the dose.

In the last years, more work that is extensive was carried out to use the propolis in amelioration the toxicity of different toxic agents. Ochratoxin A is one of the toxic metabolites that are capable of enhancing the lipid peroxidation; it is produced via *Aspergillus Ochraceus* causing anemia, nephrotoxicity, and hepatotoxicity. El-Khayat et al.²² concluded that the propolis could ameliorate Ochratoxin A-induced oxidative stress in the liver and kidney via its role in scavenging the free radicals preventing the lipid peroxidation. This amelioration is manifested by a significant reduction in the mean serum levels of alanine aminotransferase, gamma glutamyl transferase, cholesterol, and creatinine. In addition, propolis improved the antioxidant parameters of the liver and kidney such as reduced glutathione, oxidized glutathione, glutathione peroxidase, superoxide dismutase and the level of malondialdehyde that is a lipid peroxidation product.

Other researches also used propolis in modulating the toxicity of insecticides such as chlorpyrifos and cypermethrin, and biocides such as triphenyltin. In this context, El-Sheikh and Ibrahim²³ recommended using the propolis supplementation for overcoming the toxic manifestations of chlorpyrifos. In accordance with the previous study, the concurrent use of propolis with chlorpyrifos can improve the structure of thyroid and the serum hormonal levels (T3, T4 and TSH) via restoration the follicular sizes and normalization the collagen in the majority of thyroid tissues. Besides an increase in the antioxidants activities and a reduction in the reactive oxygen species by increasing the glutathione, glutathione peroxidase and superoxide dismutase activities in the thyroid tissues and reducing the malondialdehyde content.

Furthermore, Orun et al.,²⁴ emphasized the inhibiting effect of propolis on the oxidative stress that is induced by cypermethrin ameliorating its toxic hematological and biochemical manifestations. In addition to, Yousef et al.,²⁵ concluded that propolis can be effective in the protection of triphenyltin - induced reproductive toxicity wherein propolis can improve the male reproductive performance, the testosterone level, lipid peroxidation, and enzyme activities in the seminal plasma.

Finally, the propolis as an antioxidant agent may be beneficial in the hepatotoxic effect of octylphenol intoxication wherein it can restore the normal liver functions. Octylphenol is one of xenosteroids that have been found in the sewage effluent, groundwater and drinking water. Octylphenol exposure may also occur from contact with personal care products, detergents, water, and food containing octylphenol. Noteworthy, the xenosteroids are widespread environmental contaminants affecting the health of human; its action involves binding to the estrogen and androgen receptors. The ameliorative effect of propolis in xenosteroids (octylphenol) intoxication was observed in the improvement of the serum lipid profile, and diminishing the generation of free radicals by inducing antioxidant defense mechanism. Hence, propolis can minimize the cell membrane damage that is confirmed by measuring the level of DNA fragmentation besides its anabolic effect²⁶.

CONCLUSION

Propolis is a natural antioxidant based on its flavonoid content. It can scavenge the free radicals preventing the lipid peroxidation besides the activation of the antioxidant enzymes. Therefore, propolis can prevent and treat the intoxicated insults that its mechanism already depends on the toxic oxidative stress.

RECOMMENDATION

In the future, further human studies should be carried out to verified the preventive and therapeutic role of propolis in different intoxication cases.

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The Use of Propolis as Alternative Medicine in Treatment of the Toxicological Insults

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