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Biological Therapy Using Propolis as Nutritional Supplement in Cancer Treatment

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Abstract: Neoplasia cause several disorders in the affected body, such as suppression of immune function besides emotional and social impairments. Therefore, handling patients can be extremely difficult, offering several challenges in choosing the appropriate treatment option to be used. The right selection of treatment demands special attention. Chemotherapy is usually the standard treatment, although there are many other different therapeutic modalities also used in medicine. The present study is a literature review focusing on the pharmacological properties of propolis, the resinous product collected by the honeybee from different plant sources, which represents a secure and efficient option for biological therapy and cancer prevention.

Key words: Propolis, biological therapy, suppression of cancer cells

Introduction

Propolis is a resinous substance extracted from plants by bees in order to be used in the beehives for many purposes including: Protection against predators, parasites and microorganisms (Park *et al*., 2002), maintaining the temperature and promoting the asepsis of the beehive. It has been used since old Greece due to its therapeutic properties. The properties of propolis (bee glue) strongly depend on its botanical origin. The chemical composition is very variable depending on the time of the year and geographical location (Banskota *et al*., 2000). It comprises more than 180 compounds that, acting in synergy, present a healing and functional answer against many diseases (Castaldo and Capasso, 2002).

The botanical origin of propolis can either be analyzed through microscopic assessment, identifying and comparing the histological features present in the propolis sample and in plants (Bastos *et al*., 2000; Oliveira and Bastos, 1998) or by chromatographic analysis of the ethanolic extracts of propolis and its respective botanical origin; the green propolis, for instance, is originating from the tender sprouting of *Baccharis dracunculifolia* (Kasahara, 2003; Park *et al*., 2002).

The present research is a literature review on the pharmacological properties of propolis. It is generally regarded as a safe and effective choice for biological therapy and cancer prevention.

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Cancer

Neoplasia is understood as the new growth of tumor cells and usually means an abnormal proliferation. If proliferating cells are not capable of invading surrounding tissue cells, the resulting tumor is benign; in case they do, the tumor is considered malignant. These cellular aberrations are usually a consequence of genetic mutations, exposure to risk factors or abnormal secretion of hormones or enzymes. The term cancer usually implicates malignancy (Thomas, 1986). All cancer types have invasion or metastatization potential, but each specific type has singular clinical and biological characteristics that should be studied for an appropriate diagnosis, treatment and follow up (DeVita *et al*., 1997). There are four main ways to treat cancer: Surgery, chemotherapy, radiotherapy and biological therapy (National Cancer Institute, 2004).

Biological Therapy

Biological therapy is a treatment modality which works hand in hand with the immune system. Modifiers of the biological answer are used from the organism itself to face the cancer, helping it to beat the disease process. Drugs can also be used to change the differentiation pattern of the tumor cells, making them easier to control (Rosenthal, 2000). That therapeutic modality can help fighting the cancer or controlling the side effects provoked by other treatment options such as chemotherapy (National Cancer Institute, 2004). Biological therapy and chemotherapy are treatment modalities that work in different ways. While the first helps the immune system to fight the cancer, the last attacks the tumor cells directly (National Cancer Institute, 2004).

The contribution of propolis, as a coadjuvant nutritional supplement in cancer treatment is already justified due to its functional characteristics proven by many and robust scientific studies and clinical trials carried out all over the world. Some of the several biological activities of propolis that act in synergy with one another and with the conventional chemotherapy medication are: antitumoral activity, DNA protection, free radicals scavenging, immune stimulation (Banskota *et al*., 2001; Suzuki *et al*., 2002).

Anti-tumoral Activity

The cytotoxicity of propolis was documented both by animal and *in vitro* studies. It was observed that the antitumoral activity of the *Baccharis dracunculifolia* propolis is intimately related to the Artepillin C substance and the cytotoxic activity results in the apoptosis which leads to cancerous cells DNA fragmentation (Kimoto *et al*., 1998). Other hypotheses of the antitumoral mechanism of propolis suggest that this activity could be associated to the activation of lymphocyte production and the subsequent stimulation of the immune system associated to the inhibition of lipidic peroxidation (Kimoto *et al*., 2001). Artepillin C isolated from Brazilian green propolis (botanical origin: *Baccharis dracunculifolia*) and its composition revealed an *in vitro* cytotoxicity against tumor cells. After intratumoral injection of 500 mg of Artepillin C three times a week, histological apoptosis was observed, plus the combination of necrosis and mitosis suppression. Besides the inhibition of tumoral growth, it was observed an elevation in the T CD4/CD8 cell rate and in total number of defense cells (Kimoto *et al*., 1998).

The ester of caffeic acid (CAPE) is an active compound of poplar based propolis, with a simple structure, responsible for the main biological activities of this kind of propolis. About 20 similar substances were tested by Nagaoka *et al*. (2002), in cancerous cells of mice (carcinoma 26-L5; malonoma B16-BL6; Lewis lung carcinoma LLC) and humans (fibrosarcoma HT-1080; lung adenocarcinoma A549; cervix adenocarcinoma HeLa) using 5-fluorouracil (EC_{50}: 0.06 μM) as a control. It was observed that 4 out of 20 compounds presented a stronger antiproliferative activity with lower EC_{50} values (EC_{50}: 0.02 and 0.03 μM). Nagoaka *et al*., 2003, have investigated the effect of CAPE through oral administration (5 mg/mouse/day for 7 days) before and after intravenous inoculation of

the suspension on tumor cells in mice. In day 15 after the suspension was inoculated, the number of nodules on the lung surface was counted and the weight of each tumor calculated. There was no suppression of tumoral formation in the mice with administration of CAPE before the inoculation. In those mice treated with CAPE after the inoculation, a decrease in the formation of lung tumor was reported and both the weight and the number of nodules suffered reduction of 50%. In this way, the antimetastatic effect of CAPE should be either due to the cytotoxicity, inhibitory activity against tumor cells, or to the blockade of the invasive process, initial step for metastasis. In the same study, now using cisplatine (CDDP), a drug with expressive antimetastatic effect, the authors observed significant reduction of body weight, regarded as a toxic side effect. In contrast, CAPE had small impact in the body weight, suggesting metastasis suppression without significant side effects (Nagoaka *et al*., 2003).

DNA Protection

Fitzpatrick *et al*. (2001), evaluated the apoptosis inducing effects of CAPE in macrophages of mice (NR 8383) and epithelial human cells (SW 620). The cells -100,000 and 150,000 mL^{-1}, respectively-were exposed to CAPE (3-30 $\mu g\ mL^{-1}$ or vehicle (0.2% DMSO) for 24 h. The DNA fragmentation was measured by means of The cell death detection ELISA plus test method, revealing a more effective induction of apoptosis in macrophages (Fitzpatrick *et al*., 2001). Other investigators showed that CAPE is able to induce apoptosis preferably, depending on the type of cell treated with this compound-selective effect in apoptosis- (Su *et al*., 1995). CAPE, even when used in low doses, can prevent cellular transformation and induce apoptosis, without any effect on normal cells (Chen *et al*., 2003).

Free Radical Scavenging

Flavonoids and phenolic compounds are known to be antioxidant substances with free-radical scavenging activity. Both are found in high concentration in bee propolis. Free radicals, reactive oxygenated compounds, are substances continually produced by the body, resulting either from cell metabolism, generated in physiologic processes such as cellular breathing or pathological events. Those radicals act in cell membrane lipids, cytoplasmatic proteins or in the DNA, causing damages or irreversible alterations as deletions. Such events were also associated to tumoral growth, probably for they act as secondary messengers in transduction signs that regulate cellular proliferation (Havsteen, 1983; Heo *et al*., 2001). Antioxidants either block or remove excessive amounts of these radicals keeping the organism from its harmful action. Thus, reducing intracellular peroxides, antioxidants by themselves would inhibit the carcinogenesis process. Matsushige *et al*. (1996), isolated a compound of aqueous extract of *Baccharis dracunculifolia* propolis, routinely called propol, which was shown to have stronger anti-oxidant effects than the vitamins C and E. Banskota *et al*. (2000), verified that the aqueous extract of Brazilian propolis was a stronger free radical scavenger than the corresponding alcoholic extract. The Brazilian aqueous extract presented the strongest anti free radical activity if compared to the aqueous extracts of China, Peru and Holland, with ED_{50} (dose executes) of only 5.9 $\mu g\ mL^{-1}$, while the aqueous extract of Peru presented values of ED_{50} equivalent to 94.9 μg; the one in Holland, ED_{50} 14.6 μg and in China, ED_{50} equal to 7.0 μg. The ester of caffeic acid was used as control, with ED_{50} of 1.9 $\mu g\ mL^{-1}$.

Immune Stimulant

Whenever the organism presents a pathology, it becomes vulnerable and any additional stimuli for the immune system becomes very important. That can be made through the diet, for instance, with intake of products rich in vitamins as well as through food supplements. Propolis is a safe product presenting not only therapeutic action, but also a preventive one, once it presents immune modulation activity.

Ansorge *et al*. (2003), studied the effect of CAPE and of the flavonoids Hesperidine and Quercetine, coming from different propolis extracts, in human immune cells functions, such as: DNA synthesis, cytokines production (IL-1, IL-12, IL-2, IL-4, IL-10 and TGF-β1) and T lymphocytes. The data suggest the studied substances are capable, depending on the dose, of increasing the TGF- β1 production capacity in human T cells. TGF- β1 causes the inhibition of cellular growth, differentiation in several cell types, it is an immune answer regulator and an inflammatory mediator. The results demonstrate that propolis presents a direct modulator effect in basic functional activities of immune cells that probably via immune modulator T cells. It is known that intermediate metabolites of oxygen are related to the macrophages bactericidal activity. The nitric oxide (NO) is very important in the mechanism of action of macrophages against microorganisms. However, excessive production exert toxic effects in several organs, which may lead to tissue damage. Orsi *et al*. (2000), carried out a study to evaluate macrophages activation after propolis exposure. A 10% hydro alcoholic propolis solution was administered to mice; the control group received physiological solution (NaCl 0.9%). In order to evaluate macrophages activation, oxygen intermediate metabolites concentrations were determined: H_2O_2 and NO. the mice were sacrificed twenty-four hours after being treated with propolis for an *in vitro* cell evaluation. It was observed that propolis (5, 10 and 20 μg mL^{-1}) induced an increase in H_2O_2 production. In this study, propolis did not induce significant alterations in the production of NO, with discreet inhibition in the concentrations of 50 and 100 μg mL^{-1}. The conclusion of this study indicated that propolis plays an important role in the immunologic system action, specially for the host's non-specific immune response through macrophages activation. The results found in that study are in agreement with the ones found by Than *et al*. (2003), who tested the NO production inhibition, induced by aqueous and alcoholic extracts of Brazilian green propolis in cultures of macrophages cells J774.1 of mice. The culture media contained lipopolisaccharides (LPS, 10 μg mL^{-1}), one of the NO production activators. The NO production was measured by the nitrite accumulation in the culture through Griess reagent. Both aqueous and alcoholic extracts were shown to be potent in the dose dependent inhibition of NO, with values IC_{50} of 37.8 and 78.9 μg mL^{-1} respectively, in accordance with Matsushige *et al*. (1996b), who used aqueous propolis extract *in vitro* experiments to access their effectiveness in the NO synthesis. The aqueous propolis extract effect was measured in several concentrations (1000, 100, 10 μg mL^{-1}) and it was clear that it inhibited the synthesis activity of NO in J774.1 cells, varying in accordance with the applied dose.

Synergy with Chemotherapy

Its biological effects also act in synergy with conventional chemotherapy drugs such as 5-fluorouracil (Suzuki *et al*., 2002). Antioxidants have the capacity to boost the effects of the anti-carcinogenic drugs. This is a relevant fact because it reduces the side effects caused by these medicines, through decreasing the administered dose without any detriment to the therapeutic effects (Santos and Cruz, 2001). Suzuki *et al*. (2002), orally administered crude, water-soluble propolis (CWSP) together with subcutaneous 5-fluorouracil (5-FU), or mitomicine C, in ICR inoculated mice carcinoma cells, with the goal of examining the effects of CWSP in the tumor progression, the effectiveness of chemotherapy and hematopoiesis in the circulating blood. This associated therapy with propolis and chemotherapeutic agents led to the largest tumoral regression rates in advanced stages, compared with isolated chemotherapy, illustrating the auxiliary effect of oral CWSP in the tumor regression when combined with chemotherapy conventional agents. Besides, the combined therapy improved cytopenia induced by the 5-FU, resulting in recovery of the counts of white and red blood cells (5-FU + CWSP, $p<0.05$/5-FU isolated or control treated with water). Neither significant effects were observed in the platelets count with the used dosage (5-FU + CWSP, $p>0.05$/5-FU isolated or control treated with water), nor a reduction of tumor growth with the oral administration of the aqueous extract of isolated propolis. A probable mechanism of action of CWSP would be the

increase of the bioavailability of the 5-FU, in other words, CWSP would act maintaining the high levels of 5-FU in the blood stream. According to Santos and Cruz (2001), when associating antioxidants and chemotherapeutic agents, the desired effect can be reached with smaller side effects, once the antioxidants minimize the toxicity caused by drugs when interacting with free radicals.

Others recent studies suggest that nutritional supplementation with antioxidants can influence the response to chemotherapy as well as the development of side effects caused by chemotherapy. Orsolic and Basic (2005), use CBA mouse model of transplantable mammary carcinoma, to investigate a clinically potential use of a water soluble propolis in treatment of various cytopenias induced by radiation and chemotherapy. Also, the antimetastatic efficacy of water soluble compounds by propolis alone or in combination with chemotherapeutic agents and their effects on the blood cells counts were evaluated. The findings indicate that combination of water soluble propolis with chemotherapy and or radiotherapy could increase the antimetastatic potential of chemotherapeutic agents. It also suggests benefits in potential clinical trials using water soluble propolis combined with chemotherapy in order to maximize their antitumor activity and minimize side effects post chemotherapy or radiotherapy, like commonly decrease blood cells. In addition, Padmavathi *et al*. (2005), studied the therapeutic effect of paclitaxel and propolis (ethanolic extract) on lipid peroxidation and antioxidant system in, 7,12 dimethyl benz(a) anthracene, DMBA-induced breast cancer in female rats. It was observed that administration of paclitaxel and propolis effectively suppressed breast cancer, decreased lipid peroxidation and increased the activities of antioxidants enzymics or non-enzimics (superoxide dismutase and vitamin C for example) when compared to therapy of paclitaxel or propolis alone. The combination of paclitaxel and propolis offers maximum protection against DMBA induced mammary carcinogenesis.

Anti-inflammatory Activity

Inflammation is triggered by the release of chemical mediators initiated in injured tissues and in migration cells (Rankin *et al*., 1996; Serhan and Chiang, 2004). Among the identified mediators of the inflammatory process one can find: vasoactive amines (histamines and serotonin), eicosanoids (aracdonic acid metabolites-prostaglandins and leucotrienes), platelet aggregation factor (PAF), cytokines (interleukins and TNF), quinines (bradikinine), radicals free from oxygen, among others (Czermak *et al*., 1998; Ohishi, 2000). Those substances are produced by inflammatory cells that include the polimorfonuclear leukocytes (neutrofile, eosinofile, basofile), endothelial cells, mast cells, macrophages, monocytes and lymphocytes (Fiala *et al*., 2002). Besides the biological activities described previously, propolis and their byproducts enclose anti-inflammatory properties described in different inflammation models, including the formaldehyde induced arthritis, paw edema induced by PGE2, carragenine or radiation (Dobrowolski *et al*., 1991; El-Ghazaly and Khayyal, 1995; Park and Kahng, 1999; Park and Woo, 1996), as well as in the acute inflammation induced by zimozan (Ivanovska *et al*., 1995). In several of those studies it was observed that propolis presented similar effectiveness to the anti inflammatory drugs used as positive controls in experiments. Besides, the flavonoide hesperidine, present in European propolis samples, showed similar effect to the indometacine in carragenine induced edema in mice (Emim *et al*., 1994). It has been described in the literature that during the acute phase of the inflammation, the main triggering phenomenon of the process is the local production of prostaglandins (especially PGE2) and leucotrienes derived from acid aracdonic. Those prostanoids are relatively unstable and flagrantly not selective in the interaction with several subtypes of receivers prostanoids as demonstrated in prepared samples of isolated tissues (Coleman *et al*., 1994; Hata and Breyer, 2004). Studies performed with preparations of sensitized guineapig lungs with egg albumin showed that the propolis presented an inhibitory effect on the prostaglandins, leucotrienes and histamine release, helping to explain its anti-inflammatory effect observed in the *in vivo* experiments (Khayyal *et al*., 1993). Similarly, Mirzoeva and Calder (1996),

demonstrated that propolis and some of its byproducts induced a prostaglandin production suppression, including the leucotrienes, being CAPE the stronger bioactive compound for this effect. Another interesting study was done in rabbits after cornea cauterization, submitted to the treatment with propolis, alcoholic extract (Ozturk *et al*., 2000) or aqueous extract (Hepsen *et al*., 1999). In these studies, the propolis showed similar effect to the dexamethasone in the reduction of the anti inflammatory effects associated to the surgical process. It was also demonstrated that propolis promoted the inhibition of the hialuronidase enzyme, contributing to the anti-inflammatory and regenerative effects in the healing process (Ikegaki *et al*., 1999). Fourteen Brazilian commercial propolis extracts of several areas of the country were analyzed according to the model of ear edema induced by acid aracdonic in mice. Once the extracts were given, at least 4 of the tested samples presented similar anti-inflammatory effect to that produced by the indometacine (Menezes *et al*., 1999), varying significantly form area to area and depending on where it was proceeding from.

Healing Activity

Ozturk *et al*. (1999), have demonstrated that the acetylcholine (Ach) and propolis facilitated wound healing in the cornea of mice comparing with the group control, to which saline solution was administered. In the test group topical administration was used six times a day, during three days at the location of the epithelial defect of the cornea. According to Peruchi *et al*. (2000), the repair process of a skin incision begins with the release of blood and formation of the blood clot. The healing of a wound or incision in the oral mucous membrane, within a moist environment and constant movement, does not allow the blood clot retention. That would make the repair process slower being necessary the use of medicines to accelerate the healing. Propolis, then could act positively in the wounds favoring the healing due to its antiseptic, healing and anesthetic properties. In this way, many authors have verified the histological effect of the alcoholic propolis solution in wounds of oral mucosa in mice and they observed that the propolis does not create inflammatory reaction and induces the epithelial formation as well as vascular and fibroblastic neoformation of the connective tissue. The 10% propolis alcoholic solution stimulated tissue repair of the oral mucosa in mice. Bretz *et al*. (1998), used calcium hydroxide and propolis in the assessment of the potential healing of the propolis in exposed dental pulps of mice. Both tested substances were effective in maintaining low populations of inflammatory and microbial cells. The effects of a mouth rinse containing propolis in tissue repair after dental surgical procedure (sulcoplasty) in humans was tested (Magro-Filho and Carvalho, 1994). The mouth rinses used contained 5% hydro-alcoholic solution of propolis. Cytological and clinical evaluation were performed and it was observed that the oral mouth rinses containing propolis aided in the postoperative healing and the employed vehicle had minimum irritating effect in the intra-oral surgical wounds. Those findings agree with the study that analyzed histologically the reaction and repair of the subcutaneous connective tissue of mice, in contact with tubes of polyethylene filled out with comfrey ointment (*Symphytum tuberosum*), propolis and honey (Magro-Filho *et al*., 1987). Two groups were formed, with 21 animals each. Tubes were implanted without medicines (controls) and tubes with the ointment containing 90% proportions of comfrey, propolis and honey and 10% of vaseline and lanolin as vehicles. The pieces for histological evaluation were obtained after 2, 5, 10, 20, 30, 40 and 60 postoperative days and they consisted of tubes and adjacent tissues. Two areas were analyzed: One in contact with the tube opening (called area A) and other a little far from that (called area B). To the fifth postoperative day, a thick bunch of colagenous fibers was observed in the extremities of the area A. To the tenth day, a strip of colagenous fibers almost occludes the light of the tube, being thicker in the central area; in the area B there is newly formed connective tissue. It was noticed, however, that between the 20th and 60th postoperative days, the treated group presented slight neutrofile infiltration and presence of lymphocytes, histiocytes and multinucleated cells involving fragments of the material, probably due to the used vehicles, but without the occurrence of severe reactions. The study concluded that the connective neoformation was accelerated until the tenth postoperative day.

Antimicrobial Activity

The pharmacologically active compounds of propolis, as flavonoids and phenolic acids, present effects on bacteria, fungi and virus. There are indications that the solvent employed for propolis extraction can influence the strength of this antimicrobial activity. In fact, the glycerin solutions, for instance, show weak inhibition of Gram-positive bacteria, while ethanol and propylenglycol solutions show effectiveness against fungi (Castaldo and Capasso, 2002). Studies on antibiotic and antifungal activities were carried out using aqueous solutions or suspensions of the following materials: Propolis grains containing 300 mg of propolis per gram, called by authors PG; red color tablets containing 350 mg of propolis per tablet, which average weight was of 1,2 g, called by the authors of PR and yellow tablets containing 350 mg of pollen grains, with an average weight of 1.2 g, called PY. Penicillin, streptomycin, tetracycline, griseofulvine, metronidazol, phenylbutasone, flurbiprofene and hydrocortisone acetate were used as controls for comparison. The evaluation of the activity of the tested substances was accomplished under *in vitro* conditions. The microorganisms employed were five Gram-positive (*Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus viridans*, *Diplococcus pneumoniae* and *Corynebacterium diphtheriae*); five Gram-negative (*Escherichia coli*, *Salmonella typhi*, *Salmonella paratyphi* and *Shigella flexneri*); pure cultures of ten fungi (*Cryptococcus neoformans*, *Histoplasma capsulatum*, *Madurella mycetomi*, *Microsporum kennels*, *Microsporum gypseum*, *Phialophora jeanselmei*, *Piedra hortae*, *Trichophyton mentagrophytes*, *Trichophyton rubrum* and *Trichosporon cutaneum*) and a virulent lineage of Entamoeba histolytica. PR and PG exhibited antimicrobial activity, especially against Gram-positive microorganisms. PY exhibited mild antibacterial effects against four Gram-positive: *S. aureus*, *S. pyogenes*, *S. viridans*, *D. pneumoniae* and against two Gram-negatives bacteria: *E. coli* e *Sh. Flexneri.* PG and PR exhibited definite activity against the groups of superficial fungi and dermatomicosis. Activity of PG and PR against subcutaneous and systemic mycoses was not observed. None of the propolis preparations presented activity against *Entamoeba histolytica* (Dobrowolski *et al*., 1991). The effect of the ethanolic extract of commercial propolis in *Candida albicans* growth in subjects with oral candida infection was evaluated (Martins *et al*., 2002). Strains of *Candida albicans* were collected from oral lesions of pseudomembranous and eritematous candida infection of twelve patients HIV-positive and of oral lesions of atrophic erythematous candidiasis of soronegative patients. The tested solution was the ethanolic extract containing 20% of propolis (EPE) obtained from Nectar Pharmaceutica in Belo Horizonte, state of Minas Gerais, Brazil. In order to test the growth inhibiting ability of microorganisms *in vitro*, the original formula of the commercially available solution was used. Econazol disks (25 mg), clotrimazol (50 mg) and fluconazol (25 mg) were used to compare the effect of EPE. The positive control was made with nistatine (100 IU) and the negative control, with distilled sterile water (20 mL). As a result, it was observed that EPE was effective in the inhibition of the growth of all the streams of tested *Candida albicans*. There were no significant differences among the data obtained for EPE and nistatine. However, some strains of *Candida albicans* were remarkably more susceptible to EPE than to nistatine. Others have exhibited inhibition zones with similar average diameters for EPE and nistatine. Park *et al*. (1998), investigated the antimicrobial activity of propolis in oral microorganisms through an *in vitro* study and accomplished quantitative analysis of flavonoids in the samples of Brazilian propolis. All samples exhibited inhibitory effect on the growth of *Streptococcus sanguis*, *Streptococcus* sp. isolated from saliva, *Actinomyces naeslundii* and *Streptococcus mutans*. The flavonoids were analyzed through HPLC analyses, which demonstrated the presence of kaempferol, pinocembrin and galangine in different proportions (mg g^{-1}) depending on the geographical area where the sample was collected. Ito *et al*. (2001), researched the anti-HIV activity of isolated compounds of the Brazilian propolis. The appropriate amount of virus for infection between 0.1 and 0.01 units of infection/cell was added to T H9 cells. Another part of T H9 cells only received half the culture and were incubated under identical

conditions to the cells infected with HIV. The drug AZT was used in the experiment as the positive control. The compound moronic acid presented significant anti-HIV activity (EC_{50} <0,1 mg mL^{-1}, TI >186) compared to other compositions analyzed in the study and it was modified to develop more potent anti-AIDS agents.

Conclusions

In spite of constant progresses made in the medical field, cancer is not totally known, especially due to the etiologic complexity that involves this disease. Treatment options are uncomfortable, many times traumatic, impacting patient's and their relative's lives. It is important to figure out the most appropriate moment for intervention and to choose for the best therapeutic modality, taking the cancer type into account as well as its stage. The quality of life should always be considered as paramount in such decisions, to minimize the consequences on physical and psychological status of those going through oncological treatment. Propolis, for the biological activities already attributed to its compounds, presents itself as an effective food supplement to be used by people in cancer treatment besides playing an important assistant role to first choice drugs in the traditional therapies. Thus, taking advantage of the benefits of this natural product with positive pharmacological properties, can help improve the choices available to patients and professionals dealing with cancer, as well as their quality of life.

Legend

Apoptosis- programmed cellular death
T Cells-lymphocytes produced in the Thymus
CD4 - helper T lymphocytes surface markers
CD8-lymphocytes surface markers present in the cells with cytotoxic or suppression functions.
CAPE-caffeic acid phenethyl ester
Carcinoma-malignant tumor stemming from epithelial tissue
Melanoma-a form of skin cancer that flows of the melanocytes (cells that produce pigment)
Fybrosarcoma-soft tissue sarcoma that starts in fibrous tissue
Adenocarcinoma-malignant tumor that attacks epithelial glandular tissue
5-FU - fluorouracil; drug used in cancer treatment
DMBA = 7,12 dimethyl benz(a)anthracene
EC_{50} - concentration executes
CDDP - Cisplatine
ED_{50} - dose executes
IL - Interleukine
TGF - 1 - tumoral growth factor
H_2O_2 - hydrogen peroxide
CWSP-crude water-soluble propolis
PGE-Broncodilator Prostaglandine
EPE-ethanolic propolis extract
TI-therapeutic index

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