The anti-cancer effect of Honeybee venom and melittin against breast cancer cells

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ABSTRACT

Bee products made from honey, pollen, royal jelly, beewax, propolis and in particular, bee venom, and the Apitherapy is the therapeutic and medical application of them. The aim of this work is to check bee venom and its therapeutic values. It uses the application of bee venom to treat various diseases and has been used in traditional medicine since ancient times. Bee venom is produced by the venom gland in the abdominal cavity and contains several biologically active peptides, including melittin (an important component of BV), apamin, adolapin, mast cell degranulating peptide and enzymes (phospholipase A2 and hyaluronidase), as well as non-peptidic components such as histamine, and dopamine Norepinephrine. Be venom has therapeutic values against a wide variety of diseases such as arthritis, diseases of the nervous system, abnormalities of the heart and blood systems, and diseases of the skin. In addition, bee venom is widely used in the treatment of some immune system diseases and, more recently, in the treatment of various cancer cells including kidney, lung, liver, prostate, bladder cancer cells, and breast cancer, as well as leukemia cells, which can be targets of toxic ones peptides such as melittin and phospholipase A2. Research should be expanded to identify its specific component and targeted actions.

INTRODUCTION

The nature gives us many harmful and dangerous things to our health. However, the new medicine and researches establish new way to lock at many agents in the nature around us. Honeybee venom is one of these agents. The use of honey and other bee products also dates back thousands of years, and the healing properties are found in many religious texts, including the Veda, the Bible, and the Koran. Pollen, beeswax and especially bee venom (BV) Bee venom (BV) therapy, which uses the application of bee venom to treat various diseases, has been used in traditional medicine since ancient times. It is based on the fact that these raw extracts have a large variety of pharmacologically active molecules. This set of chemical compounds are consist of biogenic amine, enzymes (Phospholipase A2), peptides and basic proteins (Melittin and Apamin) and a mixture of water-soluble and nitrogenous substances. Bee venom contains a variety of different peptides, including melittin, phospholipase A2, apamin, adolapin, and mast cell degranulator peptide (MCDP). Among these compounds, melittin, a small linear peptide made up of 26 amino acids, is the main ingredient in bee venom. or ointment, by injection, acupuncture, or even directly from a live bee sting. The most common method used is bee venom acupuncture (BVA), which involves injecting diluted bee venom. It can be used as an alternative medicine in patients with Parkinson's disease, pain, and other inflammatory conditions such as rheumatoid arthritis and osteoarthritis, antiviral and anti-inflammatory effects. In addition, several studies have shown that bee venom and / or melittin have anti-cancer effects, including cancer cells of the prostate, liver, breast, cervix, and kidney. Currently, various treatments for diseases such as cancer are very expensive and have numerous side effects, so natural resource cancer drug developments are venturing around the world(Abdela, N et al, 2016).

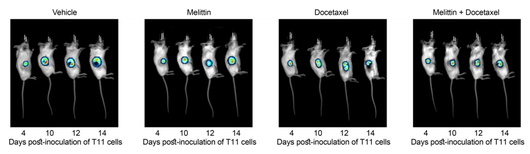

Fig 2: Bioluminescence imaging (BLI) of T11 luciferase tumors in mice at days 4, 10, 12, and 14 after inoculation of the :ells (C Duffy et al, 2020).

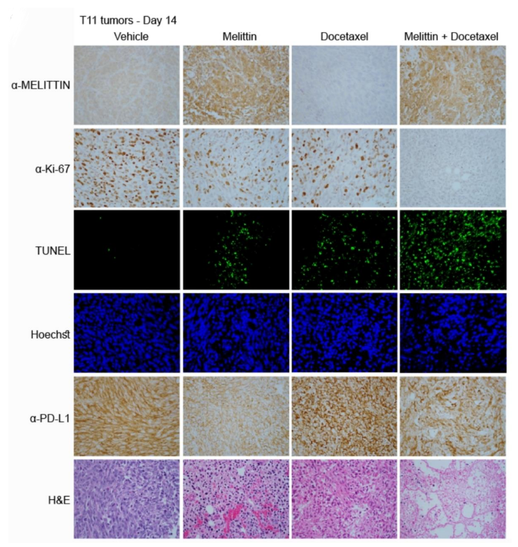

Fig 3: the images are shown using immunohistochemistry and immunofluorescence techniques in tumor biopsies from mice that were extracted on day 14 after T11 inoculation. The images are stained with anti-melittin, anti-Ki-67, TUNEL assay, Hoechst, anti-PD-L1, and H&E. and the images are divided into cells that were treated with vehicle, melittin, docetaxel, melittin + docetaxel (C Duffy et al, 2020).

MAIN BODY

bee venom Bee venom is a transparent liquid that dries easily even at room temperature, odorless, decorative pungent odor, bitter taste, hydrolytic mixture of proteins with a basic pH value (4.5 to 5.5) used by bees Defense is used. On contact with mucous membranes or eyes, bee venom causes severe stinging and irritation. Bee venom is insoluble in alcohol and ammonium sulfate and soluble in water. In contact with air it forms gray-white crystals. Dried poison turns light yellow in color, and some commercial preparations are brown in color, presumably due to oxidation of some of the poison's proteins. Collection, is considered a rich source of biogenic enzymes, peptides and amines, it has a specific gravity of 1.1331 Bee venom contains 88% water The glucose, fructose and phospholipid content of the venom is similar to that of bees Blood bee venom is a complex mixture of proteins, peptides and low molecular weight components. Its components are currently being characterized. The main components are proteins and peptides(Abdela, N et al, 2016). A study was done in 2020 to evaluate the efficacy and selectivity of honeybee venom against breast cancer. In this study, European bee venom and peptide melittin harvested in was evaluated by dose response analysis in a group of cell lines representing internal subtypes of breast cancer and untransformed cells. Bee venom shows high selectivity for cancer, and has higher efficacy on TNBC and HER2-rich breast cancer cell lines, followed by Breast cancer cavity (including MCF7 and T-47D) has the least effect on normal cells (HDFa-primary skin fibroblasts and untransformed breast cells MCF 10A and MCF-12A). Bee venom and melittin encourage caspase-mediated cell death in MCF7 cells, and reduced cell viability and migration in MDA-MB-231 breast cancer cells. Bee venom reduced metastases of breast cancer to the lung, prevent tumor growth, and prolonged survival in mice with spontaneous duct gland malignant neoplastic disease tumors(C Duffy et al, 2020).

Similarly, melittin changed into notably stronger towards HER2-enriched breast most cancers and TNBC in comparison to ordinary cells, with IC50 values from 0. Ninety four to 1.49 μM in human TNBC and HER2-enriched breast most cancers cells, and 1.03 to 2.62 μM in nontransformed cells. Cell-viability assays of honeybee venom and melittin in murine breast most cancers and ordinary mobileular strains showed improved selectivity for competitive murine tumor mobileular strains, inclusive of the p53-mutant claudin-low T11 and the BRCA-mutant B.1537,38. The venom of honeybees from distinctive honeybee populations in Ireland and England decreased the viability of SUM159 and SKBR3 cells notably greater than that of nontransformed HDFa cells. To study the mechanism and kinetics of cell death, TNBC cells were treated with melittin or melittin IC50 for 18 and 24 hours, and treated with digested caspase-3 assay to quantify cell death caused by apoptosis. For Caspase-3 in SUM159 cells, at 18 and 24 hours after treatment, only melittin caused a higher level of apoptosis than bee venom. To test Melittin sensitizes TNBC to docetaxel treatment in vivo, an exam for capability synergies among melittin and chemotherapeutic dealers to boom breast most cancers mobileular death was done . The murine p53− TNBC mobileular line T11 turned into handled with docetaxel in mixture with both honeybee venom or melittin, and mobileular-viability assays had been carried out to decide the mixture index (CI) among the treatments56 (Fig 1). In addition, they located CIs < 1 for all the concentrations examined, indicating sturdy synergistic interactions (Fig2). Synergisms had been additionally located with cisplatin, an agent used to deal with TNBCs withinside the clinic. The T11 xenograft version turned into used for in vivo experiments as it proven the maximum favorable in vitro drug interplay among melittin and docetaxel throughout a couple of mobileular strains examined, and it has an intact immune gadget allowing the immune reaction to melittin to be assessed (C Duffy et al, 2020).

DISCUSSION

from many studies Melittin contains the following properties in helping to treat cancer: The effects of melittin are with phospholipase A2, caspase and metalloproteinase 2 and kill the cells that express oncoprotein. Melittin is one of the most potent inhibitors of calmodulin, which is very important in the growth and division of cancer cells. Induces apoptosis in cancer cells by changing the potential of mitochondrial membranes. Induction of apoptosis by melittin has been confirmed in gastric, lung, liver, ovarian, breast and cervical malignancies. It has anti-metastatic properties and inhibits rac1 35expression. The substance disintegrin linker melittin (DLM) is made of melittin and disintegrin and activator of plasminogen urokinase-type (uPA). UPA breaks down in tumor cells and allows DLM to release melittin. Combination of nationality with amino terminal fragment (ATF). Combination of nationality with interleukin 2. Combination of bee venom with Cisplatin, which together have synergistic properties and cause fewer side effects. Bee-produced propyl contains Chrysin, which can be used to treat breast cancer and develop chemotherapy in the future. Using a combination of melittin and dutaxel, dutaxel-resistant tumors can be sensitive. Melittin can decrease the immune-suppressive effects of the chemotherapy. Nanoparticles, PIC13 micelles and combination of melittinaptamer can be used as safe carriers of melittin. Hespiridine, piperine and bee venom can be used to enhance the effect of tamoxifen. Melittin reduces EPC adhesion and Prevents angiogenesis. Until now the scientists are working to find the perfect doses and ways to use honey bee venom in killing breast cancer cells (Yavari M et al, 2020). So all studies agreed about the importance and the useful of honeybee venom as an anticancer therapy. In my opinion, the use of honeybee venom as a treatment to kill cancer cells has a promising future and it gives great hope to breast cancer patients.

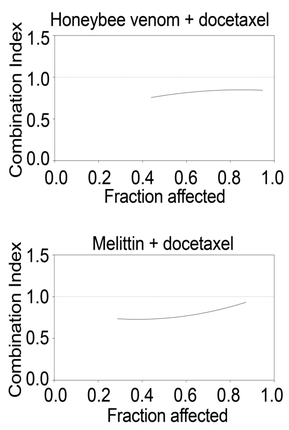

Fig 1: Index graphs of different fractions of the cells that were treated with bee venom or melittin, both with docetaxel, which are calculated with CompuSyn software (C Duffy et al, 2020).

CONCLUSION

Despite the side effects (such as allergic reactions), melittin seems to have a beneficial effect on a variety of cancers, especially breast cancer. Bee venom is seen as a potential weapon against cancer; MEL, a major polypeptide in bee venom, is believed to act as a lysing agent and has traditionally been used in various cancer therapies. However, at high treatment doses, due to its lytic properties, it exhibits severe non-specific toxicity. Though, it should not be underestimated that most research is conducted in vitro and in vivo; therefore, it can be used in humans in a variety of ways.

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