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Review Article

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A REVIEW ARTICLE ON ANTI CANCER ACTIVITY OF ELLAGIC ACID AND ITS DERIVATIVES

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ABSTRACT

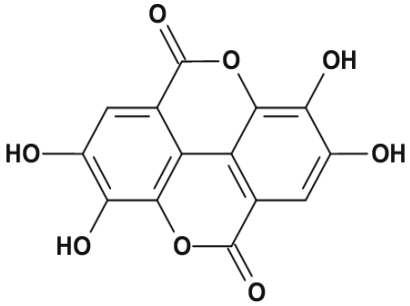
Ellagic acid is anti oxidant and anti proliferative compound present in fruit, nuts, and vegetables. Many researches based on its potential health benefits has been conducted and evidence for anti cancer activity in various cancer cell lines was found. The ellagic acid and its derivatives is used to suppress the growth of cancerous cells with enhancement of human immunity and without any undesirable side effects. It is mainly used to treat several cancer like prostate cancer, colon cancer and also used to treat bacterial infection and viral infection. The derivatives of ellagic acid like 4,4'-Di-O-Methylellagic acid and ellagic acid peracetate show anti cancer efficiency, enabling of immunity and induction of apoptosis.

KEYWORDS: Ellagic acid, anticancer agent, Derivatives, immunity, Apoptosis.

INTRODUCTION

Cancer is called as malignancy, is the abnormal growth of cells. There are several cancer that are lung cancer , colon cancer, prostrate cancer and their symptoms may vary based on type of cancer.They are several anti cancer treatment is available in the modern world , but the ellagic acid and its derivative shows an extra ordinary anti cancer activity. The commercial use of ellagic acid and its derivative show health benefits, also application and its properties.

Ellagic acid is polyphenolic compound which is obtained from tannins. The molecular weight of ellagic acid is 302g mol^{-1} and the molecular mass is 500 to 2000.



It consist of 4 ring that represents the lipophilic domain, and four phenolic groups and two lactone ring, act as a hydrogen forming sides and electron acceptors.

The ellagic acid produce high effective anti cancer activity, it show cytotoxicity towards human bladder cancer by induction P^{53} and apoptosis. The cancer growth on mouse lung can be inhibited DNA binding benzo (α) pyrene. The prostrate cancer treated by combination ellagic acid and vinorelbine estra mustine phosphate as used in chemotherapy. The acetylation of ellagic acid produce ellagic acid peracetate which produce more potent anti cancer activity.

The ellagic acid is mainly produce by fermentation as well as chemical extraction using acid-methanol with hydrochloric acid. Anti melano genic activity produced by the ellagic acid and its metabolites by chemical modification on the structure. They inhibit cell migration, cell proliferation as well as angiogenesis, this effect or reduce the metastasis of tumor cells.

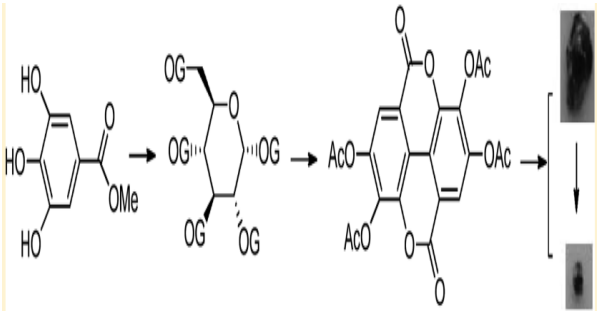
Ellagic acid also have several biological properties that is; using to prevent the joints from extremities destruction, eye, kidney heart and also which increases insulin activity. In modern world cancer is a deadly disease, the use of ellagic acid as a anticancer agent show high potential activity against the tumor.

REVIEW

Douglas Kinghorn, Jianhua Yu et al

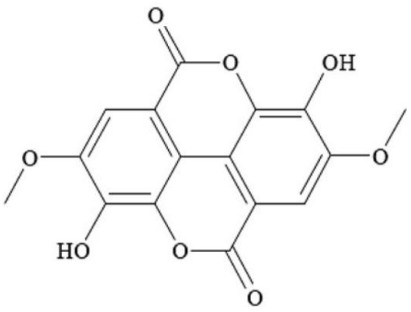
Ellagic acid was first synthesized from methyl gallate with α-pentagalloyl glucose (α-PGG) and ellagic acid peracetate (3,4,3 ', 4'-tetra-O-acid, acetylellagic acid, 2)

derived from ellagic acid on acetylation. Oral administration of melanoma growth suppressions significant in immune competent six mice without affecting the activity of Killer cells (NK). Comparison of immune-enhancing activities of Ellagic acid and its peracetate have shown that the latter compound increases the amount of white blood cells in peripheral blood and immune cells enriched with bone marrow and mouse liver. Hence the anti-tumor Efficacy and increased immunity of ellagic acid peracetate were greater than that of ellagic acid. Also, neither 1 nor 2 if Administered orally, caused changes in total body weight of normal liver or spleen in tumor-free mice, suggesting that this The compounds may not be toxic to mice. Ellagic acid peracetate was demonstrated that it inhibits the growth of B16 melanoma cells in vitro and induce apoptosis of B16 cells, which corresponds to negative regulation from BCL-2. Overall, current data imply that 2 can be deleted tumor growth by increasing the immunity of the mouse and inducing apoptosis in tumor cells without recognizable side effects.[1]



Ana Ramírez de Molina et al

Ellagic acid (EA) and certain derivatives were inhibited the proliferation of cancer cells caused the standstill of the cell cycle and modulates certain important processes of cancer cells. This study aimed to identify possible relationships of EA activity Structure and derivatives in vivo safely in its fruit effects on people's colon cancer and normal cells and compare this activity with each other polyphenols. The results showed that 4,4-di-O-methylellagic acid was the most effective connection in the inhibition of proliferation of colon cancer cells. 4,4-di-o-methylellaginic acid was 13 times more effective than other connections in the same family. In addition, DiOMEA was very active against 5-fluoroacil cancer cells of chemotherapeutic radiators, which is resistant, although no effect was achieved in non-Palm colon cells. In addition, there was no correlation between antimacroscopic and antioxidant activities, with assistance because differences in the structure can lead to various molecular targets involved in their various effects. Finally, the analysis of the microchip showed that the modulated WNT signal transmission of 4.4 DiOMEA, which may be involved in the possible antitumor action of this compound. The results suggest that differences in structure an activity between the environmental test and 4,4-DiOMEA could form the basis of a new strategy for discovery of cancer medicines on these chemical changes. The 4,4 '-DiOMEA show high anti cancer activity with IC_{50} value equal to 55µM,so it is highly used against colon cancer.[2]



Jia Li et al

Pomagrenade Peel (PPP) polyphenol extracts presented Induction of HepG2 against the anti-proliferation and apoptosis effects in the Studies. The purpose of this study was to examine the different anti-cancer effects of Ellagic acid (EA) on HEPG2 cells and their possible effects Mechanisms. Cell proliferation, morphology, cell cycle and Apoptosis was checked and the results showed that the EA did Cell cycle arrest in S and G0 / G1 phases and dose, In It is also one of the main mechanisms of the incidence of apoptosis is the implication of this in the manner of mitochondrial apoptosis. The ellagic acid on administration it show the IC_{50} values reached to 94.70 µM indicating potent anticancer activity.[3]

Imtaiyaz Hassan et al

Pyruvate dehydrogenase kinase 3 (PDK3) plays a central role in cancer metabolism through reversible phosphorylation Pyruvate dehydrogenase complex blocks the entry of Pyruvate for its catabolism in the TCA cycle, and therefore it is being considered as an important drug target for various types of cancer. We have successfully expressed full length human PDK3 and studied its Mechanism of interaction with food polyphenols in the search for potential inhibitors. Analysis of the molecular docking revealed that the certain compounds preferentially bind to the ATP binding pocket of PDK3 and interact with functionally important residues. In silico Observations were supplemented by experiments measurements of PDK3 fluorescence quenching and confirmation by isothermal titration calorimetry measurements. Ellagic acid (EA) significantly binds and inhibits the kinase activity of PDK3. In in vitro cytotoxicity and anti proliferative properties of the EAs were assessed by MTT test. Conformational dynamics of EA. The PDK3 complex in the simulation of molecular dynamics has shown this a stable complex was maintained by a large number of hydrogen bindings across the 100 ns trajectories. In summary, EA can be a promising molecule for PDK3 inhibition and could be used as a leading molecule against diseases associated with PDK3. The IC_{50} values were found to be 36.69 ± 3.22 µM for HepG2 and 23.44 ± 1.33 µM for A549 cells, this indicate that the EA is

non-cytotoxic to normal cells and also which inhibit other cancerous cells.[4]

CONCLUSION

EA can act be used as a dietary agent for preventing and treating many common forms of cancer. EA and its metabolites have preventive and therapeutic potential against human cancers. However, chemical modifications or more formulations that can bypass their poor oral bioavailability and eliminate hepatic first pass metabolism without compromising patient acceptability must be developed. From this study, It is clear that Anticancer activity is seen in Ellagic acid and its derivatives.

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