Letter to Editor

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Explore the unexplored: Potential anti-tumor properties of Rhododendron against bladder cancer.

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As cancer cases are increasing worldwide, various methods for the treatment of cancer are still ongoing. The use of medicinal plants for the treatment of both major and minor ailments have been practiced since ancient days. Rhododendron is an evergreen tree that belongs to the family Ericaceae with distribution in most regions of the world. Studies have shown cytotoxic effects of the plant against cancer cell lines supporting the anti-cancer properties .[1] However, the anticancer effect of Rhododendron on the cell lines responsible for bladder cancer remains unexplored. Bladder cancer ranks as the ninth most common cancer worldwide with developing countries contributing to more than 60% of the bladder cancer incidence and mortality above 50%. Various assays such as lactate dehydrogenase (LDH) , growth inhibition assay and techniques such as flow scytometry can be performed to examine the extract of various Rhododendron species against a variety of bladder cancer cell lines.

Various modalities are used for the treatment of carcinoma bladder including chemotherapeutic agents and surgical removal of bladder to name a few, which have their own benefits and drawbacks. Hence, exploring the anticancer effect of Rhododendron against bladder carcinoma could be promising, since it can be naturally synthesized, and is expected to have lesser side effects in comparison to the chemically synthesized drugs. The American Cancer Society estimates 83,730 new cases of bladder cancer in the United States. The carcinoma of bladder is commonly positioned in the urinary tract and gender wise distribution shows that it is the fourth most common cancer among men and eight most common cancer among women.[2] The most common risk factor for bladder cancer is smoking and it has been estimated that the exposure to aromatic amines and arsenic also possesses serious threat to bladder cancer.[3] It is found that 80% of bladder cancer are non-muscle invasive bladder cancer (NMIBC) with the remaining accounting for muscle invasive bladder cancer (MIBC). The recurrence rate for NMIBC is found to be 60 to 70%. [4] Despite Transurethral resection (TUR), the first line treatment for bladder cancer, it is still likely that 60-90% of NMIBC bladder cancer will reoccur.[5] Likewise, radical cystectomy is another standard treatment for MIBC. However, within a duration of 2 year's, approximately 50% of MIBC patients have a 50% chance of developing metastases and even after surgery, the survival rate is 50%. Cisplatin based chemotherapy is the first line treatment for advanced and critical stages of bladder cancer. Regardless of initial high response rate, the long-term survival chances are low.[7] Studies have found that the adverse side effects of cisplatin-based treatment include damage in the renal tubules, neurotoxicity, ototoxicity, and bloodstream infection. [8]

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Hence, finding an alternative treatment for bladder cancer is necessary to minimize the side effects of chemotherapy. Natural agents could be one of the potential sources of cancer treatment. Plants have been used as natural medicine since ancient days because of antioxidant properties and studies have found that medicinal plants can be used to eliminate the side effects of chemotherapy.[9] Rhododendron is one of the ornamental plants which is found especially in the Himalayan range of India, Nepal, and Bhutan. [10]

Only few studies have been conducted so far, to explore the anticancer effects of Rhododendron and has shown anti-proliferative activity against lung carcinoma cells via apoptosis. The leaf extract of Rhododendron arboreum and Rhododendron campanulatum inhibited the growth of cervical (HeLa) cancer cells by 60%.[11] Hyperin, an active metabolite in Manchurian Rhododendron, inhibits the growth of human endometrial cancer cells.[12] Based on the evidence and study, it is hypothesized that the flower of Rhododendron shows potential growth inhibitory effect against bladder cancer cell lines. It would be novel to use the extract prepared from the flower and leaf of Rhododendron species against bladder cancer. Various assays need to be carried out to explore the potential anticancer mechanism. Hence, growth inhibition assay, cytotoxicity assay (Lactate Dehydrogenase Assay), Cell Survival Assay, Flow Cytometry technique can be performed. The active metabolites present in the prepared extract can be identified by using Liquid Chromatography Mass Spectrometry (LCMS) and for structural identification of those metabolites, Nuclear Magnetic Resonance (NMR) Imaging is essential. However, demonstrative research on in-vitro and in-vivo studies are required for the potential discovery of anti-cancer molecules.

Previous studies have shown the cytotoxic properties of Rhododendron flower extract on breast and colon cancer cell lines. From the cytotoxicity assay, it is expected that the extract prepared could also have a cytotoxic effect on bladder cancer cell lines. The extract is expected to lyse the bladder cancer cell line by releasing lactate dehydrogenase (LDH) without affecting the normal cell line. From the growth inhibition assay, the growth of bladder cancer cell lines could be expected to undergo inhibition by the extract prepared from the Rhododendron as compared to the negative control. From the flow cytometry assay, it can be assumed that the extract prepared from Rhododendron could exhibit apoptosis-like effect. Furthermore, the increasing concentration of extract can induce apoptosis. Further analysis of caspase activity can be examined by zymography assay. From LCMS, it can be expected that the extract of Rhododendron species from Nepal, could have active compounds like quercetin, coumaric acid, rutin and other novel compounds. If in-vitro studies show positive results, in-vivo studies can be further performed. BALB/c Nude Mouse can be used for clinical experiments. The bladder tumor can be induced in the mouse by intraperitoneal injection (ip). The mice can be divided into three groups: control, cisplatin treated, and Rhododendron treated. The mouse should be housed in a pathogen-free condition with constant temperature and humidity. It is expected that the tumor size of the mice treated with Rhododendron extract could reduce in size with less side effects than the mice treated with cisplatin.

Despite the availability of a variety of treatment options there are chances of recurrence of bladder cancers with many side effects. There is an urgent need in finding novel alternative cancer treatment with lesser side effects. It is therefore necessary to study the potential anticancer properties of the Rhododendron plant and it's species that could lead to the development of anticancer drugs.

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