Anti-cancerous and antioxidant potential of the endophytes associated with azadir...

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Endophytes associated with a medicinal plant may be capable of producing the same metabolite as the host plant and thus may also prove to be promising from biotechnological and pharmaceutical perspective. Therefore, I aim to study anti-cancerous and antioxidant potential of the endophytes associated with three common Indian medicinal plants viz, Azadirachta indica (Neem), Momordica charantia (bitter gourd) and Curcuma longa (Turmeric). These plants are not only commonly used for food or medicine, but are known for their therapeutic benefits, including anti-cancerous properties. However reports of their endophytes with any medicinal potential are still limited. Since this avenue has not been explored in detail, studying endophytes from these plants may prove to be a promising solution for harnessing their anti-cancerous potential. Further, cancer cell lines are reliable pre-clinical models to study the efficacy of anti-cancer compounds, thus the activity of endophytic bioactive compounds can be tested in vitro using these cell lines.

A study had showed that reactive oxidative species such as superoxide anion and hydrogen peroxide also increase significantly in cancer patients (Sharma et al., 1997). Therefore, study of antioxidant compounds will be helpful in studying efficacy of the endophyte derived compounds. Thus my study will provide an insight to the endophytes associated with these plants and will also evaluate these microbes for their anti-cancerous, anti-proliferative and/or antioxidant properties. Review of Literature: Endophyte derived Bioactive compounds Bioactive compounds refer to extra- nutritional compounds that have therapeutic benefits. Use of these natural products has

gained popularity due to their advantage over synthetic chemical drugs that may have side effects (Strobel and Daisy, 2003). Moreover, owing to a rise in drug resistant diseases, specifically, Methicillin resistant Staphylococcus aureus (MRSA), Penicillin resistant Streptococcus pneumonia (PRSP), Carbapenem resistant Enterobacteriace (CRE) and Vancomycin resistant Enterococcus faecium (VRE) infections in recent years, there is an urgent need for novel/alternative drugs (Menichetti, 2005, Geisinger and Isberg, 2017).

Bioactive compounds from plants and their endophytes, alone contribute to about 80% of the natural drugs available commercially (Singh and Dubey, 2015). Moreover, about 50% of the recently developed medicines of plant origin (Cragg and Newman, 2012) have not been able to advance beyond in-vitro study stage, due to lack of potency, storage or tedious production procedure. However, if the same compounds can be extracted from microbes, the whole process becomes more commercially viable. For example, Taxol, a bioactive diterpenoid (also known as paclitaxel) is derived from the bark of trees of Taxus family, and has been approved from Food and Drug Administration (FDA) for treatment of lung cancer, advanced breast cancer and refractory ovarian cancer. Taxol was later found in a number of endophytic fungi such a Taxomyces andreanae, Taxodium districhum, Wollemia nobilis, Phyllostictia spinarum, Bartalinia robillardoides, Pestalotiopsis terminaliae and Botryodiplodia theobromae (Stierle et al., 1993; Pimentel et al., 2011).

Similarly, camptothecin (an alkaloid) is another well-known anticancer compound which was first isolated from the plant Camptotheca acuminata, and was later obtained from the endophytic fungus of the same plant. It is currently being employed successfully for ovarian and lung cancer. This compound is also a precursor of drugs such as topotecan and irinotecan, which are more soluble in aqueous medium than camptothecin (Kusari et al., 2009). Both, Taxol and Camptothecin are commercially available as anti-cancer drugs in the market. Besides these, a number of other examples of metabolites or their derivatives obtained from endophytes are under various stages of trials for their anti-cancerous properties. Plant metabolites ergoflavin (xanthane dimer) and secalonic acid D (mycotoxin) which have anticancer properties, are being derived from endophytic fungus (Deshmukh et al., 2009; Zhang et al., 2009). Phenylpropanoid, which is a large group of secondary metabolites produced from plants, has been obtained from Penicillium brasilianum, root endophyte of Melia azedarach (Chinaberry tree) (Fill et al., 2010).

Another class of compounds with a strong cytotoxic activity are Podophyllotoxin (lignan) and its analogs. Podophyllotoxin was originally obtained from the plant of Podophyllum sp. which are listed as endangered. It is a valuable precursor of anticancer drugs like teniposide, etoposide and etopophos phosphate (Kour et al., 2008; Kusari et al., 2009). Thus, the plant associated microbes have generated higher prospects of mass production for secondary metabolites (Kour et al., 2008). These are, however, only some of the prominent success stories. Owing to variable response rate towards

therapeutic compounds due to the diversity in patients, there is a need to explore novel agents. Since most cancers involve a complex crosstalk of factors affecting multiple genes and signalling pathways (Shanmugam et al., 2016), novel compounds may be able to target multi-drug resistant cancer or reduce the side effects associated with currently used cancer drugs, and may thus prove useful in medical advancement.