Hedgehog (Hh) pathway inhibitor loaded polymeric nanoparticles for anti-cancer therapy

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Abstract

Targeting the self-renewal pathways (SRPs) in cancer has become one of the futuristic treatment strategies in order to prevent cancer relapse and drug resistance. The cause of cancer recurrence and multi drug resistance (MDR) is attributed to the presence of a sub-population of cells in solid tumors called as the cancer stem cells (CSCs). These CSCs are known to possess MDR pumps, SRPs, specialized niche and altered metabolism, ultimately leading to the failure of available treatments in order to eradicate them. One of the embryonic SRPs Hedgehog (Hh) pathway is found to be aberrantly active in most of the cancers such as basal cell carcinoma, brain tumors, pancreas, prostate, leukemia's to name a few. Mutations in Hh pathway components and high expression of its ligands lead to progression in many cancers [1]. Most of the Hh pathway inhibitors available are used directly, however their successful clinical translation is hindered due to their limited aqueous solubility and poor bioavailability [2]. Hence, there arises the need for an appropriate nanoformulation of such compounds. In our work we propose to target the Hh pathway in cancer through nanomedicine approach. We have selected a novel Hh small molecule antagonist, specifically inhibiting the Gli 1/2 protein of the Hh pathway, which promises to be an aspiring candidate for future cancer therapy [3]. We encapsulated the Hh antagonist in a FDA approved polymer and it was synthesized through the single emulsion-solvent evaporation method [4]. Our prepared nanoparticles were further characterized for their size distribution, surface morphology and surface chemistry using Zetasizer, SEM, TEM and XPS respectively. *In vitro* cell studies were carried out to assess the cytotoxicity of the prepared nanoparticles and the anticancer activity.

References

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