Application Of Amorphous Solid Dispersion Technology For Improving The Solubility And In vitro dissolution properties Of *Withania somnifera* methanolic root powder extract



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Abstract

Withania somnifera is a xerophytic plant whose methanolic extract of leaves and roots powder has exhibited effectiveness against various diseases. Like other natural products, its methanolic root powder extract also displayes poor dissolution because of high lipophilicity and poor aqueous solubility. The current reseach work was intended to formulate polymeric amorphous solid dispersion (PASD) system of methanolic extract of *Withania somnifera* root powder for improving its dissolution characteristics. The solvent evaporation method with three different polymers - HPMCAS-L, PVP K-30, and soluplus® were used to prepare the amorphous system. The complete transformation of the crystalline phytoconstituents to an amorphous/molecularly dispersed state was confirmed by DSC and PXRD studies, with all tested polymers at a 1:4 polymer ratio. The stability of phytoconstituents within prepared PASDs was confirmed by FTIR study, which revealed no changes in any of the distinctive peaks of pure extract. The prepared PASDs had significantly higher saturation solubility compared to pure extract. The formulated PASDs demonstrated substantial improvement in the dissolution properties of phytoconstituents compared to a pure extract containing capsules (f_2<50).

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Importance of Research and Development

Withania somnifera (native name - Ashwagandha) is known as "Indian ginseng" due to its broad therapeutical activities [1]. Various parts of the *Withania somnifera* shrub are used to treat a variety of diseases, such as adaptogenic, aphrodisiac, tonic, narcotic, diuretic, antihelminthic, astringent etc[2]. The broad range of therapeutical applicability of *Withania somnifera* is due to the presence of diverse secondary metabolites (steroidal alkaloids and lactones - a class of constituents together known as withanolides) present in different parts to plants (roots, stems, and leaves). The root, out of all the plant parts containing secondary metabolites, is considered to be the most therapeutically active as it contains a significant amount of phytoconstituents, especially withanolides. The methanolic extract of Withania somnifera root powder has displayed anti-tumor, immune-modulatory effects, anti-bacterial effects, anti-oxidant and anti-inflammatory activity [3-5]. However, like the majority of phytoconstituents, withanolides also exhibit extremely poor solubility and hence impaired dissolution, resulting in poor bioavailability after oral administration. After oral administration, adequate bioavailability is the primary concern for converting the phytoconstituents into successful market formulations, since these molecules are commonly used to treat several diseases, such as cancer, neurodegenerative diseases, infectious diseases, and chronic metabolic disorders, which require long-term treatment [6-7]. Another limitation to converting the alcoholic extract containing phytoconstituents into a successful oral market formulation is its nature of being sticky, hygroscopic, and adhesive, which is difficult to process at an industrial scale. Based on above-mentioned facts, the present research work was aimed to formulate and evaluated the ASD of *Withania somnifera* methanolic root powder extract to enhance its dissolution characteristics. The prepared amorhous solid dispersion (ASD) was also

evaluated for its ability to improve the *in-vitro* antioxidant activity of the methanolic root powder extract.

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