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A smart innovative approach for delivery of nanosized risperidone to brain via novelistic trans vermillion route

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Abstract

Aim:

Performance evaluation of Risperidone loaded bio-flexi films using Cucurbita pepo.

Research design and Methods:

The risperidone loaded bio-flexi films was prepared using novel bio-film former isolated from fruit pulp of Cucurbita pepo by solvent casting method with different ratios (1%, 2%, 3%, 4%, 5% and 8%) and with standard polymer HPMC and CMC-Na (1%, 2%, 3%, 4% and 5%). The prepared formulations were evaluated for thickness, folding endurance, swelling index, content uniformity, in-vitro drug release, scanning electron microscopy (SEM), transmission electron microscopy (TEM), in-vitro cytotoxicity and stability studies.

Results:

The best formulation shows an R2 value of 0.9814, T50% of 29.7 hrs and T80% of 65.25 hrs respectively. According to the release kinetics the best fit model was found to be Peppas Korsmeyer with Fickian Diffusion (Higuchi Matrix) as the mechanism of drug release. Cucurbita pepo provided excellent filmability and stability having particle size of 252 nm and zeta potential of -8.91 mV. Distribution of drug in the film was studied by using SEM. TEM confirms the spherical shape of nanoparticle having range of 20 nm. Histology study shows there is no evidence of inflammation or necrosis.

Conclusion:

Cucurbita pepo act as a film former in risperidone loaded rate controlled bio-flexi film.

Introduction:

According to world health report, about 450 million people suffer from a mental or behavioral disorder. This amount to 12.3% of the global burden of disease, and predicted to rise up to 15 by 2020. Risperidone,3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl] ethyl]-6,7,8,9 tetrahydro-2-methyl-4H-pyrido[1,2-a] pyrimidine- 4-one is an approved antipsychotic drug belonging to the chemical class of benzisoxazole derivative and is available as tablet, oral liquid (Risperidal®) and orally disintegrating tablet (Risperidal® M TAB).These dosage forms exhibit low bioavailability due to extensive first pass metabolism and non-targeted delivery results in numerous side effects. Since the target site of the risperidone is brain, thereby a strategy is desirable that not only improves the bioavailability by preventing first pass metabolism but also provides targeting to the receptor site and bypasses the blood–brain barrier, so as to achieve desired drug concentration at the site of action, hence preventing availability of drug at non-targeting sites and reducing the side effects.

The skin of labial is exclusive and consists of primarily of tissue layer that has fewer and completely different glands compared with the normal skin. The lip is also in contrast to the alternative skin therein the outer layer (stratum corneum) is extraordinarily skinny or utterly absent in the general public. The translabial application of the medicine give many advantages, together with the shunning of viscous first-pass metabolism and skill to supply nearly constant drug delivery over a protracted amount, which can cut back general adverse effects. The skin forms a superb barrier against the drug permeation because of the rigid lamellar structure of the stratum lipids. Our novel translabial drug delivery sidesteps this barrier because of the terribly skinny or absent layer of stratum corneum.

Earlier studies (Madhav et al., 2013) have demonstrated that translabial platform offers a practical, non-invasive, and an alternative route of administration for rapid drug delivery to brain. It also offers the advantages of being administered simply, cost effectively and conveniently. Additionally, direct transport of drugs to brain, circumventing the brain barriers following translabial platform provides a unique feature and better option for targeting drugs to brain. However, few formulation factors should be considered while designing the drug delivery system for translabial platform. The formulation should be designed so as to provide a rapid transport of drug across translabial skin and a longer residence time at labial skin. Films by virtue of their lipophilic nature and low globule size are widely explored as a delivery system to enhance uptake across labial mucosa. Addition of mucoadhesive agents such as cucurbita pepo polymer helps in retention of the formulation on the translabial skin.

Natural polysaccharides from biopolymers have been widely used as bioadhesive materials because of their biocompatibility and biodegradability. The Cucurbita pepo biomaterial used in this study was isolated from the pulp of evergreen fruit, which belongs to the family of Cucurbitaceae. The pulp of cucurbita pepo contains carbohydrate, dietary fiber, fat, protein, vitamin and minerals. Cucurbita pepo has been reported to have neuralgia and headache, treat gastritis, purify the blood, diuretic, cure for bronchitis and fever. In our research work, cucurbita pepo was used as a bioadhesive and strip-forming agent in the dosage form.

Cucurbita pepo contains 39.25% crude protein, 27.83% crude oil, 4.59% ash, and 16.84% crude fiber; the corresponding values for the kernels were 39.22%, 43.69%, 5.14%, and 2.13% respectively. Cucurbita pepo is a rich natural source of proteins.

The objective of this investigation was to prepare, characterize bio-flexi films and evaluate their performance in animal model. It is proposed that films/patch based drug delivery system will result in greater transport and distribution into and within the brain. This can reduce the side effects, decrease the dose and frequency of administration, and perhaps even the cost of the therapy.

The potential risks arising from the use of nanomaterial on the skin, natural chemistry and natural preparation are welcomed in the design of translabial drug delivery systems. The isolated bio film former, bio-retardant was non-toxic and biodegradable as it is extracted from the natural edible sources and compatible with the translabial delivery for the treatment of depression. This is a novelistic approach significantly delivering the drug for prolonged period and the biopolymer was served as a promising excipient for delivering dosage forms. The risperidone bio-flexi film prepared by sonication solvent evaporation method. Cucurbita pepo provided excellent stability for the formulation and resulting particle size for best formulation 252nm.The bio-flexi film had PDI of 0.35 with zeta potential of -8.91mV which is permissible to the translabial delivery.

Future Scope:

The risperidone loaded bioflexi films comprises of Cucurbita pepo needs to be explored for detailed in vivo studies in both albino rabbits and rats so as to assist pharmacokinetics and pharmacodynamics behavior of the molecules upon administering through the translabial region. As it possess inbuilt neural connection to the brain via various nerves so the drug can certainly reach to the target site and show its pharmacodynamics activity and it can be reduce multi hundred folds.