FORMULATION AND EVALUATION OF METHYL PHENIDATE TABLETS FOR TRANSDERMAL DRUG DELIVERY SYSTEM


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ABSTRACT
In present study transdermal drug delivery of Methylphenidate was developed to overcome the first pass metabolism and to reduce frequency of dosing compared to oral route. Oral drug delivery system has various drawbacks like poor bioavailability due to hepatic metabolism (first pass) and the tendency to produce rapid blood level spikes (both high and low), leading to a need for high and or frequent dosing, which can be both cost prohibitive and inconvenient. Among all the 12 formulations MET3 formulation which contains Carrageenan gum and Guar gum 200mg had shown 96.15% cumulative drug release within 12 hours.

KEYWORDS: Methylphenidate, Transdermal drug delivery, Carrageenan gum and Guar gum.

INTRODUCTION
Methylphenidate is methyl 2-phenyl-2-(piperidin-2-yl)acetate. A central nervous system stimulant used most commonly in the treatment of attention-deficit disorders in children and for narcolepsy. Its mechanisms appear to be similar to those of dextroamphetamine. Binding to plasma proteins is low category central nervous system agents Methylphenidate blocks dopamine uptake in central adrenergic neurons by blocking dopamine transport or carrier proteins. Methylphenidate acts at the brain stem arousal system and the cerebral cortex and causes increased sympathomimetic activity in the central nervous system. Nervousness and insomnia are the most common adverse reactions but are usually controlled by reducing dosage and omitting the drug in the afternoon or evening.

Excipients Profile
Carrageenan gum: General Descriptions Gelatinous extracts of the Chondrus crispus (Irish Moss) seaweed have been used as food additives since approximately the 1400s.

Description: Carrageenans or carrageenins are a family of linear sulphated polysaccharides that are extracted from red edible seaweeds. They are widely used in the food industry, for their gelling, thickening, and stabilizing properties. Their main application is in dairy and meat products, due to their strong binding to food proteins. There are three main varieties of carrageenan, which differ in their degree of sulphation. Kappa-carrageenan has one sulphate group per disaccharide. Iota-carrageenan has two sulphates per disaccharide. Lambda carrageenan has three sulphates per disaccharide.

Stability and Storage Condition: Carrageenan solutions are quite stable at neutral or alkaline pHs. At lower pHs their stability decreases, especially at high temperatures. As the pH is lowered hydrolysis of the carrageenan polymer occurs, resulting in loss of viscosity and gelling capability.

Guar Gum
General Descriptions: Guar gum is a galactomannan, obtained from plant Cyamopsis tetragonolobus.

Description: Powder is whitish and yellowish consisting of slight odor. Guar gum is mainly consisting of the high molecular weight polysaccharides composed of galactomannans which are consisting of a linear chain of (1→4)-linked β-D-mannopyranosyl units with (1→6)-linked α-D-galactopyranosyl residues as side chains. The mannose: galactose ratio is approximately 2:1. The molecular weight range is 50,000-80,000,000.

Stability and Storage Condition: Aqueous guar gum dispersions have a buffering action and are stable at pH 4-10.5. The bacteriological stability of guar gum dispersion may be improved by addition of mixture of 0.15% methyl paraben and 0.02% propyl paraben as preservative.

Propylene Glycol: Synonym: 1,2-Dihydroxypropane; E1520; 2-hydroxypropanol; methyl ethylene glycol; methyl glycol; propene-1,2-diol. Functional Category:
Antimicrobial preservative; disinfectant; humectant; plasticizer; solvent; stabilizer for vitamins; water-miscible co-solvent.

METHODOLOGY
Preformulation study: Preformulation studies were primarily done to investigate the physicochemical properties of drug.

Selection of drug and other ingredients
Methylphenidate was selected as model drug based on its physico-chemical and biological properties and also based on its suitability for Transdermal drug delivery system.

Guar gum, Carrageenan gum were selected as matrix forming polymers.

Propylene glycol and PEG 400 were selected as permeation enhancer and plasticizer.

Preparation of Phosphate Buffer pH 7.4: Accurately measured 250 ml of 0.2 M potassium dihydrogen phosphate in a 1000 ml of volumetric flask and added 195.5 ml of 0.2 M sodium hydroxide and then water was added to make up the volume and adjusted pH 7.4 by using 0.2 M potassium dihydrogen phosphate/sodium hydroxide.

Construction of standard graph of Methylphenidate
Standard graph of Methylphenidate was plotted in PBS pH 7.4. Methylphenidate was estimated spectrophotometrically at $\lambda_{\text{max}}$ of 265 nm.

Preparation of standard solution: Stock solution - I was prepared by dissolving Methylphenidate 100 mg in 100 ml of buffer, so as to get a solution of 1 mg/ml concentration.

Then stock solution - II was prepared by taking 10 ml from the previous stock solution i.e. stock solution - I and dissolved in 100 ml of buffer, so as to get a solution of 100 µg/ml concentration.

Accurately measured aliquot portions of standard drug solution, from stock solution -II were taken, like 2 ml, 4 ml, 6 ml, 8 ml, 10 ml, 12ml, 14ml and 16ml were transferred in to 10 ml volumetric flasks and were diluted up to the mark with buffer pH 7.4. Absorbance of each solution was measured at $\lambda_{\text{max}}$ of 265 nm against buffer pH 7.4 as the blank, by using UV-spectrophotometer. A graph was plotted by taking concentration of drug vs absorbance was plotted.

Formulation
Development of Transdermal patches: Transdermal drug delivery patches were prepared by solvent casting method.

Solvent casting method: Transdermal patches were prepared according to the formula shown in Table 01. Carrageenan gum, Guar gum were weighed in requisite ratios and they were then dissolved in dimethyl formamide and ethanol as solvent using magnetic stirrer. Methylphenidate (100mg) with a magnetic stirrer. Propylene glycol and PEG 400 was added to the above dispersion under continuous stirring. The uniform dispersion was poured in the petri plate. The rate of evaporation of solvent was controlled by inverting cut funnel over the patches. After 24h, the dried patches were taken out and stored in desiccator.
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**Table No: 1 Formulations of Methylphenidate Transdermal Patch.**

**Fig No: 4 Calibration Curve of Methyl Phenidate.**

**Fig No: 5 %ge drug release of F1, F2, F3.**

**Fig No: 6 FTIR of Pure Drug.**

**CONCLUSION**

Oral drug delivery system has various drawbacks like poor bioavailability due to hepatic metabolism” (first “pass) and the tendency to produce rapid blood level spikes (both high and low), leading to a need for high and/or frequent dosing, which can be both cost prohibitive” and” inconvenient.

Among all the 12 formulations MET9 formulation which contain Carrageenan gum and Guar gum 100mg had shown 96.15% cumulative drug release within 8 hours.

**REFERENCES**