RESEARCH ARTICLE

Sustained release tablet of theophylline by hot melt wax coating technology

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Coating is one of the effective method used for sustaining the release of dosage form. There are various hydrophilic and hydrophilic polymers which are use to sustain the drug release. Waxes are one of the material which can be use to coat the drug in order to control the release. Coating with waxes can be achieved by dissolving it in suitable solvent or by hot melt wax coating. Hot melt coating technique defined as the application of fine layer of coating material in molten state over the substrate. Hot melt coating technique is widely used to coat granules, pellets and tablets in order to sustained the drug release, mask the bitter taste of drug, improve stability etc. Hot melt wax coatings have various advantages over wax solution coating. Toxicity of the organic solvent residues and the influence of environmental protection are major problems associated with solvent coating. The main goal of this study was to study the effect of different coating technique i.e. pan spray method and pan pour method on release pattern of theophylline and also to study the effect of different pore former like sodium laurel sulphate (SLS) and hydroxyl propyl methyl cellulose (HPMC) on release pattern. It was found that pan spray technique is the best technique to control the release due to uniform film formation, while pan pour method showed variation in release of drug from same batch this was due to non uniform coating of tablets and very low coating efficiency. If we compare the effect of pore former it was found that release of drug can be controlled by using suitable concentration of pore former while faster release was seen when SLS was used as a pore former in lower concentration than HPMC.

Key words: *Hot melt wax coating, hydrogenated castor oil (HCO), hydroxy propyl methyl cellulose (HPMC), sodium laurel sulphate (SLS), theophylline*

INTRODUCTION

Oral solid dosage forms for sustained drug release has the major attention amongst all the controlled drug delivery systems due to its conventional usage. Polymeric film coatings have been utilized widely for controlled release of an active substance from pharmaceutical dosage forms because the coated dosage forms enable the sustained and precise release of drug with good reproducibility. The performance of these drug delivery systems is evaluated primarily in terms of their release kinetics and overall ease of administration. Methods that release drug with zero order kinetics (a time-independent rate) for an extended time period is usually considered optimal.[1,2]

There are two methods used for preparation of polymeric films, one is solvent evaporation method, method and another is solvent-free hot-melt method.[3,4] The alter choosing of proper solvents for polymer dissolving is an important issue involved in solvent evaporation method. The solvent with large molar volume is preferred due to easy evaporation during film formation process. However, the toxicity of the organic solvent residues and the influence of environmental protection are major problems incurred in this method.[5-7] The solvent-free hot-melt method is an alter choosing native method to overcome these problems. Blended polymers play an important role in developing a sustained drug delivery system. There can be combined two types of polymers in the blended films: one is remained in the end-use, and another is removed as a pore-forming agent to produce porous structure. The controlled-porosity in case of hot melt wax coating can been developed via incorporation of leachable water-soluble small molecules, such as hydroxyl propyl methyl cellulose, sodium chloride, potassium chloride, urea, and sucrose etc[8,9] and surfactant such as laurate, sodium alkylsulfates such as sodium dodecyl sulfate, hexadecyl sulphonic acid, sodium dioctylsulphosuccinate, dodecylpyridinium chloride, hexadecyl(cetyl)trimethylammonium bromide into major component of film coating material. These pore-forming agents are leached when contacted with an aqueous medium, and the pores are created on the surface to allow drug release.[10]

HCO is a white to slightly yellow fine powder obtained

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by hydrogenation of castor oil using a catalyst. HCO has been used in formulation technology as a sustained-release coating material and hardening agent.[11] When tablet components are compressed, HCO forms a thin coating on the surface of the drug particles; thus, HCO may function as a binder. Physical mixing of drug with HCO to obtain the prolonged release was described penetration of the solvent molecule was hindered due to hydrophobic coating of the HCO on the drug particle leading to slow drug release for a prolonged period.[12]

MATERIALS AND METHODS

Hydrogenated Castor Oil flakes was obtained from Sret Rayalastma Alkalies and allied Chemicals Ltd, Kurnolol, Mumbai as a gift sample. HPMC was obtained as gift sample from Colorcon Asia Ltd, Goa. Sodium laurel sulphate was provided by Iatros pharmaceutical Ltd.

Preparations of core tablet

Tablet containing 100 mg of theophylline (batch size, 4000 tablets) were prepared using microcrystalline cellulose, lactose as diluents by wet granulation method [Table 1]. Hardness was kept at 6 kg/cm^2. Compression was carried out on a 8 station rotary machine with 8-mm standard concave punches.

Coating of theophylline core tablet

Tablet (batch size, 250) was film coated in a 15-inch coating pan by atomizing the coating solution 9 spray gun 100 ml S68; pilot at 10-psi pressure for all formulation except formulation F1 where pan pour technique was used. Pan speed kept at 40 rpm [Table 2]. Hydrogenated Castor oil was melted at 80°C and was use along with HPMC and SLS in varying proportion as pore former to coat the theophylline core tablet [Table 3].

Evaluation of physical parameters of theophylline coated tablet

Hardness

For each formulation the hardness values for 6 tablets were determined using Monsanto hardness tester.

Thickness

The thickness of a tablet was the only dimensional variable related to the process. 10 tablets were measured for their thickness and diameter with a Vanier Caliper. Average thickness was calculated.

Percent weight gain

Weight gain by tablet is one of the important parameters monitored during formulation, process and scale up development. Weight gain was calculated from the difference in the tablet weight before and after coating.

Drug release study

Release of Theophylline from the coated tablets was studied in 0.1 N HCL (900 ml) as prescribed in the dissolution rate test of theophylline tablets in USP XXIV employing apparatus 2. A six station dissolution rate test apparatus was used. One tablet containing 100 mg of theophylline, a speed 100 rpm and a temperature of 37 ± 0.5°c were employed in each test; samples were withdrawn through a filter at different time intervals, suitably diluted and assayed for theophylline at 270 nm. Drug release studies were conducted in triplicate. The results are shown in Figure 1-3.

RESULTS AND DISCUSSION

All the hot melt wax coated tablet formulation, showed thickness values in the range of 3.51 ± 0.002 to 3.52 ± 0.001 mm while the hardness values range in between 6-7 kg/cm^2.

Percent weight gain by tablet was also determined and it is represented in Table 4.

[Figure 1] shows the effect of coating method on release of theophylline from coated tablet. It is observed that the

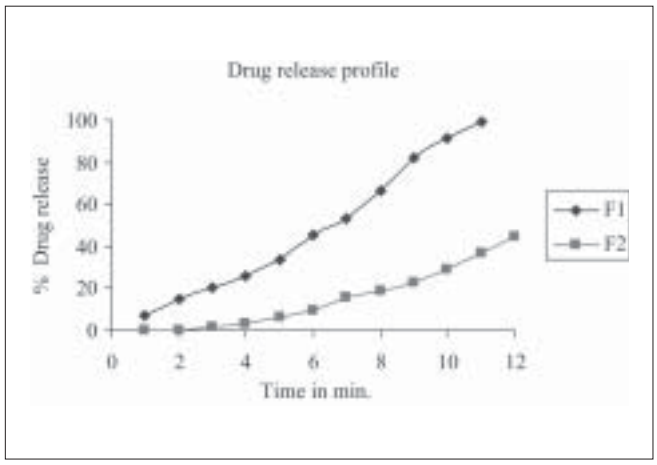

Figure 1: Release profile of theophylline coated tablet prepared by two different techniques i.e. Pan pour method for formulation F1 and pan spray method for formulation F2

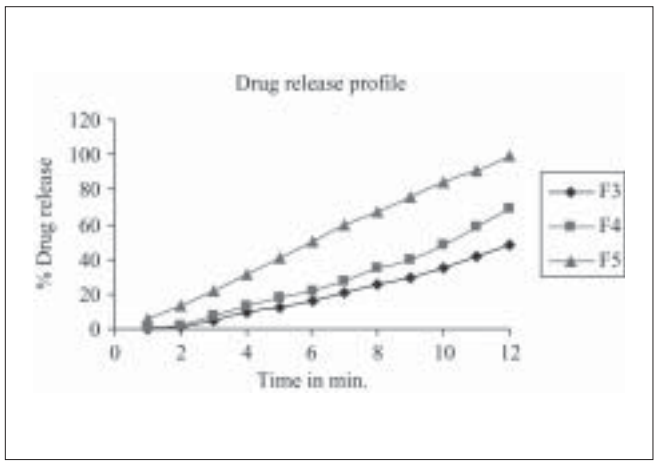

Figure 2: Release profile of theophylline coated tablet prepared by using SLS as pore former by pan spray method

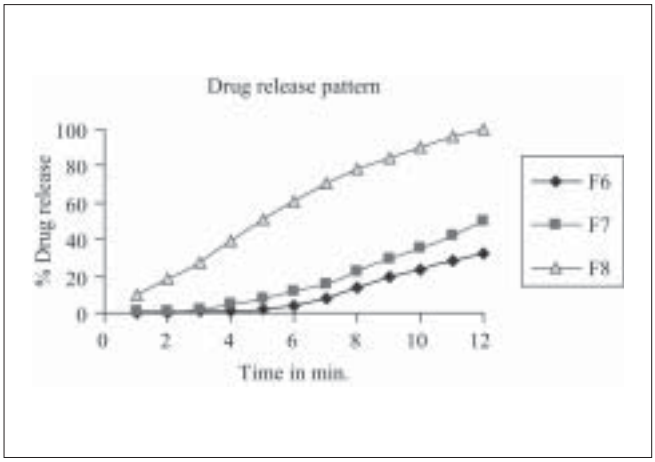

Figure 3: Release profile of theophylline coated tablet prepared by using HPMC as pore former by pan spray method

Table 1: Formulation of theophylline core tablet

Ingredients	Quantity (mg/tab)
Theophylline	100
Lactose	62.5
Preservative	5
starch	12.5
Microcrystalline Cellulose	12.5
Talc	5
Magnesium Stearate	2.5

Table 2: Coating parameters for coating process

Batch size	50 g (~250 tablets)
Spray rate	2 ml/min
Atomizing air pressure	15 psi
Tablet bed temperature	30-70°C
Pan speed	40-60 rpm

Table 3: Formulations for hot melt wax coating

Ingridient	Quantity							
	F1	F2	F3	F4	F5	F6	F7	F8
Hydrogenated castor oil	10	10	9.75	9.5	9	9	6.6	5
HPMC	-	-	-	-	-	1	3.3	5
SLS	-	-	0.25	0.5	1.0	-	-	-

Table 4: Physical parameters of coated tablet

Test	Quantity							
	F1	F2	F3	F4	F5	F6	F7	F8
Hardness (kg/cm^2)	6-7	6-7	6-7	6-7	6-7	6-7	6-7	6-7
Thickness (mm)	0.37	0.43	0.40	0.45	0.42	0.39	0.39	0.43
% weight rise	3.48	6.53	6.12	6.81	6.34	6.04	6.0	6.45

release of drug through tablet prepared by pan spray coating method for F1 formulation was slow as compare to pan pour coating method for F2 formulation this effect was mainly due to the effective smooth coating of the core tablets by pan spray coating technique where the release of the drug was through fine pores. While in case of pan pour coating method the release of the drug was faster this was due to non uniform coating on the tablet, from where the release of drug occurs. Another reason for slow release was the low coating efficiency of pan pour method as compare to the pan spray method where uniform spry patter is obtained by using spray gun.

In case of formulation F3, F4, F5 the drug release is as show in [Figure 2]. It shows the effect of pore former SLS on release pattern of theophylline from coated tablet. The dissolution data revealed that the drug release for formulation containing SLS as pore former in high concentration was faster than formulation containing SLS in low concentration. For formulation F3, F4 and F5 the percent release of drug at 12hr was 49%, 68% and 100% respectively. This was due to the carrier effect of SLS which decrease the interfacial tension between the drug and dissolution medium which leads to easy release of the drug from the pores.

While in case of formulation F6, F7, F8 the drug release is as show in [Figure 3]. The initial decrease in the drug release after coating for formulation F6 could be due to prevention of penetration of water into the coated tablet. To aid the initial drug release, hydrophilic excipients such as HPMC were incorporated in the coating composition. The results of the dissolution studies indicated that incorporation of water-soluble excipients aided in the initial drug release. Moreover it was observed that one could control the initial drug release by altering the amount of HPMC in the coating composition [Figure 3]. For formulation F6, F7 and F8 the percent release of drug at 12 hr was 33%, 50% 100% respectively. This was due to the hydrophilic nature of the polymer which when comes in contact with the dissolution medium hydrates the polymeric film and there occurs the formation of the pore through which the drug diffusion occurs.

From the dissolution data, one can conclude that the combination of hydrophilic and hydrophobic polymer matrices is not suitable in the development of a controlled-release dosage form for water-soluble drugs. Incorporation of hydrophilic excipients such as HPMC in the coating formulation was found to facilitate the drug release from the hydrophobic coating materials.

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