Evaluation of Taste Masking Efficiency of Kollicoat® Smartseal 100P Using Hot Melt Extrusion Techniques

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PURPOSE

Formulations containing bitter active pharmaceutical ingredients (APIs) are poorly accepted by patients and because of this adherence to treatment is affected. HME is a proven technique being applied to mask the unpleasant taste of APIs using polymers. Theophylline, model drug used here, is a bronchodilator with bitter taste and effective in the treatment of acute and chronic asthma..

OBJECTIVE

The objective of this study is to evaluate the taste masking ability of Kollicoat® Smartseal 100P with theophylline as model drug.

METHODS

Fomrulation:

- Theophylline (TPL) was blended with kollicoat® Smartseal 100P and Poly Ethylene Glycol (PEG) 1500 in Maxiblend™ (GlobePharma, New Brunswick, NJ, USA) at 25 rpm for 15 minutes. The blends were extruded using a 11mm corotating twin screw extruder (Thermo Fisher Scientific, Waltham, MA, USA). Modified screw configuration was used to improve the processability. The obtained extrudates were pelletized into 3mm pellets.

Characterization:

- Differential Scanning Calorimetry (DSC) and X-Ray Diffraction (XRD) studies were done to investigate the nature and miscibility of drug with the excipients.
- FTIR spectroscopy was performed to check the interactions between the excipients and drug
- In vitro evaluation was carried out by release study in simulated salivary fluid(SSF) of pH 6.8 and also in 0.1N HCl using type I apparatus (SR8-plus, Hanson) at 50rpm.
- Different formulations with three drug loads and two PEG concentrations were formulated and studied to check the impact of PEG 1500 on processability and taste masking. The extrusion parameters are shown in Table 1.
- Bitter threshold comparison: Solubility of pure theophylline was compared with the amount of theophylline from the formulations, dissolved in 1 min.

RESULTS

- The DSC thermographs (Fig.1) of the extrudates showed a small dip at around 50-55°C which corresponds to the glass transition temperature of PEG 1500.
- The melting peak of Theophylline at 276°C disappeared in the thermograms of the extrudates, inferring that the drug converted into amorphous form.
- Though, in one formulation containing 30% Theophylline and 40% polymer, it can be observed that there is a small peak at 275°C, as the drug retained some of its crystallinity, the enthalpy of the crystalline drug is significantly reduced from 157 J/Kg to 12.5 J/Kg, which means that the crystalline nature is greatly decreased and the drug is mostly converted to amorphous form. This partial conversion might be due to high drug load in the formulation.
- The solubility results of extrudates showed that the amount of drug released by formulation is lower than the bitterness threshold level, while for free drug it is much higher.
- The FTIR results showed that there is no interaction between drug and polymer, As similar characteristic peaks of pure drug appeared in formulation.
- The unpleasant taste of theophylline was effectively masked as the formulations containing Kollicoat® Smartseal 100P released not more than 3% drug in 2 minutes in formulations with 20% PEG 1500.
- The release studies in 0.1N HCl (Fig 3) show that formulations containing 30% PEG 1500 showed faster drug release as compared to formulations containing 20% PEG 1500, probably due to more PEG 1500, which further increased the solubility.
- While free drug showed 81% release in 2 hours, formulations with 30% PEG 1500 demonstrated 100% drug release in 45 minutes. Drug release from formulations with 20% PEG 1500 were 100%, 94% and 87% in 2 hours, at theophylline concentrations of 10%, 20% and 30%, respectively.

S.no	Theophylline (%)	PEG 1500 %	Kollicoat® Smartseal 100P (%)	Temperature (°C)	RPM
F1	10	30	60	130	100
F2	20	30	50	120	100
F3	30	30	40	110	100
F4	10	20	70	140	100
F5	20	20	60	130	100
F6	30	20	50	130	100

Table 1. Formulation and process parameters

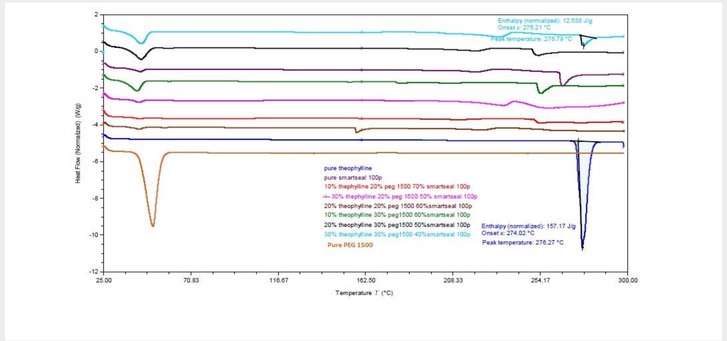

Fig 1. DSC thermograms of the formulations

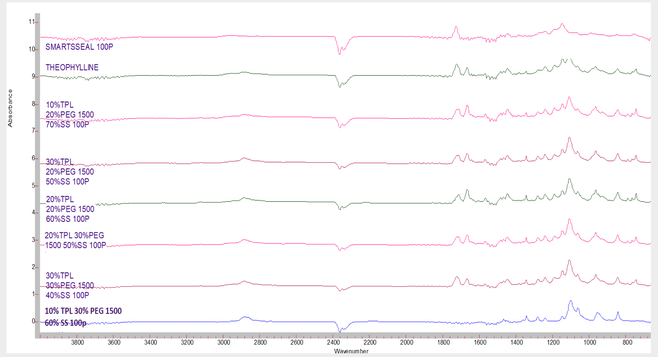

Fig 4. FTIR spectra of the formulations

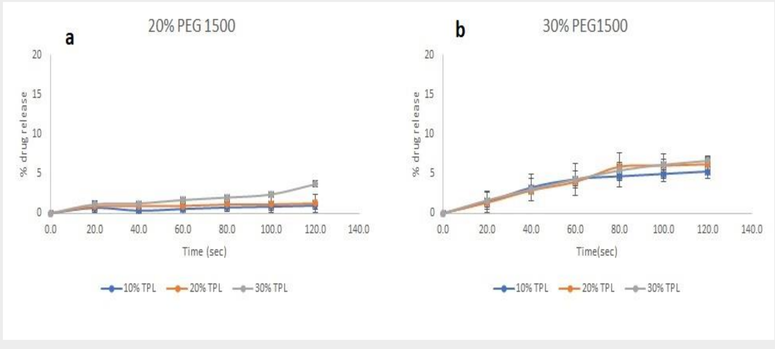

Fig 2. Release study of formulations in SSF. a. Formulations containing 20% PEG 1500 b. Formulations containing 30% PEG 1500

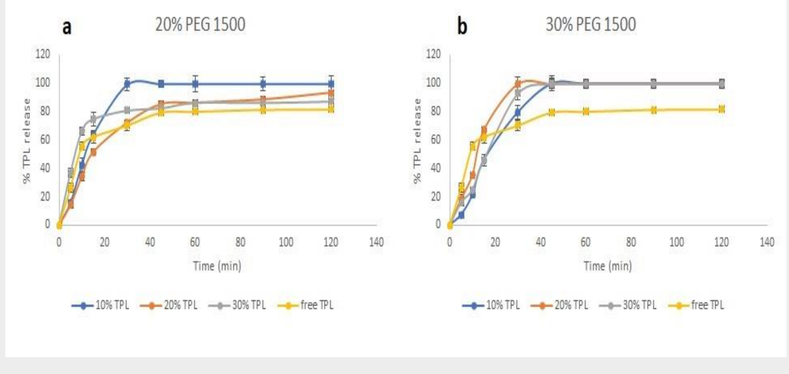

Fig 3. Release study of formulations in 0.1N HCl. a. Formulations containing 20% PEG 1500 b. Formulations containing 30% PEG 1500

CONCLUSIONS

- The study demonstrated that Kollicoat® Smartseal 100P was found to hinder the release in salivary pH media.
- Theophylline significantly in salivary pH. PEG 1500 was used as a plasticizer to aid the extrusion process and improve the feasibility.
- Formulations containing lesser PEG 1500 showed better retardation of drug release as compared to those with higher amounts of PEG1500 in pH 6.8 as well as in 0.1N HCl.
- Thus, Kollicoat® Smartseal 100P was demonstrated to be a taste masking agent.

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