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INTRODUCTION

Undesirable taste is one of the important issues observed with pharmaceutical formulations specifically with bitter tasting drugs. Effective taste masking can be achieved by various reported approaches such as fluidized-bed coating, supercritical fluids, complexing agents, or pro-drug approaches. However, lipid-based formulations have gained interest in recent times and are applied for numerous purposes such as controlled release, improvement of swallowability, moisture protection, and taste masking applications.

PURPOSE

The objective of the current study was to investigate the potential of different lipids to mask the unpleasant/ bitter taste of caffeine citrate by hot melt extrusion techniques.

METHODS

Two lipids, glyceryl dibehenate (Compritol® 888 ATO) and glyceryl palmitostearate (Precirol® ATO were investigated with caffeine citrate as a model drug. Caffeine citrate was blended individually with Compritol® and Precirol® at high drug loads. The physical mixtures of drug and lipids were extruded using an 11mm co-rotating twin-screw extruder (Process 11 twin screw extruder, Thermo Fisher Scientific) utilizing Thermo Fischer standard screw configuration.

The extrusion was performed over the melting range of 70-75 °C for Compritol® formulations, and 50-60 °C for Precirol® formulations at a constant screw speed of 50 rpm.

Solid-state characterization of the extrudates was performed by Differential Scanning Calorimetry (DSC). Further, the flow properties of prepared formulations was studied. Dissolution studies were performed on the milled extrudates in 500mL of simulated salivary media (pH 6.8) to assess the extent of drug release in the salivary pH and gastric drug release was assessed in 0.1N HCl using USP apparatus I (50 rpm).

RESULTS

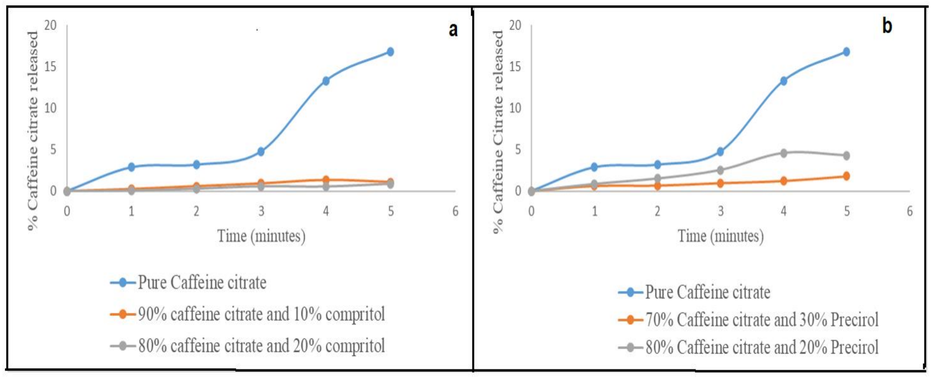

Figure 1. Salivary dissolution profiles of caffeine citrate with (a) compritol (b) precirol

- The extrusion process was carried out at higher drug loads of 90%,80% and 70% (w/w) with lipids in 10%, 20% and 30% (w/w) concentrations, respectively.
- The die plate was removed and the extrudates were collected as granules with torque in the 2-5% range.
- Thermal behaviour of the physical blend and the extruded formulations examined by differential scanning calorimetry (DSC) showed the presence of two characteristic endothermal peaks for Compritol® formulations,
- The peak at 168°C shows the presence of crystalline caffeine citrate and the other at 72.9°C Compritol® melting point as shown in Figure 3.
- Similarly, for Precirol® formulations, there were two characteristics peaks observed one at 168°C and the other at 52°C (Precirol® melting point).These observations reveal that caffeine citrate is in crystalline form.
- Dissolution testing in simulated salivary media (pH 6.8) was used as a primary screening method for assessing the taste masking ability of the formulations. All the formulations showed low drug release (1%-2%) in simulated salivary media (Figure 1).
- Dissolution studies in 0.1N HCl for 20% (w/w) and 30 %(w/w) compritol® formulations showed a drug release of 67.83% and 54% respectively at the end of two hours (Figure 2a).While for formulations with 20% (w/w) and 30% (w/w) precirol® as lipid, the drug release was observed as 61.87% and 66.13% respectively (Figure 2b).
- The flow properties of pure caffeine citrate, lipids and the formulations were predicted using Carr's compressibility index and Hausner's ratio. **The formulations with precirol®** demonstrated good flowability as shown in Table 1.

Table 1. Compressibility Index and Hausner's Ratio of pure caffeine citrate and the extrudates

Formulations	Compressibility Index	Hausner's Ratio
Pure caffeine citrate	20.8 (fair)	1.25 (fair)
Compritol	25.04 (passable)	1.33 (passable)
Precirol	9.90 (excellent)	1.11 (excellent)
70% API and 30% Compritol	28.6 (poor)	1.17 (poor)
70% API and 30% Precirol	12.46 (good)	1.14 (good)

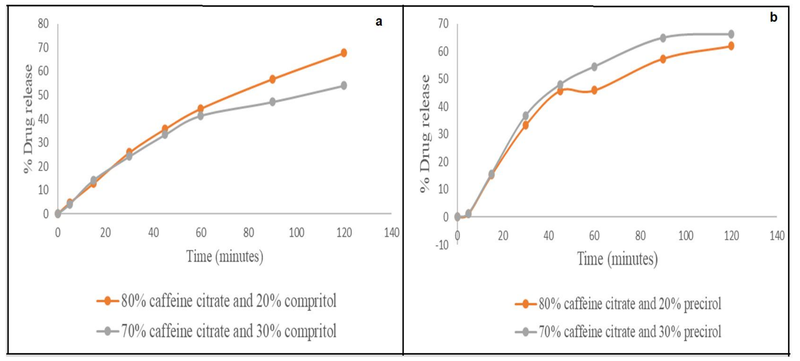

Figure 2. Gastric dissolution profiles of caffeine citrate with (a) compritol (b) precirol

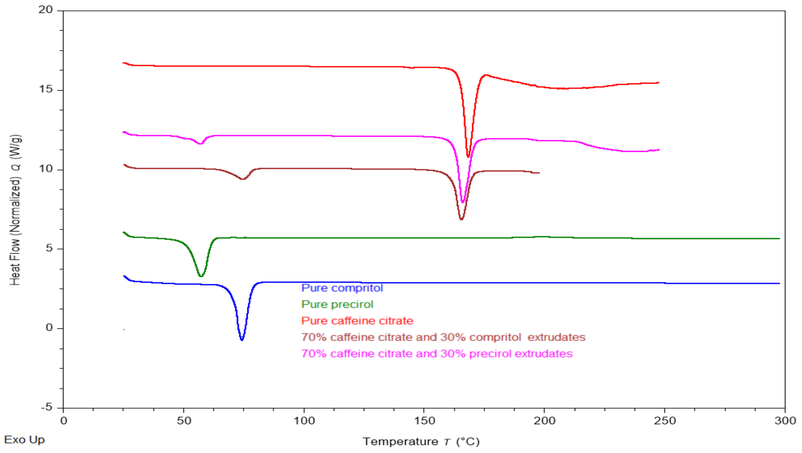

Figure 3. DSC thermograms of pure caffeine citrate, pure compritol, pure precirol and corresponding extrudates

CONCLUSIONS

- Caffeine citrate was extruded with various concentrations of lipids using HME technology.
- The results from salivary dissolution demonstrated the taste masking ability of lipids.
- DSC studies indicated the crystalline nature of caffeine citrate in the formulations.
- Hot melt extrusion can be considered as an efficient method and promising technique for the development of taste masking formulations by the incorporation of lipids.

ACKNOWLEDGEMENTS

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