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MALTODEXTRIN FAST-DISSOLVING FILM: A FEASIBILITY STUDY

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INTRODUCTION

Fast-dissolving drug delivery is rapidly gaining interest in the pharmaceutical industry. These systems either dissolve or disintegrate generally within a minute, without needing water or chewing. An important benefit is the accurate dosing as compared to liquid dosage forms, mostly used with paediatric patients or in case of dysphagia. Moreover, these systems may offer superior clinical profiles with potential oromucosal absorption, thus increasing the drug bioavailability with respect to oral administration. Fast-dissolving drug delivery systems are mainly tablets, and their rapid disintegrating properties are obtained through special process (freeze-drying or tablet moulding, over all) or formulation modifications (superdisintegrants and sugar-based ingredients). Recently thin films has been proposed as an alternative fast dissolving dosage form.

Films can be produced by solvent cast methods or hot-melt extrusion technology. It is well known that the solvent cast method suffers from several disadvantages over the hot-melt extrusion method due to the solvent residues within the film and the environmental risks in the case of organic solvent. In addition, extrusion facilities are economic as compared to solvent cast ones. The fast dissolving films reported in literature are generally made of an hydrocolloid (e.g. pullulan or cellulose derivatives) and a plasticizer.

AIM OF THE WORK

The aim of this work was to evaluate the feasibility of a fast dissolving film made of a maltodextrin plasticized by glycerin by solvent free hot-melt extrusion technology. Loading capacity and the in vivo performances of the film were assayed by using paracetamol as model drug because its bioavailability can be determined in saliva.

MATERIALS and METHODS

Materials Glucidex IT12[®] (D.E.-12) (Gdx IT12) (Roquette, F); Glycerin (Gly) (AFOM Medical, I); Paracetamol (Flaror, CH); Avicel PH 101[®](Avi 101) (FMC BioPolymer, USA); Menthol (Menth) (Fluka, I).

Film preparation

	Gdx IT12	Gly	Avi 101	Paracetamol	Menth
F1	58.12	19.54	21.47	-	0.81
F2	45.40	18.65	18.92	16.22	0.78

The placebo and drug loaded films were realized into a mono screw extruder, with an heating system spited into 4 zones (Tecnova srl, I). The film is then pressed into a cylindrical calender in order to obtain the thickness of 300 μm , cut with a simple system of swords in strips of 25 cm and stored at 25 \pm 1 $^{\circ}\text{C}$ until use.

Tensile properties were evaluated according to ASTM International Test Method for Thin Plastic Sheeting (D 882-02). An electronic dynamometer AG/MC1 (Acquati, I) was used.

Thickness was evaluated by using an electronic micrometer MI-1000 (Cheminstruments, USA). Three strips for each batch were analyzed in defined position by measuring at the extremities and in the center.



Disintegration test was performed according to Ph.Eur 5 Ed.

Dissolution test was carried out according to paddle apparatus Ph.Eur 5 Ed. (900 ml; phosphate buffer pH 5.8; 37 $^{\circ}\text{C}$; 50 rpm). Paracetamol concentrations were assayed spectrophotometrically at 241 nm (DU-640, Beckman Coulter, USA).

In vivo testing Fourteen healthy volunteers (10 females and 4 males) aged from 23 to 30 years, participated in this study, after giving informed consent. Each volunteer received a single oral administration of a film containing 50 mg of paracetamol. Two weeks later they received the same dose of drug in syrup (Tachipirina sciroppo, ACRAF, I). After 5 minutes they rinsed their mouth with a wash of 10% (v/v) ethanol solution. Saliva samples were collected at 10, 20, 30, 45, 60, 120, 240, 360 minutes after intake. 200 μl of saliva and 200 μl of mobil phase were mixed by vortexing (15 s); after centrifugation (3000 rpm, 5 min) the supernatant was collected and analyzed. Paracetamol was quantified in saliva by HPLC assay (HP Chemstation 1100, Agilent Technologies, USA). Column: C18 reverse-phase cartridge (Licrospher 100 RP-18E, 5 μm , 4x125 mm - Agilent, USA). Injected volume: 10 μl ; flow 1.0 ml/min; wavelength: 240 nm; temperature: 25 $^{\circ}\text{C}$. Mobile phase: 80% 0.025 M sodium acetate, 0.01 M triethanolamine (pH 5.05); 20% acetonitrile; v/v. Assay: A standard calibration curve (0.1-20 $\mu\text{g/ml}$) for paracetamol was used.

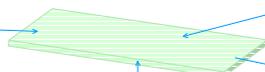
Kamali F., Bell G.D., Salivary secretion of paracetamol in man, Journal of Pharmacy and Pharmacology, 39: 150-152 (1987).

RESULTS

Tensile properties

Placebo film:
Maximum load: 10.0 N
Elongation at break: 5.0 mm

Paracetamol film:
Maximum load: 12.2 N
Elongation at break: 5.9 mm



Thickness

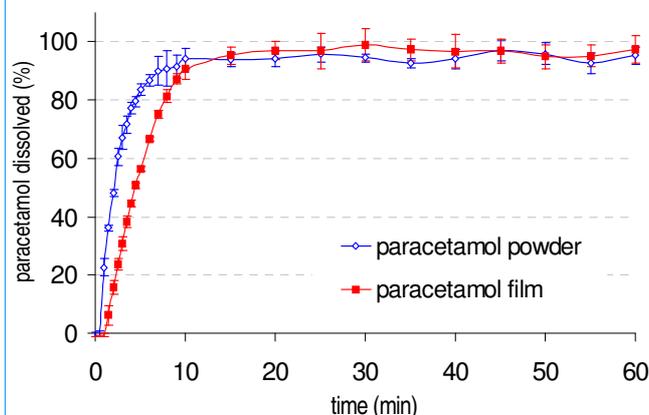
Placebo film: 301 \pm 2 μm
Paracetamol film: 317 \pm 3 μm

Paracetamol content: 7 mg/cm²

Disintegration time < 1'30"

Dissolution test

After 5 minutes more than 50% loaded drug was dissolved and the dissolution can be considered complete within 10 min.



In vivo testing

The volunteers reported that the paracetamol film disintegrated within a minute.

The main pharmacokinetic parameters calculated from the saliva concentration after syrup and film intake resulted:

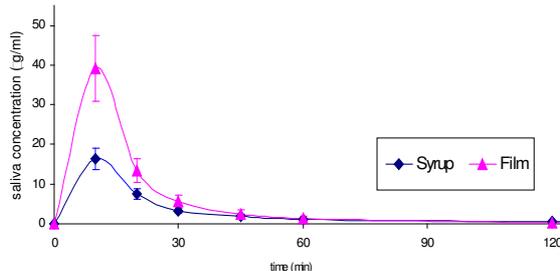
$C_{\text{max, syrup}}$: 14.7 \pm 2.5 $\mu\text{g/ml}$

$C_{\text{max, film}}$: 42.2 \pm 5.6 $\mu\text{g/ml}$

AUC_{syrup} : 377.8 \pm 83.8 $\mu\text{g} \times \text{min/ml}$

AUC_{film} : 664.6 \pm 125.2 $\mu\text{g} \times \text{min/ml}$

AUC and C_{max} obtained after film administration were higher than those determined after the syrup intake. These results can be attributed to a partial oromucosal absorption of paracetamol following the film administration.



Conclusion

Maltodextrin can be used to produce fast-dissolving films with a high drug loading capacity by hot-melt extrusion technology

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