



HAL
open science

Effect of baobab pulp powder on controlled release properties of matrix tablet formulated with whey protein and alginate

Arthur Chervet, Améline Delanne, Ghislain Garrait, Khaled Fadhlou, Sandrine Chalancon, Sylvain Denis, Eric Beyssac, Emmanuelle Laine

► To cite this version:

Arthur Chervet, Améline Delanne, Ghislain Garrait, Khaled Fadhlou, Sandrine Chalancon, et al.. Effect of baobab pulp powder on controlled release properties of matrix tablet formulated with whey protein and alginate. 4th European Conference on Pharmaceutics: Advanced technologies enabling new therapies, Mar 2023, Marseille, France. . hal-04104108

HAL Id: hal-04104108

<https://hal.science/hal-04104108v1>

Submitted on 23 May 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution 4.0 International License

Effect of baobab pulp powder on controlled release properties of matrix tablet formulated with whey protein and alginate.

Arthur Chervet¹; Améline Delanne¹; Ghislain Garrat¹; Khaled Fadhlou¹; Sandrine Chalancon¹; Sylvain Denis¹; Eric Beyssac¹ and Emmanuelle Lainé¹

¹ UMR 454 MEDIS, 28 pl. Henri Dunant, 63000 Clermont-Ferrand, France, emmanuelle.laine@uca.fr

INTRODUCTION

Tablet is the most convenient dosage form for oral administration to control the release of drug. Baobab pulp (BB) has been used as excipient in tablet formulation as lubricant and binding agent but also as hydrophilic excipient for modified release tablets [1]. An association of whey protein (WP), alginate (ALG) and BB has never been tested in tablet formulation and could be promising for peptides and live biotherapeutic products. We evaluated influence of the independent variables (mass and hardness) and dependent variables (polymers proportion) on friability, swelling and dissolution profile of a model drug, theophylline (TPH).

MATERIALS AND METHODS

Design of experiments

Three powder blends (Free-TPH, F2 and F10, Table I) based on a mixture composed of 36.5% (w/w) of powder of the three natural polymers and a diluent (qsp 36.5% lactose): denatured WP, BB and ALG powder. Direct compression was executed via an alternative tableting press machine. Each tablet unit weighed 530 mg.

Formulas	Percentage (%)							
	TPH	BB	WP	ALG	Diluent	Flow agent*	Lubricant	Total
Free-TPH	62	0	0	0	36.5	0.5	1.0	100
F2	62	8	18	2	8.5	0.5	1.0	100
F10	62	25	8	2	1.5	0.5	1.0	100

(*) the amount of added bulking agent was selected so that the total weight of the polymer(s) and flow agent is 36.5% by weight of the total tablet weight.

Table 1. Composition of the tablet

Powders Flow Properties

Bulk and tapped density were determined as described in the European Pharmacopea (P.E. 10.0). Compressibility index were calculated according to P.E. 10.0 in order to provide a measure of the flowability and compressibility behavior of samples.

Tablets characterization

Pharmacotechnical characterization.

Tablets were characterized by weight, hardness, friability, dimension according to PE 10.0 technical procedures.

In vitro dissolution.

To evaluate the controlled release of TPH, dissolutions of the tablet were realized in USP2 apparatus in buffer pH 1.2 for

30 min follow with buffer pH 4.5 for 1h30 and pH 6.8 until 6h at 37°C. TPH release was estimated by UV dosage. All experiments were performed in triplicate. To analyze the release mechanism, several release models were tested such as Korsmeyer-Peppas and Harland. The swelling behavior of tablets was evaluated after 120 min of dissolution in buffer pH 6.8 at 37°C in USP2 apparatus. After 120 min, all tablets were withdrawn, accurately weighed and measured.

Artificial Digestion of Drug Loaded-tablets.

The artificial digestive system (Figure 1, TIM1; TNO, Zeist, the Netherlands) consists of four serial compartments simulating the stomach and the three segments of the small intestine: duodenum, jejunum, and ileum.

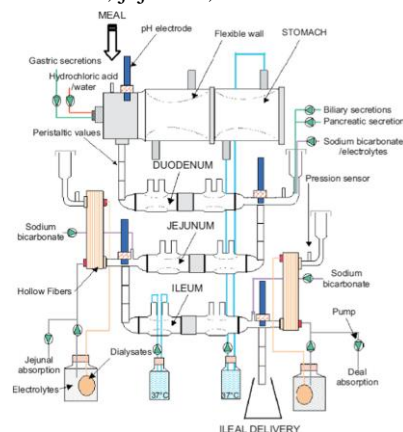


Figure 1: Schematic representation of TIM

Each compartment is composed of glass jacket with flexible wall between which heated water flows to control both the temperature inside compartment (37°C) and the pressure on flexible walls inducing the mixing of the chyme by alternate compression and relaxation (Figure 1). Two tablets or free-TPH corresponding to two tablets (660 mg) were introduced into the gastric compartment simultaneously with 200 g of water to simulate the fasted state in an adult. All experiments of digestion were performed in triplicate.

RESULTS AND DISCUSSION

All the formulations permitted the compression process and tablets were successfully produced by direct compression with a target hardness of 90 N (Table 2).

Formulas	Powder flow	Tablet compression (Hardness)	Tablet friability	Water uptake	Diameter change	TPH release
				(%, 2 h pH 6.8)	(%, 2 h pH 6.8)	
Free-TPH	E	C	NC	ND	ND	91 ± 11
F2	E	C	NC	97 ± 12	42 ± 15	28 ± 1
F10	G	C	C	66 ± 1	28 ± 1	34 ± 6

For flow measurements and tablet friability, the meaning of the abbreviations E, B, EM, C, NC, and ND is as follows: E: Excellent, G: Good, EP: extremely poor, C: Compliant, NC: Non-compliant, ND: Not determined. For tablet compression and friability: C: compliant, NC: non-compliant

Table 2. Powder flow, tablet friability, swelling and theophylline release after 2h of dissolution in pH 6.8.

A deviation of less than 5% was obtained for all formulations so this deviation is in accordance with the PE. For the 3 formulations, only one have a friability lesser than 1%. This formulation corresponds to a lot of BB. TPH release in dissolution apparatus from free-TPH, F2 and F10 tablet was investigated (Figure 2A).

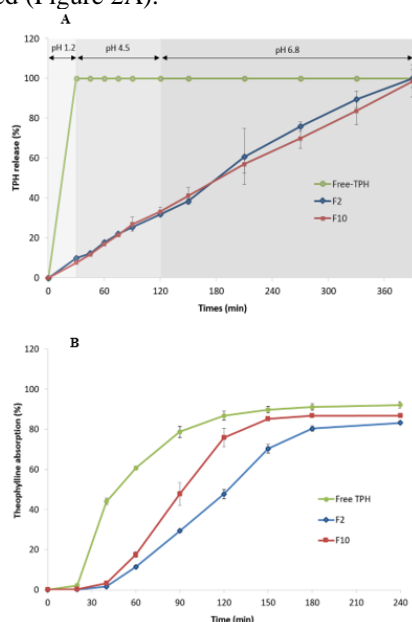


Figure 2: Release kinetics of free-TPH and TPH from Tablet (A) in USP2 (B) and cumulative TPH absorption during digestion in TIM1 (n=3, mean ±SD).

TPH powder dissolution was fast and complete for free-TPH, which is characteristic of a BCS class I drug. On the contrary, TPH release from F2 and F10 tablet was similar with a controlled release in pH 1.2, 4.5 and 6.8 of drug during 390 min. Incorporation of polymers slowed down drug release and modified the behavior of the formulation to achieve a controlled and sustained release. The polymers thus constitute a pH-dependent matrix excipient allowing a prolonged release of TPH. There are different types of active substance release from tablet. The first one, diffusion, appeared during the contact of tablet with the gastrointestinal juices. The liquid will diffuse inside the tablet and leads to a diffusion of the active substance towards the outside through the matrix. The second type is erosion, the contact between the juices, the enzymes and the peristalsis

will allow the erosion of the tablet and thus the release of the active substance. A mathematical model was used to define the type of release. For F2 and F10, the value of n in the Korsmeyer-Peppas equation is greater than 0.89 indicating a release mechanism predominantly dominated by erosion. The use of the Harland equation confirms these results since the study of the parameters of the equation (A for diffusion and B for erosion) indicates for the formulations a release mechanism of erosion type. The release is due to the water intake and diameter change of the tablets (Table 2) proves the hydration capacity of WP > BB polymers which may be due to the formation of hydrogen bridges between the polymer chains and the water molecules.

Taking into consideration the protein and fiber character of our novel excipient BB, drug release was also evaluated with gastric and intestinal enzymes. Percent represented the amount of TPH released and dialyzed through hollow fibers considered thus as available for *in vivo* absorption (Figure 2B). We can conclude that absorption of free-TPH was fast with T50% absorbed in approx. 45 min and a T80% of 90 min which is characteristic of a BCS class I drug [2]. On the contrary, for F2 and F10 tablets, TPH absorption percentages were significantly slowed down with a prolonged T50% at 120 min and 90 min and a T80% reached in 180 and 135 min of digestion for F2 and F10 respectively. TPH release from F2 and F10 was similar in dissolution apparatus without enzymes but different with enzymes. These results indicated that WP was more resistant to enzymes digestion than BB. Moreover, the profile of release was similar between formulation F2 (18% WP, 8% BB and 2% ALG) and a tablet formulated with 30% WP [2]. A part of WP could be substitute by BB and ALG for the controlled release of TPH.

CONCLUSION

Add BB to the formulation improve WP/ALG tablet process. Polymers influence TPH release in dissolution apparatus in gastric or intestinal pH with a slow and complete release of TPH during 6.5 hours and controlled via swelling and erosion mechanism. Controlled release was confirmed in the artificial digestive. However, proteolytic enzymes accelerated the drug release. BB was more sensitive to enzymes than WP polymer. BB powders can be considered as a new excipient for sustained release applications particularly when absorption is targeted to take place in the jejunum or ileum.

REFERENCES

1. Arama, E.; Michaud, P.; Rouffiac, R.; and Rodriguez, F. A new excipient in pharmaceutical formulation of theophylline tablets of the hydrophilic matrix type: the pulp of the baobab fruit. *Farmaco Prat.* 43, 303-15 (1988).
2. Hsein, H.; Garrait, G.; Tamani, F.; Beysac, E.; and Hoffart, V. Denatured Whey Protein Powder as a New Matrix Excipient: Design and Evaluation of Mucoadhesive Tablets for Sustained Drug Release Applications. *Pharm. Res.* 342, 365–377 (2016).