

# THE FORMULATION AND PHARMACOTECHNICAL CHARACTERISATION OF FAST DISPERSING TABLETS WITH ACETAMINOPHEN

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**ABSTRACT.** The present study has been carried out for the formulation and characterisation of orodispersible acetaminophen tablets. This type of tablet offers certain advantages over conventional tablets, being suitable for administration to patients with difficulties in swallowing, such as elderly and pediatric patients, their main characteristic – a fast disintegration in the saliva – conveying an improved compliance and improved bioavailability. Acetaminophen was selected as active pharmaceutical ingredient because it is an analgesic antipyretic drug used in the treatment of moderate pains, fever and other symptoms that request a rapid onset of the therapeutic effect. The formulations were prepared by direct compression or after wet granulation and various/different superdisintegrants were employed/ used (in the different formulations, the aim being) to obtain tablets with suitable tensile strength/ hardness and a fast disintegration. The pharmacotechnical characterization of the formulations has revealed that the optimal formulas resulted by associating sodium starch glycolate with sodium carboxymethylcellulose, (an optimal balance between the disintegration time and the tablet hardness).

**Keywords:** acetaminophen, direct compression, superdisintegrants, orodispersible tablets, disintegration time

## INTRODUCTION

Oro-dispersible tablets are uncoated tablets designed to rapidly disperse in oral cavity, in less than 3 minutes after administration, before being swallowed [\*\*\* Romanian Pharmacopoeia X-th edition, 2004 Supplement; 2. European Pharmacopoeia, 6th edition]. The origin of this type of tablet is represented by sublingual tablets. Generally, these tablets are obtained by moistening a mix of lactose and the active substance with a mix of ethanol and water resulting a paste that is then moulded into tablets, which are later dried and packed. The most popular example of such tablets is the nitro-glycerine sublingual tablets. Also, this dosage form provides an adequate formulation for drugs which are inactivated in the gastrointestinal tract and for drugs for which the sublingual absorption minimizes the first-pass effect (Ansel et al., 1999). More recent approaches of the design of such tablets are represented by Fast Dissolving/ Dispersing Oral Tablets. This type of tablets is characterized by their capacity to rapidly dissolve or disperse in saliva (in 15-30 seconds) once placed on the tongue, before being swallowed. These

The following substances of pharmaceutical grade were used in the formulation of the acetaminophen tablets: acetaminophen DC (Nantong Desheng Chemical Co Ltd., China), DC lactose (Tabletose 80, Meglle Pharma, Germany), microcrystalline cellulose (Vivapur 102, S&D Chemicals Ltd.), polyvinylpyrrolidone K 30 (BASF AG, Germany), sodium starch glycolate (Explotab – Ed. Mendell Co.), sodium carboxymethylcellulose (Crosscarmellose sodium – Carefarma, India), magnesium stearate (Union Derivan SA / Arnaud Romania), colloidal silica

tablets are suitable for patients with swallowing difficulties, such as elderly patients and children, HIV patients or patients following radiotherapy (Dobetti, 2000; Popa et al., 2003; Hirjau et al., 2009). The manufacturing technology involves tablet moulding, freeze-drying, sublimation, spray-drying, addition of superdisintegrants and direct compression and the use of sugar-based excipients (Sreenivas et al., 2005). Acetaminophen is a p-aminophenol derivative with moderate analgesic and antipyretic effect. Its indications are minor to moderate pain (nerve or muscle pain, headaches, dysmenorrhea), fever of various aetiology (microbial or viral infections). It is considered an antipyretic of first election for young children, in viral infections and in rheumatic pains (Cristea, 2005). The aim of this study was to obtain acetaminophen oro-dispersible tablets as an alternative to conventional oral dosage forms containing this drug (tablets and capsules), for paediatric use.

## MATERIALS AND METHODS

dioxide (Aerosil 200, Degussa/Astron Chemicals), banana flavour, aspartame.

The tablets were obtained by direct compression technique on a Triowin tableting press (Shanghai Triowin Tech. Co., Ltd., China) and a pharmacotechnical characterization, consisting of the determination of uniformity of mass, hardness, friability, disintegration, was carried out on all four experimental formulations.

### The formulation of the acetaminophen orodispersible tablets

The formulation of the tablets was aimed at selecting the excipients and choosing a manufacturing technology suitable to produce rapidly dissolving / dispersing tablets with an adequate hardness. Also, the aim was to mask the unpleasant taste of the drug,

considering that by dispersing the tablet in saliva, the taste buds come in direct contact with the tablet components for a few seconds.

Four experimental tablet formulations were taken into study. The following table shows the components for each formulation and also their function.

Table 1

The formulations of orodispersible acetaminophen tablets					
Tablet components	Function in formulation	Formula 1 (g/tablet)	Formula 2 (g/tablet)	Formula 3 (g/tablet)	Formula 4 (g/tablet)
Acetaminophen DC	Active ingredient	0.1205	0.1205	0.1205	0.1205
Lactose DC	Filler	0.1385	0.1385	0.1735	0.1000
Manitol	Filler	0.0850	0.0850	0.0500	0.0500
Microcrystalline cellulose	Filler / Dry binder	0.1000	0.1000	0.1000	0.1735
Sodium starch glycolate	Superdisintegrant agent	0.0250		0.0125	0.0125
Sodium carboxymethylcellulose	Superdisintegrant agent		0.0250	0.0125	0.0125
Magnesium stearate	Lubricant / antiadherent	0.0200	0.0200	0.0200	0.0200
Colloidal silica dioxide	Glidant	0.0100	0.0100	0.0100	0.0100
Saccharin	Sweetener	0.0010	0.0010	0.0010	0.0010
Banana flavor	Flavor	q.s.	q.s.	q.s.	q.s.
<b>Total</b>		<b>0.5000</b>	<b>0.5000</b>	<b>0.5000</b>	<b>0.5000</b>

Due to the poor compressibility properties of acetaminophen, a directly compressible type was included in the tablet formulations. Also, the filler excipients used are of directly compressible types (lactose DC and microcrystalline cellulose).

Two superdisintegrating agents were used, formulations 3 and 4 containing an association of these two agents.

### Preparation of acetaminophen orodispersible tablets with acetaminophen

All experimental formulations were obtained by the direct compression technique, carried out in the following stages: weighing the components, dry mixing, lubricating the mix and tableting.

### Pharmaco-technical evaluation of the orodispersible tablets with acetaminophen

In this stage of the study, the following parameters were determined, using compendial methods (European Pharmacopoeia, 6th ed., Romanian Pharmacopoeia, Xth ed.) and acceptance criteria:

- appearance, color, odor, taste: organoleptic examination;
- tablet thickness : Vernier caliper;
- tablet diameter and hardness (VanKel VK 200 Tablet Hardness Tester), on 20 tablets, according to method 2.9.5. described in Eur. Ph. 6th ed.;
- friability (VanKel Friability Tester), according to method 2.9.7. described in Eur. Ph. 6th ed., on a sample of whole tablets corresponding to 6.5 g;

- uniformity of mass (Sartorius pharmaceutical scale) (by determining the individual weight on 20 tablets for each formulation and calculating the average weight, according to method 2.9.5. from the European Pharmacopoeia 6th ed.);

- disintegration of the tablets (method 2.9.3, apparatus 1, as described in the European Pharmacopoeia, 6th ed.).

## RESULTS AND DISCUSSIONS

### Organoleptic characteristics

All four experimental formulations have resulted in plane, disc-shaped tablets, 12 mm in diameter, white in color, spotless, with no cracks and with intact margins. The taste of the tablets was sweet, producing a cool sensation after administration, due to the inclusion of manitol in the formulation. Also, all the resulting tablets were odorless. The organoleptic characteristics meet the usual requirements for such tablets, described in literature.

### Tablet thickness and diameter

Regardless the technological process applied (direct compression or compression after wet granulation), the tablet thickness and diameter had similar values and have shown only small variations, indicating that the material that was to be compressed has good flow properties and that the compression stage was properly conducted.

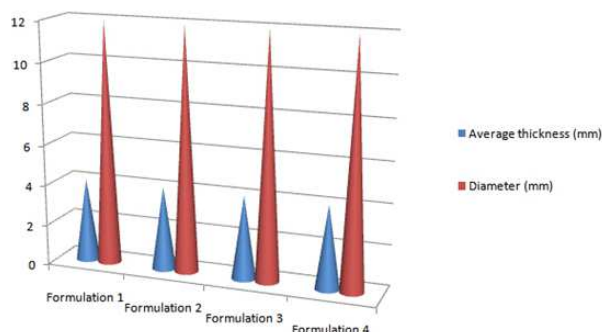


Fig. 1. Average thickness and diameter (mm) of the experimental orodispersible tablet formulations

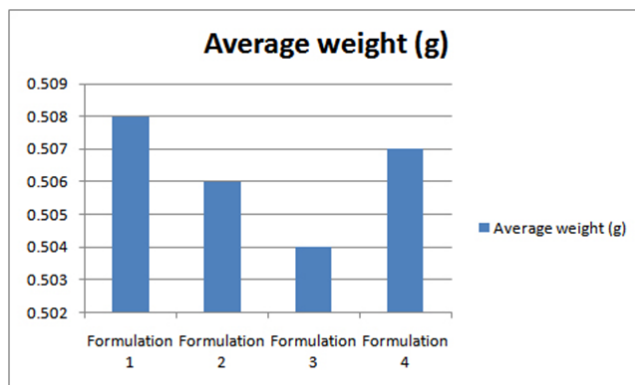


Fig. 2. Average weight (g) of the experimental orodispersible tablet formulations

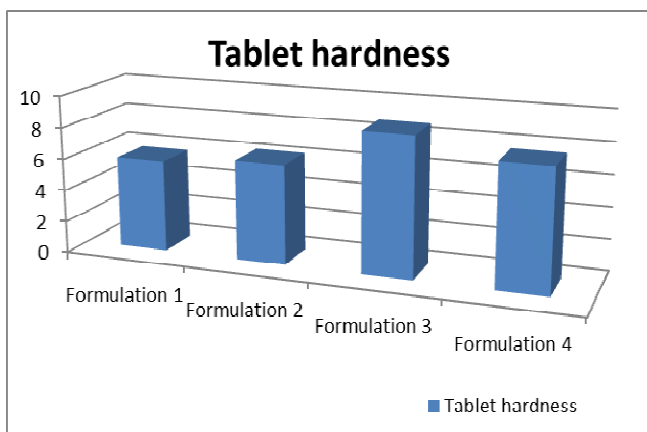


Fig. 3. Tablet hardness of the experimental orodispersible tablet formulations

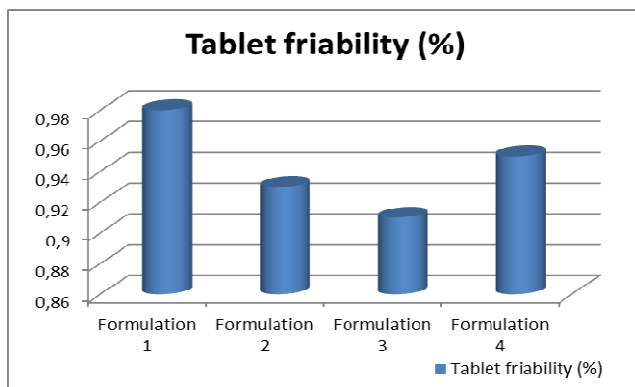


Fig. 4. Tablet friability of the experimental orodispersible tablet formulations

### Uniformity of mass

The results of this test are shown in figure 2.

The results show that the tablets meet the requirements of the Romanian Pharmacopoeia (average mass  $\pm 5\%$ ).

### Tablet hardness and friability

Figures 3 and 4 show the average values recorded in the determination of tablet hardness and friability.

The experimental results reveal a correlation between the tablet hardness and the friability. The tablet hardness is sufficient to ensure their integrity during handling (ranged between 5.8 and 8.8 Strong Cobb units) and the friability is within accepted limits (less than 1%).

### Disintegration

All formulations have disintegrated rapidly, in less than 180 seconds.

The results of the test are shown in figure 5.

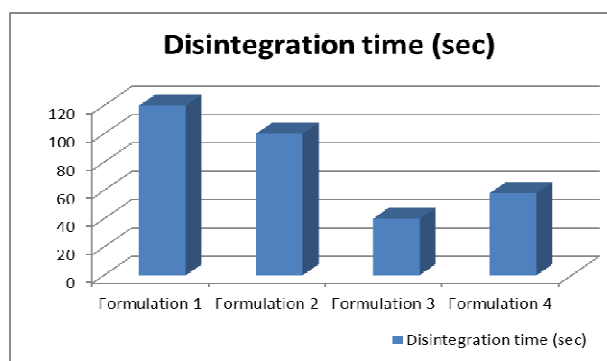
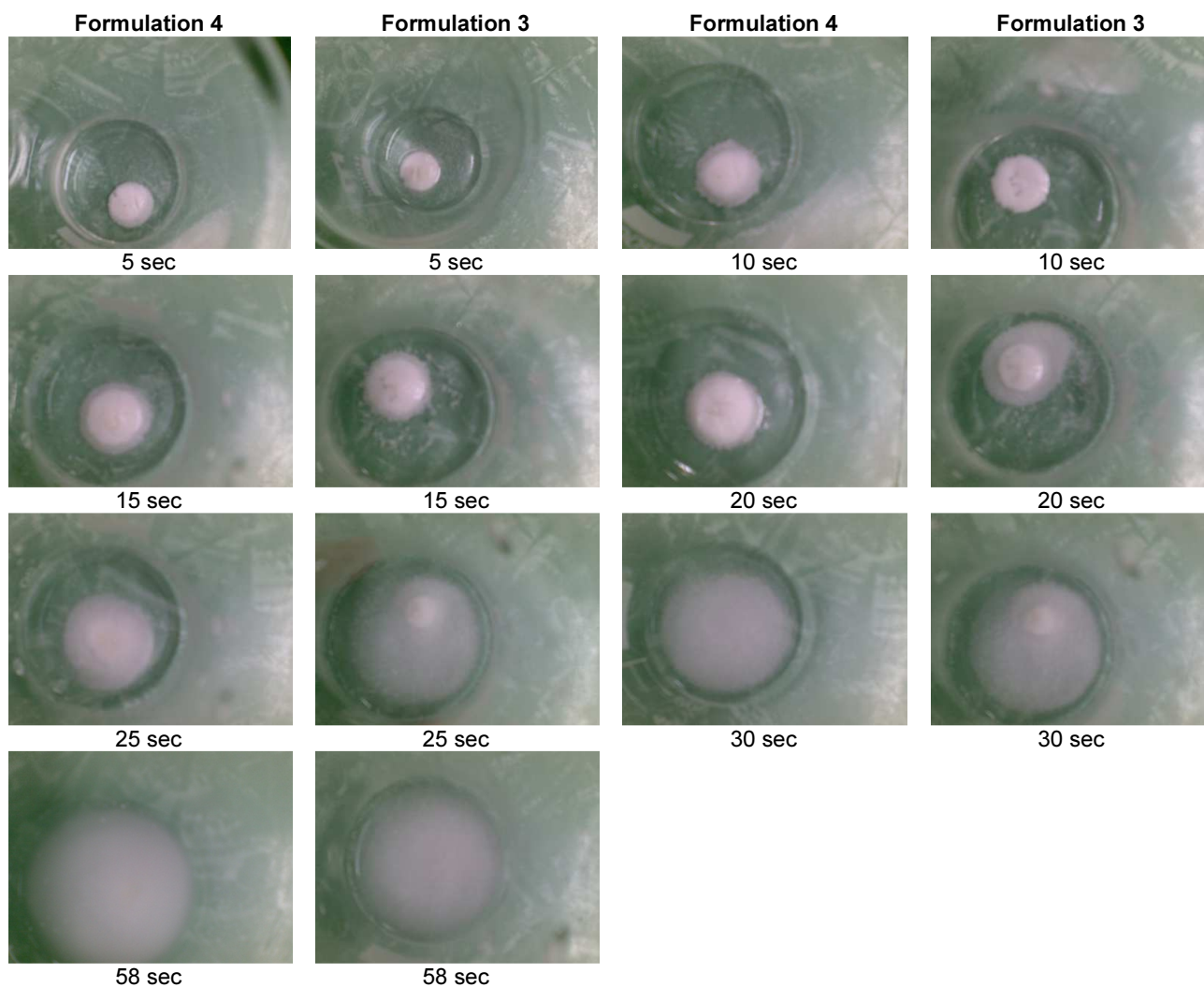


Fig. 5. The results for the disintegration test

The fastest disintegration (40 seconds) could be observed for formulation 3, the disintegration stages being shown in figure 6. This formulation contains a blend of the two superdisintegrating agents, in equal parts, amounting to 5% of the tablet weight. It differs from formulation 4 by its higher content in lactose DC.



**Fig. 6.** The stages of disintegration of the tablets from the Formulations 3 and 4

## CONCLUSIONS

Four orodispersible tablet formulations containing acetaminophen were prepared by direct compression. The aim was to optimize the disintegration time by using two superdisintegration agents, included in two different concentrations (2.5% and 5%, respectively), individually (formulations 1 and 2) or in association (formulations 3 and 4).

The resulting tablets exhibited had an acceptable hardness and disintegration time according the compendial criteria. Formulation 3, containing a higher proportion of lactose DC and the blend of superdisintegrants, has had the shortest disintegration time.

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