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DEVELOPMENT AND CHARACTERIZATION OF ORODISPERSIBLE TABLETS CONTAINING PARACETAMOL GRANULES COATED WITH TASTE-MASKING TECHNOLOGY

L. C. A. Laís Costa Ayub [1, * 2], H. T. T. M. Helena Teru Takahashi Mizuta [1] and V. M. Vinícius Müller [2]

Industrial Pharmacy Residency Program [1], State University of the West of Paraná - UNIOESTE.
Ourofino Animal Health [2], Ribeirão Preto, SP - Brazil.

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Correspondence to Author:
L. C. A. Laís Costa Ayub

Ourofino Animal Health,
Ribeirão Preto, SP - Brazil.

E-mail: l.costaayub@gmail.com

ABSTRACT: Orodispersible tablet technology allows tablets to be administered without the need for additional water, which would increase pediatric patient compliance. In this paper, an orodispersible paracetamol tablet formulation with flavor masking technology was developed. For this purpose, the methacrylic acid-derived polymer, Eudragit® E100, has the ability to form films on particles, which are insoluble at pH higher than 5.0 and soluble lower than it. The coated granules were obtained by coating the paracetamol with the Eudragit® E100 polymer (20% w/w) in Hüttlin Oystar fluidized bed. The tablets were obtained by direct compression with 800 mg as average weight, and the formulations were differentiated by the used disintegrant: Pharmaburst® 500, Prosolv® ODT G2 or Starlac®. Characterization of the granules and afterward of the obtained tablets were carried out. All formulations reached average weight, hardness, friability, disintegration in accordance with the proposed specifications. The mean disintegration time of the tablets was 20 seconds. Taste masking was evaluated *in-vitro* from a dissolution method adapted from the 41st United States Pharmacopeia, where the dissolution profile in simulated saliva and simulated gastric fluid was assessed in order to mimic the passage through the oral cavity and posterior passage through the stomach. When at basic pH (6.8), after 30 seconds of the trial the dissolved amount of paracetamol was less than 20%, evidencing that all tested formulations have the potential for taste masking.

INTRODUCTION: The orodispersible tablet technology, also known as immediate-release (IRT), is defined as a dosage form in which the drug is released very rapidly, taking from a few seconds to one minute to disintegrate [1, 2].

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This feature is attributed to the disintegrants used in the formulation, where they can act by forming pores in the tablet structure. The pores can be made by the immediate solubilization of the excipient, causing the erosion of the system, or by its expansion, causing swelling [3]. Crospovidone, pregelatinized starch, and lactose are examples of disintegrants.

Currently, large companies promote the improvement of these inputs, producing them in coacervation, improving their flow characteristics for direct compression and even flavor [4, 5].

IRTs can be administered without the need for additional water, which is useful for children, elderly patients and those with difficulty swallowing. During the development of such dosage form for the pediatric patient, it is critical to provide adherence to the treatment, in which two aspects are addressed: Unpleasant drug taste masking, such as bitter and ease of swallowing [6-8].

After disintegration, soluble substances in an aqueous medium dissolve and interact with taste receptors, which are distributed on the surface of the tongue [1, 9]. Saliva is composed of small organic molecules and inorganic ions, forming an aqueous solution, whose pH might vary from 5.5 to 7.0, which, among other functions, acts on the movement of particles to the taste buds [2]. The papillae, in turn, acts as a safety sensor against toxic materials, leading to the reflex of preventing the ingestion of bitter molecules, which resembles toxic substances [10].

An alternative to promote taste-masking would be by physical methods such as granulation, extrusion or by coating the active pharmaceutical ingredient (API) with polymers [11-13]. The fluidized bed is a viable option to perform the coating of powdered ingredients, obtaining coated granular particles with low size distribution in the population, considering the technological advances in its process control parameters [14, 15, 16].

Polymers derived from methacrylic acids, such as the monoalkyl methacrylate copolymer, commercially known as Eudragit® E100, have become a focus on taste-masking technology because of their ability to form film on particles, which becomes insoluble at pH higher than 5.0 and soluble lower than it. Thus, during the disintegration of the orodispersible dosage form in the oral cavity (pH 6.8-7.2) the coated API is not dissolved in large amounts due to the insolubility at this pH of the polymer film around the particles. However, when it reaches the stomach fluid, it is released from the polymer matrix and continues with the characteristic dissolution process [17].

Paracetamol is a well elucidated active substance, soluble in water and rapidly absorbed in the gastrointestinal tract, as well as widely prescribed and administered for the treatment of pain and fever. However, the active ingredient has a bitter taste, and currently, the available oral dosage forms for pediatric patients remain unpalatable [8, 18, 19, 20]. In this paper, an orodispersible paracetamol tablet formulation with taste-masking technology was developed. The fluidized bed was used to coat the crystalline particles. For the proposed formulations, the effect of the disintegrant on the results of the quality control analyzes was studied.

MATERIALS AND METHODS:

Raw Materials: Paracetamol, from Hebei Jiheng Pharmaceutical CO. Ltd., was kindly provided by Prati-Donaduzzi e Cia Ltda. Eudragit® E 100 coating polymer was supplied by EVONIK, São Paulo, Brazil, as well as the Starlac® disintegrant. Pharmaburst® 500 disintegrant was supplied by SPI Pharma, São Paulo, Brazil. Prosolv® ODT G2 disintegrant was supplied by JRS Pharma, São Paulo, Brazil. The other used ingredients **Table 1** were supplied by Prati-Donaduzzi.

Obtaining the Coated Granules: Eudragit® E100 polymer solubilized in alcohol at 96°GL was used to perform paracetamol taste masking, forming the solution at 12.5%, while the polymer was at 10% (w/w) of paracetamol.

The coating was performed in Oystar® Hüttlin type fluidized bed (Bosch, GERMANY). The used parameters were: 125 m^3/h of inlet airflow, inlet temperature 60 °C, product temperature was maintained at 42 °C, microclimate at 0.12 bar, air spray 0.22 bar, pump application speed at 5 rpm, and the filter beat time 0.5 s.

The procedure was performed again by taking the granules obtained from the first step as ingredients to the second coating, which was carried out under the same conditions described previously.

Content of the Granules: Determination of the content of the granules was determined by UV-Vis spectrophotometry. A calibration curve was initially obtained with concentrations of 0.001 to 0.01 mg/mL in 0.1 N HCl medium. Paracetamol was used as the standard considering the content of the manufacturer's certificate of analysis (99.8%) and the stock solutions were prepared in triplicate. The UV-Vis Cary 50 (Varian®, USA) spectrophotometer was read at a wavelength of 243 nm. Thereafter, 10 mg of the granules were weighed, and serial dilutions were performed with the 0.1 N

HCl medium until a concentration of 0.01 mg/mL was obtained. The procedure was performed in triplicate and read under a wavelength of 243 nm.

Obtaining the Tablets: The studied variable was the effect of the commercial pre-mix disintegrant (Pharmaburst® 500, Prosolv® ODT G2 and Starlac®) on the results of quality control analyzes.

TABLE 1: FORMULATIONS OF ORODISPERSIBLE 160 mg PARACETAMOL TABLETS. F1 = PHARMABURST; F2 = PROSOLV; F3 = STARLAC ANDCOMPONENTS OF THE EXTERNAL PHASE OF THE TABLETS

	F1 (mg)	F2 (mg)	F3 (mg)
Coated API	195,123	195,123	195,123
Pharmaburst 500 (SPI Pharma)	528,920	-	-
Prosolv ODT G2 (JRS Pharma)	-	528,920	-
Starlac (Evonik)	-	-	528,920
Mannitol	32,000	32,000	32,000
Colouring erythrosine red	0,500	0,500	0,500
Solid strawberry flavour	1,180	1,180	1,180
Solid red fruits flavour	1,180	1,180	1,180
Sucralose	1,900	1,900	1,900
Crospovidone	24,000	24,000	24,000
Colloidal silicone dioxide	2,400	2,400	2,400
Sodium ditrate	8,000	8,000	8,000
Magnesium stearate	4,800	4,800	4,800
Tablet weight	800,000	800,000	800,000

The formulations were compressed in a Piccola-type D 8 punch compressor (Riva Europe, UK).

Optical and Polarized Light Microscopy: To confirm the coating, part of the granules obtained in item 2.2 prior to sieving were selected, so coated granules and uncoated paracetamol crystals were present in the same sample. The EclipseE200 binocular optical microscope (Nikon, USA) was used in the analysis. The sample was added to a glass slide, without coverslip and in the 10x objective a field was chosen, in which there were the two stock populations. When a suitable field was recognized, it was photographed, and then the same field was submitted to polarized light, another photo was captured. If the used paracetamol was in its crystalline form, without the coating, there would be the polarization of light through the crystals.

Mean Weight: The test was performed in accordance with the 41st United States Pharmacopeia, where twenty tablets were randomly selected, weighed in Ohaus Adventurer®, model AR2140 (Toledo do Brasil, BRAZIL). The mean weight was determined by the arithmetic mean of the values obtained for each tablet. For uncoated tablets with a mean weight equivalent to 800 mg, the allowable weight variation is up to ± 5.0%.

Hardness: The test was performed in accordance with the 41st United States Pharmacopeia. For each tested formulation, ten tablets were randomly selected. The hardness test was performed on the TBH 125 Series hardness tester (Erweka®, GERMANY), subjecting each selected tablet to the apparatus.

Friability: The test was performed in accordance with the 41st United States Pharmacopeia. Ten tablets were weighed and rotated, at a speed equivalent to 25 rpm/min, for 4 min in a TAR Series friabilometer (Erweka®, GERMANY). At the end of the spin, the tablets were weighed again. For uncoated tablets, the allowable weight variation is ≤1.5%.

Tablet Thickness and Diameter: Ten tablets were randomly selected, whose thicknesses and diameters were determined with the aid of an OD-8 "VC (Mitutoyo®, CHINA) pachymeter. From the individual results, the arithmetic mean was determined.

Disintegration: Six (6) tablets were randomly selected. The used medium was purified water, maintained at 37 ± 2°C. The product must be disintegrated within 3 min, specification for orodispersible tablets according to the 41st United States Pharmacopeia. The analysis was performed on the ZT 320 Series disintegrator (Erweka, GERMANY).

Tablet Content: The content of the tablets was determined by UV-Vis spectrophotometry. First, a calibration curve with concentrations of 0.001 to 0.01 mg/mL in 0.1N HCl medium was obtained. Afterward, three randomly selected tablets had the individual weight determined and each one was added to a 50 mL volumetric flask. The volume was made up to 0.1N HCl medium. Each tablet contains the equivalent of 160 mg of paracetamol. Dilutions were carried out until a concentration of 0.005 mg/mL was obtained for Cary 50 UV-Vis spectrophotometer (Varian®, USA) reading, in λ at 243 nm.

Adapted Dissolution Assays: The dissolution assays were performed in an adapted manner to the proposed method for paracetamol at 41st United States Pharmacopeia, for all tablet formulations at two different pHs, one close to neutral and the second in acid medium. Thus, the passage of the tablet through the saliva was mimicked, followed by swallowing into the stomach fluid.

The used dissolution medium: simulated saliva pH 6.8 (250 mL) and simulated gastric fluid pH 1.2 (500 mL). For this test, apparatus 2 (paddle) was used at a stirring speed of 75 rpm. Collection times for the basic medium were: 0.25, 0.50, 0.75, 1, 1.25, 1.50, 1.75 and 2 minutes. Meanwhile, the sample collection times for acid medium were: 5, 10, 15, 20, 30 and 35 min. The tests were carried out in a dissolver (Erweka®, GERMANY) and the paracetamol quantification was performed in a UV spectrophotometer (λ= 243nm). The corresponding concentrations were calculated by the equation of the straight line obtained from the calibration curve constructed in the range of 0.001 to 0.01 mg/mL (one for simulated saliva pH 6.8 and another for simulated gastric fluid pH 1.2).

Statistical Analysis: Descriptive statistical analyses were performed in Microsoft® Excel 2017, version 16.17. The analyses of normality, one-way ANOVA and Tukey's test were performed in Graph Pad Prism 8, version 8.0.0.

Year and Site of Experiments: All experiments were conducted in 2018 to 2019 at Prati-Donaduzzi.

RESULTS AND DISCUSSION:

Obtaining Paracetamol Granules: The coating process was carried out in two steps, the first on paracetamol powder and the second on the granules from the first coating step. Thus, the granules received approximately 20% (w/w) coating with the E100 polymer. **Fig. 1** shows the granules obtained after the coating steps. The granules were sieved (60 mesh) in order to remove the uncoated crystals from the remainder of the sample.

Moreover, coating can be evidenced by the differentiation of the refringence (A) and polarization (B) of the samples. The crystals of paracetamol behave characteristically when exposed to light: Under normal light there is the appearance of refringence in the crystals, while under polarized light, there is polarization. Such phenomena are not observed in the coated granules in their entirety; the coating polymer E100 lacks the light polarizing characteristic and also does not allow refringence.

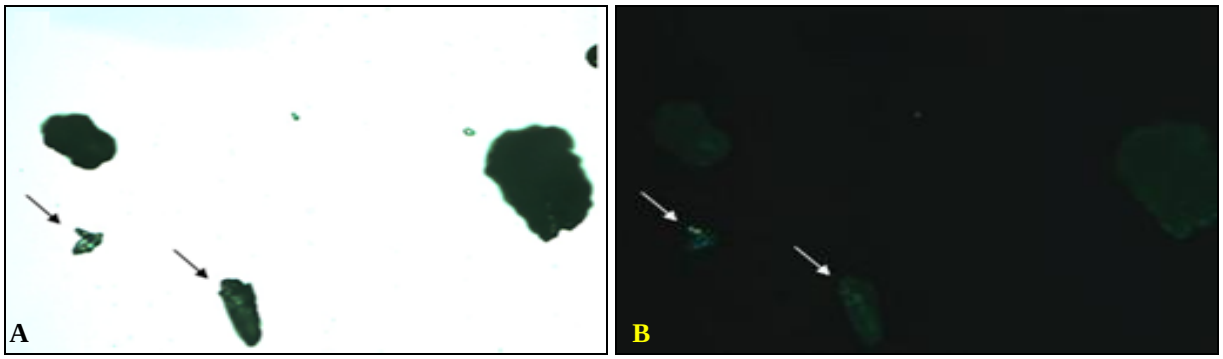

FIG. 1: (A) OPTICAL MICROSCOPY OF THE GRANULES AND CRYSTALS (INDICATED BY THE ARROWS) RESULTING FROM THE COATING STEP. (B) MICROSCOPY OF POLARIZED LIGHT, CONFIRMING THE COATING OF THE GRANULES BUT NOT OF THE CRYSTALS (INDICATED BY THE ARROWS). BOTH IMAGES WERE CAPTURED UNDER 10X MAGNIFICATION

Due to the heterogeneity of the material obtained after the coating, the content of the granules obtained after sieving the material was analyzed in order to calculate the equivalent amount of paracetamol required to obtain 160 mg IRT tablets. The obtained content was 82%, a value quite close to the calculated theoretical value of 80% due to the second coating step. From the granule content result, it was possible to weigh the granules equivalent to 160 mg paracetamol to obtain the formulations of the IRTs.

Obtaining Tablets: Although the used matrix for compression of the blends was the same for each formulation **Table 1,** the obtained tablets had different thicknesses and diameters among the

formulations. **Table 2** shows the values obtained from the measurements with digital caliper for each group and the result of the Tukey multiple comparison analysis.

TABLE 2: DATA OF THICKNESS AND AVERAGE DIAMETER OBTAINED AFTER THE COMPRESSION OF THE FORMULATIONS AND RESULTS OF THE TUKEY TEST

Comparison	Mean 1	Mean 2	Mean differences	Adjusted p-value
Thickness (mm)				
F1 *vs.* F2	5.85	5.23	0.6020	< 0.0001
F1 *vs.* F3	5.85	4.84	0.9840	< 0.0001
F2 *vs.* F3	5.23	4.84	0.3820	< 0.0001
Diameter (mm)				
F1 *vs.* F2	14.44	14.19	0.2450	< 0.0001
F1 *vs.* F3	14.44	14.27	0.1690	< 0.0001
F2 *vs.* F3	14.19	14.27	-0.0760	< 0.0001

From the results of the multiple comparison analyses, the obtained p-value for thickness and diameter was less than 0.05, presenting statistical significance in all comparisons. Thus, the difference of the obtained measurements is due to the used disintegrant, since it is the input that differs between the formulations.

Pharmaburst® 500 is a mixture of polyols and crospovidone, its bulk density is 0.44 g/mL and the tapped density is 0.51 g/Ml [21]. On the other hand, Prosolv® ODT G2 disintegrant consists of a more complex matrix of microcrystalline cellulose, silicon dioxide, mannitol, fructose and crospovidone, considering the bulk density 0.57 g/mL and the tapped density 0.65 g/mL [22]. Starlac® is an α-lactose and maize starch spray-dried compound, whose bulk density is 0.54 g/mL and tapped density is 0.64 g/mL [4].

The combination of inputs with viscoelastic and plastic characteristics is common in co-processed disintegrators. Such inputs provide different attributes to the tablets from their formulations. The viscoelastic characteristic of polyols and microcrystalline cellulose may be responsible for the increased thickness presented in the formulations F1 (Pharmaburst®) and F2 (Prosolv® ODT G2). After the compressive strength is exerted on such compounds, they expand again until they reach the level of stable expansion energy [23, 24, 25].

In the formulation F3 (Starlac®), it was possible to note that the reached thickness 4.84 ± 0.025, was lower than in the other formulations. However, such behavior can be attributed to the lactose present in the disintegrant and to the density of the excipient. Lactose has a viscoelastic and plastic aspect, resisting the applied strength without great variations in the compaction mode of the formulation [25]. In addition, the input density is higher compared to the disintegrators used in the study, which may have an influence on the higher particle compaction and consequent reduction of thickness and diameter measurements.

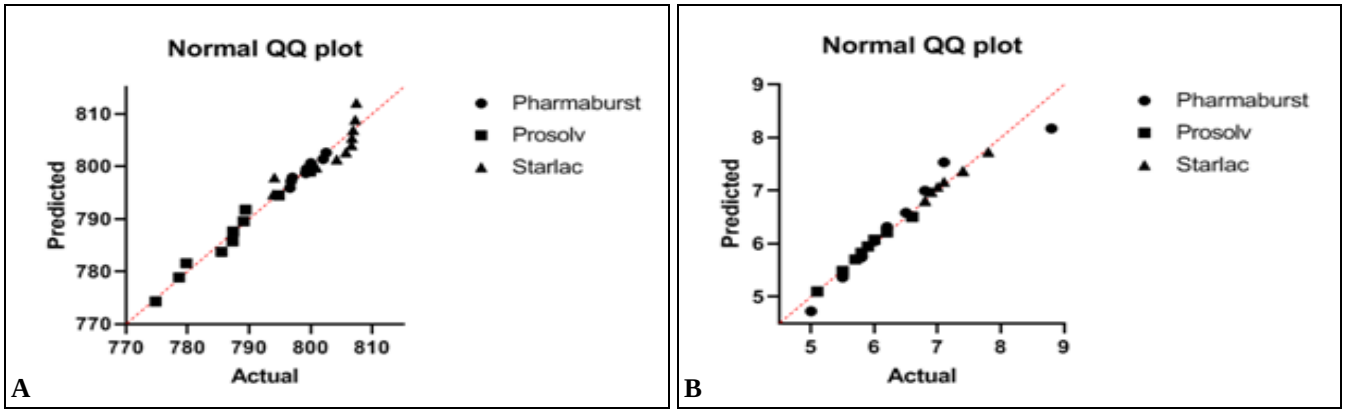

FIG. 2: GRAPHS OF DATA NORMALITY OF (A) MEAN WEIGHT AND (B) HARDNESS

Table 3 shows the analysis of mean weight and hardness. When the data were interpreted, we opted for evaluating if the difference between the formulations would be due to chance or if it would

be bound to the used disintegrant. For this, the normality test was performed by Shapiro-Wilk **Fig. 2** in order to determine if the data present normal distribution. Then, the same data were submitted to the one-way ANOVA statistical test, and the result of the obtained significance is shown in **Table 3**. With $p<0.05$ for both methods, the difference between the groups was assigned to the disintegrant used in the formulation.

The characteristics already mentioned above have an influence mainly on the results of hardness. Depending on the elastic or plastic behavior of the disintegrating compounds, the compaction of the formulations' inputs after the application of the compression strength is different for each formulation, which can make it more or less porous. Therefore, for the formulations F1 (Pharmaburst®) and F2 (Prosolv® ODT G2), which have more viscoelastic characteristic disintegrants, the possibility of having internal pores is higher than in F3 (Starlac®). This is confirmed by the lower hardness results in the formulation F1 (6.45 ± 1.05) and F2 (5.89 ± 0.48), while in F3 this attribute is higher.

In the mean weight analysis, the predominant characteristic of the obtained result is the particle size of the used disintegrant, since this input comprises more than 50% of the formulation, favoring the more or less constant flow of the blend contained in the feeder of the matrix compressor.

TABLE 3: COMPARATIVE TABLE OF THE RESULTS OF MEAN WEIGHT AND HARDNESS, WITH ONE-WAY ANOVA STATISTICAL ANALYSIS

Formulation	Mean weight (mg)	ANOVA (p value)	Hardness (Kgf)	ANOVA (p value)
F1	799.25 ± 2.03	<0.0001	6.45 ± 1.05	0.0022
F2	786.66 ± 7.53		5.89 ± 0.48	
F3	803.36 ± 0.96		7.12 ± 0.37	

In **Table 4** the results of friability, disintegration and content are presented. As evidenced in the previous analyses, the difference in the composition of the inputs of the used co-processed disintegrants in this study is responsible for the difference between the analyzed samples. The content analysis was performed again on the tablets in order to verify the content of paracetamol in the formulations, and all the formulations obtained satisfactory results.

TABLE 4: TABLE COMPARING THE RESULTS OF THE TABLET FRIABILITY, DISINTEGRATION AND CONTENT, OF THE THREE FORMULATIONS

Formulation	Friability (%)	Especification	Desintegration (s)	Especification	Content (%)
F1	1.32	< 1.5%	16	<3 min	99.4
F2	1.09		21		104.5
F3	0.86		25		105.8

The friability analysis relates the level of porosity of the compacted material with the resistance to mechanical shocks. Values greater than the ones specified in 41st United States Pharmacopeia indicate that the tablet is susceptible to rupture under mechanical shocks and therefore does not comply with the quality attributes required for the oral solid dosage form. By observing the results, the friability can be related to disintegration time and hardness; the lower the hardness and the higher the friability, shorter the time needed for the tablets to disintegrate. The formulations fall under this assumption, where F1, with characteristic elastic disintegrant, had a higher thickness, which favored pore formation among the constituent powder from the mixture after compression. The evidence that this pore formation originated from the results of hardness (intermediate), friability, which almost exceeded the specification (<1.5%) and the low disintegration time of 16 seconds.

The matrix of Prosolv® ODT G2 disintegrant is more complex and has microcrystalline cellulose. For this reason, it has a slower disintegration rate when compared to the matrix used in F1. Also, the F2 obtained lower friability, suggesting higher compaction and cohesion of the powder at the moment of compression, although the hardness was kept.

From **Fig. 3**, it is possible to see that the disintegration process occurs in two forms, swelling (F1 and F2) or erosion (F3).

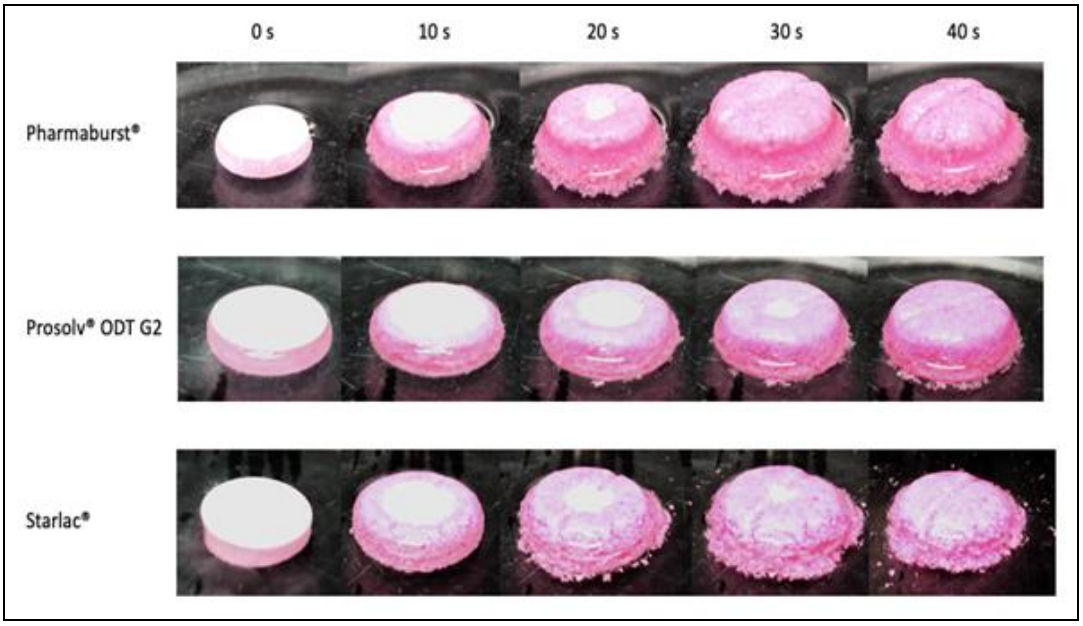

FIG. 3: DISINTEGRATION BEHAVIOR OF FORMULATIONS WHEN IN CONTACT WITH WATER

F3, having a disintegrant with more plastic characteristics than the others studied, obtained lower friability and consequently a longer disintegration time. Furthermore, F3 goes through all the analyses referring to quality attributes assigned to solid oral dosage forms.

***In-vitro* Taste Masking (Dissolution):** In order to prove the taste masking of Paracetamol, an analysis was performed to mimic the passage of the tablet through the oral cavity and subsequent release of the polymer into the gastric fluid.

Firstly, the tablets were subjected to analysis in simulated saliva medium, where the medium was at pH 6.8. In this environment, it was expected that the Eudragit® E100 polymer would preclude total solubilization of paracetamol. **Fig. 4** shows the dissolution profile in this condition.

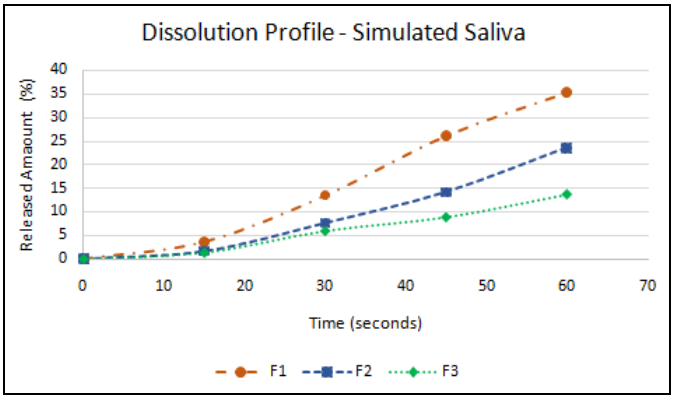

FIG. 4: GRAPH OF DISSOLUTION PROFILE IN SIMULATED SALIVA OF THE THREE IRT FORMULATIONS OF PARACETAMOL 160 mg

It is possible to identify that up to about 40 sec after disintegration (around 20 s), the highest concentration of released drug was approximately 35%, which may provide partially coated granules or which contained the active in its external layer. However, shortly after the disintegration period, the dissolved amount of paracetamol was less than 20%, evidencing the masking power provided by the Eudragit® E100 polymer.

Studies carried out with other polymers of the same action mechanism showed that the amount of polymer to be used is dependent on the drug and its biopharmaceutical classification[11, 16, 26].

Drašković *et al.*, (2017), when performing paracetamol and caffeine coating, determined a sensory analysis scale for bitter taste by training volunteers. Formulations containing the coated active ingredients obtained better taste-related notes than formulations that did not contain the coated particles. The authors concluded that the active ingredients coated with Eudragit® E PO (30% w/w) were effective in masking the flavor of the formulation. Thus, the formulations F1, F2 and F3 have potential for taste masking in this research.

Compared with other powder coating techniques, the performance of this fluidized-bed process results in more uniform coated granules and consequently possesses greater taste-masking power. When evaluated formulations obtained by coating pan or fluidized bed, the volunteers

established that the IRTs that had granules from the fluidized bed, had bitter flavor masked compared to the granules of another coating process [26].

When the dissolving behavior in the simulated gastric fluid is evidenced. **Fig. 5**, the characteristic rapid behavior of paracetamol (> 80% in 30 min) is evidenced. Therefore, the coating process of paracetamol does not influence its acidic solubilization. This means that when in the stomach, all the active ingredients will be rapidly dissolved and will be available for absorption.

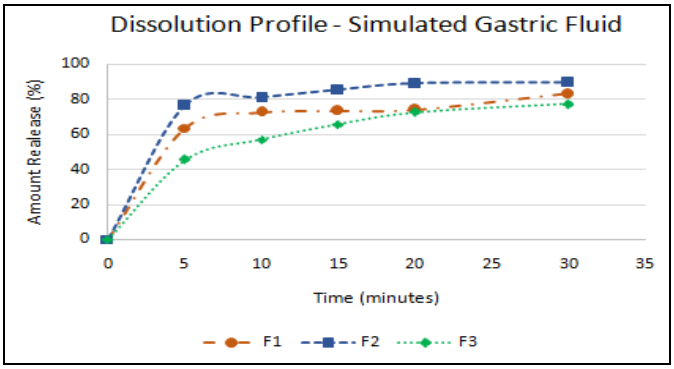

FIG. 5: SIMULATED GASTRIC FLUID DISSOLUTION PROFILE GRAPH OF THE THREE FORMULATIONS OF IRT 160 mg PARACETAMOL

It is expected that all proposed formulations, when subjected to the analysis of pharmaceutical equivalence, behave in a similar way, evidencing that the API coating does not compromise its availability or its absorption process.

Thus, all presented formulations reached the quality parameters compared to the carried out analyses. Hence, it was possible to develop three commercially viable formulations of taste masking orodispersible paracetamol tablet.

CONCLUSION: In sum it was possible to develop three ODT formulations with taste masking technology, among them, the formulation F2 stands out because it does not approach any limit proposed in the specifications and does not contain lactose in its composition, as well. *In-vivo* studies are still required to prove taste masking, as well as stability and pharmaceutical equivalence studies to determine their similarity regarding both the dissolution and absorption profile, in relation to conventional paracetamol formulations.

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CONFLICTS OF INTEREST: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

REFERENCES:

1. Rao Y, Bandari S, Mittapalli R and Gannu R: Orodispersible tablets: An overview. Asian Journal of Pharmaceutics 2008; 2(1): 2-11.
2. Garg G, Siddiqui N and Kumar SP: A short review on a novel approach in oral fast dissolving drug delivery system and their patents. Advances in Biological Research. 2015; 5(6): 1-14.
3. Rowe RCR, Sheskey PJS and Cook W: Handbook Pharmaceutical Excipients. Sixth Edition, Pharmaceutical Press 2009.
4. Evonik Nutrition and Care GMBH. Starlac ® Brochure 2015b.
5. Usman S, Ejaz RR and Safdar KA: Formulation development and optimization of orally disintegrating tablets of montelukast sodium by Design- Expert. Tropical Journal of Pharmaceutical Research. 2018; 17(9): 1701-09.
6. Saxena A, Tiwari RK and Singh L: Embracing the quality in alternative oral drug delivery system: Oral Disintegrating Tablet (ODT). European Journal of Biomedical and Pharmaceutical Sciences 2019; 6(2): 219-25.
7. Comoglu T: Orally disintegrating tablets (ODTs): a new approach to solid dosage forms. Macedonian Pharmaceutical Bulletin 2020; 66(1): 95-96.
8. Almurisi SH: Taste Masking of Paracetamol encapsulated in chitosan-coated alginate beads. Journal of Drug Delivery Science and Technology 2020; 56(A): 101520.
9. Chauhan R: Taste Masking: A Unique Approach for Bitter Drugs. Journal of Stem Cell Biology and Transplantation. 2017; 1(12): 1-6.
10. Pytko-Polonczyk J, Jakubik A, Przeklasa-Bierowiec and Muszynska B: Artificial Saliva and its Use in Biological Experiments. 2017; 68(6): 807-13.
11. Belugina RB: Distinguishing paracetamol formulations: Comparison of potentiometric "Electronic Tongue" with established analytical techniques. Journal of Pharmaceutical and Biomedical Analysis 2020; 188: 113457.
12. Thakker P, Shah J, Mehta T and Agarwal G: Taste masking of pharmaceutical formulations: review on technologies recent trends and patents. International Journal of Lifescience and Pharma Research 2020; 10(3): 88-96.
13. Amelian A and Winnicka K: Polymers in pharmaceutical taste masking applications 2017; 62(6): 419-27.
14. Drašković M, Medarević D, Aleksić I and Parojčić J: *In-vitro* and *in-vivo* investigation of taste-masking effectiveness of Eudragit E PO as drug particle coating agent in orally disintegrating tablets. Drug Development and Industrial Pharmacy. Polimery 2017; 43(5): 723-31.
15. Kumar RS and Kiran AS: Taste masking Technologies: A Boon for Oral Administration of Drugs. Journal of Drug Delivery and Therapeutics 2019; 9(4): 785-89.
16. Alotaibi HF: Design of taste masked enteric orodispersible tablets of diclofenacsodium by applying fluid bed coating

technology. Saudi Pharmaceutical Journal 2019; 27: 354-62.
17. Evonik Nutrition and Care GMBH. Eudragit E100, Eudragit E PO and Eudragit E 12, 5. Specification and Test Methods. Evonik Technical Information 2015.
18. Sangnim T and Huanbutta K: Development and evaluation of taste-masked paracetamol chewable tablets using a polymer and/or wax dispersion technique. Journal of Drug Delivery Science and Technology 2019; 54: 101361.
19. Athersuch TJ: Paracetamol metabolism, hepatotoxicity, biomarkers and therapeutic interventions: a pespective. Toxicology Research 2018; 7(3): 347-57.
20. Tittarelli R: Hepatotoxicity of paracetamol and related fatalities. European Review for Medical and Pharmacological Sciences 2017; 21(1): 95-101.
21. SPI PHARMA. Pharmaburst ® 500 Brochure (2016).
22. JRS. Prosolv® ODT G 2 Brochure [n.d.].
23. Svačinová P: Comprehensive study of co-processed excipients F-Melts: Flow, viscoelastic and compacts properties. Powder Technology 2019; 355: 675-87.
24. Desbois L, Tchoreloff P and Mazel V: Characterization and modeling of the viscoelasticity of pharmaceutical tablets. International Journal of Pharmaceutics 2020; 587: 119695.
25. Sikistirma S: Evaluation of lactose-based direct tableting agents' compressibility behavior using a compaction simulator. Turkish Journal of Pharmaceutical Sciences 2020; 17(4): 367-71.
26. Sujitha V, Bhattacharyya S and Geetha T: Preparation and evaluation of orally disintegrating taste masking tablet of paracetamol with kollicoat smart seal 30 D. Der Pharmacia Lettre 2014; 6(2): 82-89.

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