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Original Article

FORMULATION AND CHARACTERIZATION OF EFFERVESCENT TABLETS FROM A TRADITIONAL MEDICINE RECIPE FOR DENTAL CARE

BOLADE CONSTANTIN ATCHADE[1,2*], SALFO OUEDRAOGO[1,2], TATA KADIATOU TRAORE[2], ISANORELLE BONOU-SELEGBE[1], RASMANE SEMDE[1]

[1]Laboratory for Drug Development (LADME), Center for Training, Research and Expertise in Drug Sciences (CEA-CFOREM), Doctoral School of Health Sciences (ED2S), Joseph KI-ZERBO University, BP-7021, Burkina Faso. [2]Phytomedicine and Drug Research and Development Laboratory (LR-D/PM), Health Sciences Research Institute (IRSS), National Center for Scientific and Technological Research (CNRST) BP 7047 Ouagadougou 03, Burkina Faso

[*]Corresponding author: Bolade Constantin Atchade; [*]Email: constantinatchade@yahoo.fr

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ABSTRACT

Objective: Plant use to treat pathologies is increasingly common in Africa. Our study focuses on a recipe (active ingredient) of traditional medicine that has proven itself in treating dental caries and oral pathologies. This study aims to formulate and evaluate the quality of effervescent tablets based on the recipe (active ingredient) for treating dental caries and oral hygiene.

Methods: A physicochemical and pharmacotechnical characterization of the recipe (RMC, pH, Hausner index, Carr index, flow rate) was carried out. Five stoichiometric ratios of the citric acid/sodium bicarbonate combination were used (1:3.32; 1:3.11; 1:3; 1:2.93; 1:2.87). The tablets were obtained after wet granulation. Pharmacotechnical tests were carried out according to the European Pharmacopoeia 10th Ed to determine the most optimal formulation that could promote rapid release of the active ingredient.

Results: The recipe constituting the active ingredient has properties with an apparent density of 0.50, and a density after tamping of 0.65. The compressibility index is 23.61, and the Hausner index is 1.30. These fairly weak rheological properties required improvement through granulation. A total of 5 formulations were obtained. Formulations F2 to F5 had a disintegration time of less than 5 min. The friability rate was less than 4.60%, 0.86%, 0.91%, 0.75%, and 1.22 for the formulations respectively F1 to F5 and the hardness 95N, 81.8N, 118N, 103.6N, 89.8N. The stoichiometric ratio of 1:3.11 gave us the most optimal formulation with a disintegration time of 156 sec, a friability rate of 0.86%, and a pH of 5.13.

Conclusion: These results demonstrate the feasibility of a solid form to be redispersed for use in oral hygiene.

Keywords: Oral disease, Recipe, Formulation, Effervescent mouthwash tablet

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INTRODUCTION

Oral diseases and conditions, although largely preventable, represent a significant burden of disease in many countries and have lifelong effects, causing discomfort, pain, disfigurement, and even death, affecting nearly 3.5 billion people [1]. Dental caries is an oral disease that occurs when plaque that forms on the surface of the teeth converts free sugars present in food and beverages into acids that, over time, destroy the tooth [2, 3]. Untreated caries in permanent teeth is the most common disease, according to the Global Burden of Disease 2019 report [4]. Aside from dental caries, several factors could contribute to developing other infectious oral diseases. These factors are often linked to a deterioration in the general condition (malignant diseases, prematurity, Human immunodeficiency virus infection), hormonal imbalance (diabetes, pregnancy, hypothyroidism), favorable local factors, or even heavy therapies (long-term antibiotic therapy) or immunosuppressive (immunosuppressant's). In people suffering from cancer, the main causes of oral infectious diseases are the alteration of the salivation process, ulcers in neutropenic patients, and iatrogenic stomatitis of drug origin.

Therapies that control the excess of a specific tissue reaction use drugs composed of anti-inflammatories, analgesics, and antimicrobials (antibiotic, antifungal) [5, 6]. Most drugs in these therapeutic groups are synthesized molecules [7]. One of the galenic forms used in the treatment of oral and dental pathologies is mouthwashes. The stability of its liquid galenic forms is very often questioned [8, 9]. An alternative could be the formulation of solid forms that can improve not only stability but also compliance. In traditional medicine, several studies have proven the effectiveness of plants in the treatment of oral and dental diseases [10]. This study was initiated to promote this traditional medicine. Indeed, a traditional medicine practitioner developed a recipe to treat oral diseases. According to the traditional practitioner's instructions, the treatment consisted of taking a pinch of the recipe in the mouth for a few moments before swallowing the powder or using it as a gargle. To improve the traditional form of use of the recipe, but also to develop a stable dosage form that could promote good monitoring of patient treatment, the choice was made for a solid dosage form.

Among the different solid forms that can promote local action and can be used by gargling after dispersion or solubilization in a solvent, we distinguish dispersible, soluble, and effervescent tablets.

The choice was therefore made for effervescent forms. This choice is justified by the accelerated release of the active ingredient due to the presence of effervescent agents (Citric acid/Tartaric acid/Sodium bicarbonate/Sodium carbonate) [11]. In addition, the excipients used are accessible. The solution obtained after dissolution will be gargled before being swallowed. The recipe powder was characterized to determine the pharmacotechnical properties and define the formulation strategy. Once the formulations were made, the tablets were subjected to quality control to verify whether the requirements of the pharmacopoeia were met.

MATERIALS AND METHODS

Physicochemical and pharmacotechnical studies of powder

The physicochemical and pharmacotechnical tests of the powder of the recipe were carried out according to the prescriptions of the 10th edition of the European Pharmacopoeia [12]. These tests make it possible to determine the powder's physicochemical and pharmacotechnical characteristics and will help define tablet formulation strategies.

Macroscopic observation

The powder's organoleptic characteristics (color, odor, texture, and taste) were determined by macroscopic observation using the appropriate sense organs.

Determination of pH

The pH of the powder was determined by making a 10% solution of distilled water of the powder from the recipe and using an electrode pH meter (WTW pH meter 3210). The experiment was carried out in triplicate.

Residual moisture contents (RMC)

The determination of THR was carried out using a Mettler Toledo HS153 halogen desiccator. A mass of 1 g of the recipe powder was weighed and placed in the desiccator previously set at a temperature of 105 °C and time of 15 min. After the beep signalling the end of the process, the powder was removed, and the percentage of humidity was noted. The process was carried out in triplicate.

Apparent solubility

The solubility test of the recipe was determined in the following solvents: distilled water, 96° ethanol, methanol, and chloroform, following the procedure described in the European Pharmacopoeia 10th Ed [12].

Particle size distribution

A stack of sieves of sizes ranging from 100 µm to 900 µm was arranged with a receptacle. A quantity of 100 g of the recipe powder was placed in the upper sieve (900 µm). The sieves were shaken for 20 min at 50 vibrations per minute. The sieves were carefully removed without material loss and weighed [12].

$$\text{D average} = \sum \text{FDm}/100$$

-Da: Average diameter of the powder; F: frequencies; Da: Average diameters of the sieves

Rheological properties of the powder

The methodology used was adapted to that proposed by the European Pharmacopoeia 10th Ed [12]. The measurement of the angle of repose, the Carr index, the Hausner index, and the flow time through an orifice are the tests carried out to determine the rheological capacities of the powder.

A mass (M) of 50 g of the recipe powder was weighed and transferred into a graduated cylinder of 250 ml. The apparent volume (AV) occupied by the powder of the recipe was measured, and the apparent density (AD) was calculated according to the formula [13].

$$\text{AD} = \text{M}/\text{AV}$$

The powder was mechanically compacted until a constant volume called the tapped volume (TV) was obtained. The tapped density (TD) was calculated using the following formula.

$$\text{TD} = \text{M}/\text{TV}$$

The compressibility index and Hausner ratio were calculated from the measured AD and TD values.

$$\text{Compressibility index} = ((\text{TD} - \text{AD})/\text{TD})\text{x}100$$

$$\text{Hausner's Report} = \text{TD}/\text{AD}$$

Flow time

A mass of 50g of the powder was weighed; the test determines the time it takes for the powder to pass through the orifice of a funnel.

The angle of repose was determined by using 100 g of the recipe passed through a funnel held 3 cm from the top of the powder pile. The height and diameter of the powder cone from the following formula:

$$\text{Angle of repose} = \tan^{-1}\text{h}/\text{r}$$

Testing of tablet formulations

The Drug Development Laboratory (LADME) of Joseph KI ZERBO University and the Health Sciences Research Institute (IRSS) of Burkina Faso provided the active ingredients and excipients of European pharmacopoeia quality.

Determination of the effective dose

The interview with the traditional health practitioner revealed that a pinch of two fingers (middle and index) is required once a day for treatment in adults. On this basis, we chose 10 people, including 5 men and 5 women. The choice took into account height and weight in order to take into account the different possible corpulences. Each volunteer took a pinch in triplicate and the average of the three values was taken for each volunteer. The average mass of the doses was determined and considered as the daily dose.

Justification of the dosage form

Treating oral diseases requires local or systemic action. In this case, the use of mouthwash is one of the first resorts. However, studies have shown the instability of some liquid oral preparations, calling into question their effectiveness and therefore their compliance [8, 9]. An alternative would therefore be to produce a solid form that can be dissolved extemporarily for use. One of the galenic forms that could be produced is the effervescent form. Indeed, the powder in the recipe is a mixture of poorly soluble plant powders. It is necessary to find a formulation whose composition promotes the dissolution of the active ingredient to improve its dissolution and therefore have a better effect. Effervescent agents (citric acid, tartaric acid, sodium bicarbonate, or sodium carbonate) are known for their ease in increasing the solubility of poorly soluble compounds. In addition, the powder in a dispersed form will allow longer contact with the oral cavity, thus better treating oral diseases.

A similar study was already investigated by Singh *et al.*, who manufactured a solid preparation for oral hygiene in the form of an effervescent tablet for mouthwash using *Azadirachta indica* and curcumin [14].

Formulation strategy

There are several reasons for choosing to perform wet granulation. The rheological properties of the powder do not favor direct compression, so wet granulation could improve the flow of the powder and therefore a uniform distribution of the mass of the tablets. Better wet granulation improves the quality of the compression [15]. Indeed, the water added to the mixture to be compressed allows the binder to dissolve and coat the particles of the powder mixture. Strong bonds are formed within the tablet during the drying phase. These bonds, therefore, allow the tablets to acquire greater mechanical strength than that obtained by other compression methods [16].

The formulation strategy is based on improving the rheological properties of the powder to facilitate compression. Three criteria are sought for compression: good compressibility, flow, and wettability. The powder in the recipe did not meet any of the required properties. Therefore, wet granulation was used to improve flow and compressibility.

Polyvinyl pyrrolidone (PVP) was used as a binding agent to promote the bonding between the powder particles and form granules. Wheat starch is used as a disintegrant to promote microdisintegration of the granules. Lactose 200 mesh is the diluent used to complete the volume, and magnesium stearate is used as a lubricant. The combination of citric acid and bicarbonate was used in different proportions to obtain the formulation, allowing rapid disintegration of the tablets.

1 g Citric acid (MM = 210) reacts with 1.2 g sodium bicarbonate (MM = 84) [11]:

The molar ratios used are inspired by the study of Rani *et al.* [17] with some modifications. Five molar ratios of effervescent agents (citric acid and sodium bicarbonate) were used, namely 1:3.32,1:3.11,1:3,1:2.93,1:2.87. The weight ratio of citric acid and sodium bicarbonate in these five formulations was 3:4, 4:5, 5:6, 6:7 and 7:8 for formulations 01 to 05, respectively.

Table 1: Composition quantitative et qualitative des formulations

Formulations	Compositions (%)							Granulation liquid(ml)
	Active ingredient	Citric acid	Sodium bicarbonate	PVP	Wheat starch	Lactose 200 mesh	Magnesium stearate	
F01	45.4	8.56	11.44	4	8	21.6	1	SQ
F02	45.4	8.92	11.08	4	8	21.6	1	SQ
F03	45.4	9.08	10.92	4	8	21.6	1	SQ
F04	45.4	9.2	10.8	4	8	21.6	1	SQ
F05	45.4	9.32	10.68	4	8	21.6	1	SQ

SQ: Sufficient quantity

Granules preparation

A mixture of the formulation components was carried out in a mortar and pestle, except citric acid and sodium bicarbonate [17]. Citric acid and bicarbonate were added separately to the mixture and initially divided into two to reduce effervescence when adding the granulation liquid. The water mixture was made to obtain grains that were neither too wet, nor too crumbly, nor too hard and, without clogging the 1.6 mm mesh opening grid of the oscillating granulator (ARWEKA AR 402). The granules were dried at 45 °C in an oven (memmert) for twelve hours, and the moisture content of the grains was measured to ensure that the water content was less than 5%. A screening was carried out to obtain grains of the same particle size. The flow time was carried out to confirm the improvement of the rheological properties of the grains and move on to compression.

Tablets fabrication

The tablets were made in the drug development laboratory of Joseph KI ZERBO University. The mixture of granules and lubricant was carried out in the mortar equipped with a spatula to obtain a homogeneous mixture with a uniform lubricant distribution. A manual rotary tablet press was used, and the lower and upper punch adjustments made it possible to adapt the compression chamber to the volume of granules necessary to have the tablets of the desired mass and hardness.

Pharmacotechnical testing of tablets

The requirements of the 10th edition of the European Pharmacopoeia carried out the physicochemical tests of the tablets.

Macroscopic characteristics

The macroscopic and organoleptic characteristics of the tablets obtained were described. It is about the appearance, the homogeneity of the color, the taste, and the smell of the tablets.

Mass uniformity

Twenty (20) tablets were randomly selected and weighed, and the average mass was determined. The test meets the European Pharmacopoeia requirements when the individual mass of 2 at most of the 20 °Cp cannot deviate from the average mass by 5% of the tolerated deviation. Still, the mass of no unit can deviate by more than 10%.

Hardness

The hardness of the tablets was determined on ten (10) tablets using a device consisting of two jaws facing each other, one moving towards the other. The tablet was placed between the jaws, taking into account its shape. The force exerted causing the tablet to break is considered the tablet's hardness and is expressed in Newton [12].

Friability

The friability test was performed with 10 tablets units using a horizontally fixed rotating drum (PHARMA TEST) rotating at 25±1 rpm. The drum was rotated 100 times, and the tablets were removed. All loose dust from the tablets was removed before accurately weighing the tablets. A maximum loss in mass (obtained from a single test or the average of 3 tests) not exceeding 1.0% is considered acceptable [12].

$$\%F = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Initial Weight}} \times 100$$

Tablet dimensions

The measurement of the diameter and thickness of the tablets was carried out using the caliper.

Disintegration/Effervescence test

One (1) tablet in a beaker containing 200 ml of distilled water at 25 °C was used. The tablet is considered to disintegrate when it is either dissolved or dispersed in water with a total absence of particle agglomerate. The test was repeated on 5 other tablets. The tablets comply with the test if each of the 6 tablets used disintegrates in the prescribed manner with in 5 min or 300 sec.

Determination of the pH of the effervescent solution

The pH of the solution was determined with one tablet in 200 ml of distilled water at 25±1 °C using a pH meter immediately after completing the dissolution time. This experiment was repeated 3 times for each formulation.

Data analysis

The physicochemical and pharmacotechnical characteristics, including organoleptic properties, moisture content, angle of repose, Hausner ratio, and particle size distribution, described descriptively. The results were compared with the requirements of the European Pharmacopoeia 10th Edition. In parallel, the effect of differences in the ratio of citric acid to sodium bicarbonate as effervescent agents was analyzed by statistical analysis using GraphPad Prism software version 10.3.1. One-way ANOVA followed by Dunnett's comparisons test was performed. Differences were considered significant if P (p-value) was less than 0.05.

RESULTS

Physicochemical and pharmacotechnical properties of recipe powder

Table 2 provides information on the physicochemical and pharmacotechnical characteristics of the prepared powder, which constitutes the active ingredient in the formulations.

Macroscopic and organoleptic observations showed that the powder was gray, with a bitter taste, odorless, and fine in texture. Residual moisture content was less than 10% at acidic pH. The particle size distribution of the powder showed a predominance of particles between 0.1 and 0.25 mm in size. The particle diameter was 0.148 mm (148 µm), and they are therefore classified as fine particles. The characterization of the powder's rheological properties demonstrated its flow difficulties. Therefore, taking into account the particle size and rheological results (angle of repose, compressibility index, and Hausner ratio), the prepared powder was suitable for wet granulation.

Tablet quality control tests

Following the formulation strategies implemented, tablet quality control tests were carried out. These tests focused first on the flow capacity of the granules carried out and secondly on the average mass of the tablets, the disintegration or effervescence time, their pH in solution, the hardness, the reliability, and the size of the tablets. The results from these tests are recorded in the table.

Table 2: Physicochemical and pharmacotechnical properties

Physicochemical and rheological properties	Powder	Interpretation	Specifications Eur Pharm 10th Ed
pH	5.58±0,01	Acid	
RMC	6.18%±0,03	Adequate	< 10%
Solubility (Water)	Slightly soluble	-	-
Particle size	148 µm	Fines particles	-
Bulk density	0.50±0.00	Weak	-
Taped density	0.65±0.00	Weak	-
Compressibility index	23.61±0.35	Poor	1-15%
Hausner ratio	1.30±0.00	Poor	1.00-1.18
Flow time	Infinity	-	4-10 g/s
Angle of repose (α)	62.5°±0.50	Fair	25-35°

Data expressed as mean±SD, n=3.

Table 3: Pharmacotechnical properties of the tablets (*p<0.05 Vs F1)**

Formulation	Standard (Ph Eur 10th)	F01	F02	F03	F04	F05
	Evaluation of the characteristics of the effervescent tablets					
Organoleptic	Light brown, Smooth appearance, Tart taste					
Granule flow time (sec)		<10	<10	<10	<10	<10
RMC (%)	< 10%	3.06	4.15	4.27	3.5	4.28
Mass uniformity (mg)	< 5%	513.2±13.68	508.2±10.29	451±29.33	480.5±19.5	521.8±17.59
Hardness (N)	-	95±14.14 ns	81.8±6.76**	118±26.83	103.6±4.72 ns	89.8 ±9.4 ns
Friability (%)	< 1%	4.60±0.01	0.86±0.02	0.91±0.06	0.75±0.03	1.22 ±0.09
Diameter (mm)	-	11.1	11.1	11.1	11.1	11.1
Thickness (mm)	-	4.28	4.28	4.28	4.28	4.28
	Evaluation of the characteristics of the effervescent tablets after reconstitution					
Organoleptic	Preparation: Dispersion; Taste: Bitter and tangy; Color: Dark orange; Aroma: Smell of henna					
pH	5-6	5.89±0.12	5.13±0.3***	4.27±0.16***	4.39±0.04***	4.19±0.06***
Disintegration time	< 300s	307***	156	263***	209***	261***

n=3; Data expressed as mean±SD; sec: second

The test results show that the tablets of the different formulations have a mass that varies between 450 and 521 mg; only the F3 formulation respects the 5% margin tolerated in the European Pharmacopoeia 10th Ed. The hardness of the tablets was between 81.8 and 118N. Friability is a parameter that starts from the compressive force and, therefore, from the hardness. In the case of our formulations, we note a friability rate higher than the requirements of the European Pharmacopoeia 10th Ed with the F1 and F5 formulations. For measuring the pH of the tablets after disintegration, it was found that the formulations had a pH that varied depending on the proportion of the acid-base couple. A significant difference was noted between the pH of formulation F1/F2 and formulations F3 to F5. The size of the tablets is practically identical, which shows the homogeneity of the tablet masses. The disintegration time of the tablets of the formulations F3 to F5 respects the standards of the European Pharmacopoeia, which requires total disintegration within 5 min or 300 sec. There is a significant difference between the disintegration time of the tablets of formulation 2 and formulations F03, F04, and F05, the time of which complies with the standards of the European Pharmacopoeia.

DISCUSSION

Powder characterization tests help define the formulation strategy of the galenic form and constitute parameters for powder recognition [18–21]. In producing improved traditional medicines, the exact identification and quality of raw materials are essential because they contribute to the safety and quality of the finished product [19, 22]. Thus, the color, taste, texture, and odor are all characteristics that allow a powder to be recognized and, above all to avoid any confusion during large-scale preparation [16]. The raw powder in the recipe was gray and had a slightly bitter taste characteristic of the presence of tannin. Its pH was 5.8. The macroscopic and organoleptic characteristics of the powder constitute identification parameters, allowing recognition and avoiding falsification. However, the characteristics of the powder, depend on the particles obtained during grinding and conservation of the medicinal plant.

Among the parameters that can vary, we note the residual humidity rate, which is less than 10%; the recipe can, therefore, be stored for a long time without contamination and proliferation of molds or yeasts [23]. The recipe powder is slightly soluble in water. This result is justified because the recipe is a mixture of vegetable powder without prior treatment.

The powder particle size analysis shows a homogeneous and uniform distribution with a strong predominance of particles less than 0.25 mm and an average size of 0.148 mm. According to the terminology of the European Pharmacopoeia [23], it is uniform and classified as a powder of fine particle size. The particle size is a parameter that influences the solubility and rheological properties of the powder [19]. The rheological qualities of the powder were tested using 3 methods. Indeed, the results of the compressibility index and the Hausner ratio allow us to qualify the flowability of the powder as poor. One of the reasons that can justify the poor flow properties of the powder is the particle size. Indeed, several studies have proven particle size's impact on powders' flow properties. Several techniques have been used to solve the flow problem. Among the methods used, we can cite dry or wet granulation [16], high-shear wet granulation, crystal-co-agglomeration [24], or spherical crystallization [25]. Others to improve flow properties use flow regulators such as colloidal silica [26–28] or talc [29].

The technique used in our case to improve the flow properties of the powder is wet granulation. This technique was used to reduce the number of excipients in the formulation.

Granules obtained by wet process, in general, improve not only the flow properties of the powder and compression [16].

After obtaining the granules, screening was conducted to obtain the same size and homogeneity. The flow time of the grains justifies this method. Indeed, the flow time of the grains through the funnel orifice was less than 10 sec. Another important parameter in the quality of the granules before the compression phase is the residual humidity rate. Indeed, effervescent granules are hygroscopic [17], and a change in hygroscopic parameters can alter the flow of

granules [30]. The formulations produced had a relatively low water content. The moisture content of the granules varies between 3.08 and 4.28. According to some authors, the moisture content requirements of the granules are approximately 3 to 5% [31, 32]. Based on these requirements, the granules have an acceptable moisture content. This low moisture content is not conducive to the proliferation of microorganisms that could contaminate the formulations and promotes good preservation.

A total of 5 formulations of 500 mg tablets were produced. The formulation strategy that was developed allowed the use of some excipients, including the flow regulator, to be limited. However, for its swelling properties, starch was used as a disintegrant and PVP as a binder. Magnesium stearate was used as a lubricant to facilitate the compression of the granules. The citric acid and sodium bicarbonate couple was used as an effervescent agent due to their solubility and ability to mask the powder's bitter taste.

The tablets of each formulation were subjected to quality control tests after preparation.

According to the European Pharmacopoeia 10th Ed., the maximum permissible deviation from the average mass percentage for 250 mg tablets is 5% [12]. Tablet mass should therefore be between 475 mg and 525 mg. Variations in tablet mass percentage were within this acceptable limit, except for formulation F3. This parameter demonstrates that the tablets have the desired mass. Furthermore, this parameter could be used in stability studies, as any increase in mass during storage indicates moisture absorption, highlighting inappropriate tablet packaging conditions [16].

A hardness test was conducted to assess the tablet's fracture toughness. Tablet hardness ranged from 81.8 to 118 N. There was no significant difference ($p<0.05$) between formulation F3, which had the highest hardness, and formulations F1, F4, and F5. This variation may be explained by the use of a hand press, which could result in a variation in compression force during the process. Indeed, a hand press was used; therefore, the compression force applied to produce the tablets may not be uniform at each process. The European Pharmacopoeia does not specify tablet hardness requirements. However, it is important that this parameter not be set too high, as this could prevent the release of the active ingredient and thus delay the drug's effect.

The friability test determines a tablet's resistance to mechanical disturbances to maintain its shape[33]. Formulations F2, F3 and F4 had a friability rate meeting the requirements (1%) of the European Pharmacopoeia 10th Ed. These formulations will therefore have good resistance to shocks due to transport or storage. The use of the binding agent and the choice of the compression method (granulation) could therefore be responsible for this result. Indeed, studies have demonstrated good resistance to crumbling and good cohesion of the particles during compression following the use of binding agents such as PVP, but also compression by granulation. PVP is a hydrophilic polymer with good binding properties and an ability to form films, thus allowing good adhesion of particles and granules. This low percentage of loss was also made possible by granulation, which improves the cohesion characteristics of the grains and therefore better compactibility [16]. The bonds formed during the granulation process allow the tablet to acquire better mechanical strength by dissolving the binder and coating the particles in the mixture [34]. The formulations F1 and F5 had a friability rate above the requirements (1%) of the European Pharmacopoeia 10th Ed. The hardness of the tablets of these formulations could justify this. The formulation F2, despite a hardness significantly identical to the formulations F1 and F5, has a reliability rate that meets the requirements. The non-uniformity of the compression forces of the different tablets explains this. Given this observation, we can, therefore, justify the complementarity between the hardness and friability of the tablets. According to some authors, hardness alone cannot provide information on the physical resistance of the tablet [35]; a combination of the two tests is necessary. These crumbling rates of less than 1% also indicate good cohesion of the particles during compression, and therefore, justify the use of the binder and the granulation technique. Wet granulation improves the compressibility, fluidity, and hardness properties [36, 37]. In their study, several authors, including Ouedraogo *et al.*, have proven the advantages of compression by wet granulation.

The pH of the effervescent preparation is one of the parameters affecting consumer acceptance and, therefore important in treatment compliance. The difference in the ratio of citric acid and sodium bicarbonate as effervescent had a significant impact on the pH of the preparation. The pH of the suspension tablets for the five formulations varied between 4 and 5. The acid-base ratios used favor this balance. A significant difference ($p<0.05$) was noted between the pH of formulation F1/F2 and that of formulations F3 to F5. The decrease in the pH of the formulation was inversely proportional to the increase in the citric acid/sodium bicarbonate ratio. Increasing the proportion of acid increases the concentration of unreacted [H^{30+}] ions in the solution [38], which is explained by the pH of the formulations being lower than 6. The resulting acidity increases the patients' taste perceptions [39]. The relationship between the proportions of citric acid and bicarbonate is closely linked to the pH of effervescent forms [40]. According to some authors [41], an acidic pH irritates the stomach, while a basic pH can promote a bitter taste in the preparation.

The parameter promoting the release of the active ingredient responsible for the activity was evaluated using the disintegration test, which defines the time after which the entire solid form disperses into particles in water. According to the recommendations of the European Pharmacopoeia, 10th ed., tablets pass the test if each of the 6 units disintegrates in less than 5 min or 300 sec. The results of statistical analysis by one-way ANOVA test showed a significant difference ($p<0.05$) in the dispersion time of five formulations. The dispersion time of formulation 2 was significantly different from that of formulations 1, 3, 4 and 5 according to Dunnett's comparison test ($p<0.05$). Formula 2 with a citric acid/sodium bicarbonate ratio (1:3.11) produced the best disintegration time, which was 156 sec. A rapid disintegration time accelerates the release of the active ingredients in the formula and thus promotes better therapeutic action. Indeed, the presence of the acid-base pair in the formulation promotes the rapid disintegration of the tablets. The production of carbon dioxide results from this chemical reaction between sodium bicarbonate and citric acid in the presence of water. Studies have shown that the more effervescent the mixture used, the better the carbon dioxide production [42]. His carbon dioxide acts as a disintegrant for the effervescent tablets [43]. The higher proportion of base to acid in formulation 2 resulted in a more pronounced effervescent reaction, hence the rapid dispersion and dissolution of the tablets observed. Giyatmi and Lingga, in their study on the effect of citric acid and sodium bicarbonate concentration on the quality of effervescent red ginger extract, observed practically the same results [44]. The acid-base ratio of formulation 2 showed that the citric acid and sodium bicarbonate had completely reacted.

This phenomenon was observed with formulation F2, where the bicarbonate content was high. Furthermore, this result could be due to the hygroscopic properties of the bicarbonate, which is higher in proportion, allowing it to absorb water more easily and react more quickly than the other formulations. Furthermore, the characteristics of the excipients also promote water penetration. The hydrophilic nature of PVP as a binder facilitates the penetration of water into the tablet pores, and the tablet dissolution process begins with this penetration. This penetration causes an effervescent reaction between the acid and the carbonate, releasing carbon dioxide to dissolve the effervescent tablets [43].

The disintegration of the dosage form produces a dispersion that will have a local action after use as a mouthwash. Its systemic action is thought to be due to the high carbonate salt content. Upon ingestion of the drug solution, gastric pH is temporarily elevated, accelerating gastric emptying and promoting drug absorption with increased bioavailability [45].

The cavities in the granules that make up the tabl*et al.* so facilitate the disintegration process. It has been shown that liquids penetrate more efficiently and facilitate the disintegration of the granules due to the high porosity caused by the presence of citric acid and sodium bicarbonate [43].

Conversely, increasing the acid content lengthens the solubility time [46]. Decreasing sodium bicarbonate results in reduced porosity and carbonation rate [35, 45]. This observation was made with formulations F3, F4 and F5, with a significant increase in disintegration time compared to formulation F2.

From the results of the pH and disintegration time analysis, it appears that these two parameters reveal a clinical importance both in improving compliance with the treatment of oral pathologies but also in the effectiveness of the treatment by patients.

This study allowed us to develop a formulation that complies with pharmacopoeia standards, promoting better therapeutic action of the drug.

The next step would be to work on parameters likely to improve treatment compliance. Indeed, the taste of the tablets produced is tangy and slightly bitter; for good dosage compliance and therefore treatment, their taste should be improved [47–49]. In this sense, we can draw inspiration from the formulation D. L. Aulifa *et al.*, who used sucrose as a sweetener and diluent in their formulation. This excipient could complete the mass of the galenic form and therefore overcome the slightly bitter taste left by the drug after taking it [50].

CONCLUSION

This work led to the development and characterization of effervescent tablets containing the formula, aimed at improving the use of a traditional recipe used for the treatment of oral and dental conditions. This dosage form was chosen based on the rheological properties of the powder. The Carr and Hausner index associated with the flow rate revealed poor compressibility and flow of the powder. The improvement of rheological properties by wet granulation made it possible to produce tablets that mainly met the specifications of the European Pharmacopoeia 10th Ed. The molar ratios influenced the disintegration time, which was more favorable when the proportion of citric acid decreased with the increase of sodium bicarbonate. Formulation 2, whose ratio is 1:3.11, presented the best disintegration time, i. e., 156 sec, and a friability rate of less than 1%. Its pH was 5.13. This formulation appears to meet the desired formulation objectives. On the one hand, it could therefore provide a basis for the continuation of formulations aimed at improving taste and color. These parameters are essential for treatment compliance. On the other hand, a one-year stability study would confirm that formulation F2 is the most optimal and that it maintains these characteristics throughout its shelf life. Given that it is an effervescent tablet, it is recommended to store it away from moisture to preserve the integrity of the solid form.

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Laboratoire de Recherche et Développement de Phytomédicaments et de Médicaments (LR-D/PM)/IRSS/CNRST

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CONFLICT OF INTERESTS

All authors declare no conflict of interest

REFERENCES

1. World Health Organization. Global oral health status report: towards universal health coverage for oral health by 2030. World Health Organization; 2022 Nov 21. Available from: https://www.who.int/publications/i/item/9789240061484.
2. Moynihan P. Sugars and dental caries: evidence for setting a recommended threshold for intake. Adv Nutr. 2016;7(1):149-56. doi: 10.3945/an.115.009365, PMID 26773022.
3. National Institute of Dental and Craniofacial Research. Across the lifespan: working age adults oral health and aging information for caregivers. Oral Health; 2020 Aug. Available from: https://www.ncbi.nlm.nih.gov/books/NBK578294.
4. Qin X, Zi H, Zeng X. Changes in the global burden of untreated dental caries from 1990 to 2019: a systematic analysis for the global burden of disease study. Heliyon. 2022 Sep 21;8(9):e10714. doi: 10.1016/j.heliyon.2022.e10714, PMID 36193522.
5. Alalwani A, Buhara O, Tuzum MS. Oral health-related quality of life and the use of oral and topical nonsteroidal anti-inflammatory drugs for pericoronitis. Med Sci Monit. 2019 Dec 3;25:9200-6. doi: 10.12659/MSM.918085, PMID 31860632.
6. Elashiry M, Morandini AC, Cornelius Timothius CJ, Ghaly M, Cutler CW. Selective antimicrobial therapies for periodontitis: win the battle and the war. Int J Mol Sci. 2021;22(12):6459. doi: 10.3390/ijms22126459, PMID 34208697.
7. Shanu Wilson J, Coe S, Evans L, Steele J, Wrigley S. Small molecule drug metabolite synthesis and identification: why when and how? Drug Discov Today. 2024;29(5):103943. doi: 10.1016/j.drudis.2024.103943, PMID 38452922.
8. Jolivot PA, Dunyach Remy C, Roussey A, Jalabert A, Mallie M, Hansel Esteller S. Etude d activite *in vitro* et de stabilite de suspensions antifongiques pour bain de bouche: vers une remise en question de pratiques empiriques? Pathologie Biologie. 2012;60(6):362-8. doi: 10.1016/j.patbio.2012.01.002.
9. Barbara B, Martina F, Debora C. Long-term stability of glycopyrrolate oral galenic solution composed of different storage conditions. Pharmacieutics. 2024 Jul 31;16(8):1018. doi: 10.3390/pharmaceutique16081018.
10. Camara AK, Keita T, Camara AA. Ethnobotanical survey on the use of medicinal plants in the treatment of oral diseases in the commune of Kindia in the republic of Guinea. Pharmacopoeia Trad Afr Med. 2023;21:107-15. doi: 10.1016/j.jksus.2024.103350.
11. Ansel HC, Allen LV. Pharmaceutical dosage forms and drug delivery systems. Wolters Kluwer 20e Ed; 2014.
12. European directorate for the quality of medicines and healthcare of the Council of Europe (EDQM). In: European pharmacopoeia. 10th ed. Vol. 1. France: Council of Europe; 2019.
13. Abdelkader A, Moos C, Pelloux A, Pfeiffer M, Alter C, Kolling S. Tablets made from paper an industrially feasible approach. Pharmaceuticals (Basel). 2022;15(10):1188. doi: 10.3390/ph15101188, PMID 36297300.
14. Singh M, Sharma D, Kumar D, Singh G, Swami G, Rathore MS. Formulation development and evaluation of herbal effervescent mouthwash tablet containing Azadirachta indica (neem) and curcumin for the maintenance of oral hygiene. Recent Pat Drug Deliv Formul. 2020;14(2):145-61. doi: 10.2174/1872211314666200820142509, PMID 32819253.
15. Pharmaceutical Granulation Technology Manual Parikh DM, editor. Handbook of pharmaceutical granulation technology. 3rd ed; 2010. p. 57.
16. Ouedraogo S. Development of tablets based on Lannea microcarpa Engl. Et K. Krause (Anacardiaceae) extracts for arterial hypertension therapy. GJPPS. 2021;9(1):1-12. doi: 10.19080/GJPPS.2021.09.555752.
17. Rani KC, Parfati N, Ekajayani NI, Kurniawan IM, Kristiani NP. The development of Moringa leaves effervescent granules with effervescent agent of citric acid and sodium bicarbonate. Pharmaciana. 2021;11(2):225. doi: 10.12928/pharmaciana.v11i2.20873.
18. Ouedraogo S, Yoda J, Traore TK, Nitiema M, Sombie BC, Diawara HZ. Production de matieres premieres et fabrication des medicaments a base de plantes medicinales. Int J Bio Chem Sci. 2021;15(2):750-72. doi: 10.4314/ijbcs.v15i2.28.
19. Acharya S, Pandey J, Joshi HP, Parajuli G, Poudel N, Poudel S. Formulation and evaluation of gastroretentive floating tablet of amlodipine besylate using natural organic polymers. Int J Appl Pharm. 2022 Jul;14(4):227-34. doi: 10.22159/ijap.2022v14i4.44600.

20. Roy A, Arees R, Madhavi BLR. Formulation development of oral fast dissolving films of rupatadine fumarate. Asian J Pharm Clin Res. 2020 Nov 7;13(11):67-72. doi: 10.22159/ajpcr.2020.v13i11.39185.
21. Ouedraogo S, Sombie BC, Ouedraogo JC. Quality control of trunks barks of Lannea microcarpa engl. and k. krause and anogeissus leiocarpus (DC) guill. and perr. for the manufacture of phytomedicines for the treatment of hypertension. International Journal of Phytopharmacy. 2017;11(5):7. doi: 10.22270/jddt.v11i5.4988.
22. Nayak BS, Patel KN. Pharmacognostic studies of the Jatropha curcas leaves. Int J Pharm Tech Research. 2010;2(1):140-3.
23. European directorate for the quality of medicines and healthcare of the Council of Europe (EDQM). European pharmacopoeia. 6th ed. Council of Europe Stratbourg; 2008.
24. Gupta MM, Chatterjee A, Kumawat T. Troubleshooting the poor flow problem of valsartan drug powder using the crystallo-co-agglomeration technique. Cureus. 2023;15(5):e38590. doi: 10.7759/cureus.38590, PMID 37288190.
25. Chatterjee A, Gupta MM, Srivastava B. Spherical crystallization: a technique use to reform solubility and flow property of active pharmaceutical ingredients. Int J Pharm Investig. 2017;7(1):4-9. doi: 10.4103/jphi.JPHI_36_16, PMID 28405573.
26. Majerova D, Kulaviak L, Ruzicka M, Stepanek F, Zamostny P. Effect of colloidal silica on rheological properties of common pharmaceutical excipients. Eur J Pharm Biopharm. 2016 Sep;106:2-8. doi: 10.1016/j.ejpb.2016.04.025, PMID 27163240.
27. Tran DT, Majerova D, Vesely M, Kulaviak L, Ruzicka MC, Zamostny P. On the mechanism of colloidal silica action to improve flow properties of pharmaceutical excipients. Int J Pharm. 2019;556:383-94. doi: 10.1016/j.ijpharm.2018.11.066, PMID 30529657.
28. Blanco D, Antikainen O, Raikkonen H, Yliruusi J, Juppo AM. Effect of colloidal silicon dioxide and moisture on powder flow properties: predicting in-process performance using image based analysis. Int J Pharm. 2021;597:120344. doi: 10.1016/j.ijpharm.2021.120344, PMID 33545294.
29. Ajayi OM, Amin S. Flow and performance effects of talc alternatives on powder cosmetic formulations. Int J Cosmet Sci. 2021;43(5):588-600. doi: 10.1111/ics.12733, PMID 34411305.
30. Mutahar RK, Ramesh R, Nagesh C, Omer S. Formulation development and *in vitro* evaluation of effervescent tablets of niacin for dyslipidemia. Biomed Pharmacol J. 2008;1(1):107-14.
31. Sun CC. Mechanism of moisture-induced variations in true density and compaction properties of microcrystalline cellulose. Int J Pharm. 2008;346(1-2):93-101. doi: 10.1016/j.ijpharm.2007.06.017, PMID 17669609.
32. Crouter A, Briens L. The effect of moisture on the flowability of pharmaceutical excipients. AAPS Pharm Sci Tech. 2014;15(1):65-74. doi: 10.1208/s12249-013-0036-0, PMID 24092523.
33. Albadry AA, Ali WK, AL Saady FA. Formulation and evaluation of prochlorperazine maleate sustained-release floating tablet. Int J Pharm Pharm Sci. 2017;9(2):89-98. doi: 10.22159/ijpps.2017v9i2.15665.
34. Liu Z, Sun X, Liang T, Luo Y, Chen X, Li T. Preparation and characterization of the biological compound effervescent granule of calcium acetate. Curr Pharm Biotechnol. 2019;20(11):934-44. doi: 10.2174/1389201020666190628144637, PMID 31264545.
35. Herlina KN, Kuswardhani N, Belgis M, Tiara A. Characterization of physical and chemical properties of effervescent tablets temulawak (*Curcuma zanthorrhiza*) in the various proportion of sodium bicarbonate and tartaric acid. E3S Web Conf. 2020;142:7. doi: 10.1051/e3sconf/202014203006.
36. Aslani A, Fattahi F. Formulation characterization and physicochemical evaluation of potassium citrate effervescent tablets. Adv Pharm Bull. 2013;3(1):217-25. doi: 10.5681/apb.2013.036, PMID 24312839.
37. Aslani A, Jahangiri H. Formulation characterization and physicochemical evaluation of ranitidine effervescent tablets. Adv Pharm Bull. 2013;3(2):315-22. doi: 10.5681/apb.2013.051, PMID 24312854.
38. Lestari AB, Desihapsari BN. The optimization ratio of tartaric acid sodium bicarbonate on the green tea extract effervescent granule by dry granulation method. J Ilmu Kefarmasian Indones. 2011;9(2):136-42. doi: 10.37275/ehi.v4i4.89.
39. Jassim Z, Ayash N, Mohammed Ali N. Study the effect of wet granulation and fusion methods on preparation characterization and release of lornoxicam sachet effervescent granules. Drug Invent Today. 2018;10(9):1612.
40. Nurahmanto D, Prabawati DI, Triatmoko B. Optimasi asam tartrat dan natrium Bikarbonat granul, Jurnal Farmasi Fkik. 2019;7(2)11573. doi: 10.24252/jfuinam.v7i2.11573.
41. Grajang IB, Wahyuningsih I. Formulation of Sechium edule extract effervescent granule with the variation of citric acid tartrate acid and sodium bicarbonate. In: Proceedings of the 1st muhammadiyah international conference on health and pharmaceutical development. Scitepress Science and Technology Publications; 2018. p. 54-60. doi: 10.5220/0008239300540060.
42. Kaur P, Deswal G, Chopra B, Kriplani P, Grewal AS, Dhingra AK. Formulation development and evaluation of effervescent tablet of green tea (*Camellia sinensis*). Cent Nerv Syst Agents Med Chem. 2025;25(4):1-12. doi: 10.2174/0118715249333134250116112001, PMID 39936415.
43. Julianti TB, Bakar MF, Wikantyasning ER. Formulation and optimization of an effervescent tablet containing *Kaempferia galanga*. Int J Appl Pharm. 2024;16(5):133-9. doi: 10.22159/ijap.2024v16s5.52464.
44. Giyatmi G, Lingga DK. The effect of citric acid and sodium bicarbonate concentration on the quality of effervescent of red ginger extract. IOP Conf Ser Earth Environ Sci. 2019;383(1):012022. doi: 10.1088/1755-1315/383/1/012022.
45. Lodhi VD, Jadon AS, Sen J, Jain PK, Thakur BS, Khare B. Effervescent tablets: everything you need to know. Asian J Dental Health Sci. 2022;2(4):1-8. doi: 10.22270/ajdhs.v2i4.18.
46. Siregar CJ. Teknologi Farmasi Sediaan tablet penerbit buku kedokteran. Jakarta; 2010.
47. Nakama KA, Dos Santos RB, Serpa P, Maciel TR, Haas SE. Organoleptic excipients used in pediatric antibiotics. Arch Pediatr. 2019;26(7):431-6. doi: 10.1016/j.arcped.2019.09.008, PMID 31611144.
48. Ghatole S, Ashokbhai MK, Sanjay LR, Kaity S. Taste masking polymers. In: Polymers for oral drug delivery technologies. Amsterdam: Elsevier; 2025. p. 631-57. doi: 10.1016/B978-0-443-13774-7.00015-3.
49. Kapoor DU, Garg R, Gaur M, Patel MB, Minglani VV, Prajapati BG. Pediatric drug delivery challenges: enhancing compliance through age-appropriate formulations and safety measures. J Drug Deliv Sci Technol. 2024;96:105720. doi: 10.1016/j.jddst.2024.105720.
50. Aulifa DL, Wibowo DP, Safitri N, Budiman A. Formulation of effervescent granules from red ginger (Zingiberis officinale roscoe var. rubrum) extract and its antioxidant activity. Int J Appl Pharm. 2022;14(1):112-5. doi: 10.22159/ijap.2022v14i1.43377.