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Research Article

Formulation and Evaluation of Paediatric Oral Vehicles for the Administration of Sildenafil and Omeprazole in Infants

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Abstract

When it comes to dispensing medicines to children, the use of a suspension agent is sometimes necessary. To ensure that children and adolescents have timely access to safe and effective medicines, including paediatric formulations. The overall objective of this work was to develop an oral paediatric dispensing solution representing the vehicle for suspensions. The specific objectives were to formulate different suspension agents and to determine the physico-chemical characteristics of the paediatric oral suspensions formulated. The suspension preparation method is based on dissolution/dispersion to produce different formulations. Parameters such as pH, viscosity and PA release were determined. The oral suspensions obtained are pleasant and well tolerated, providing precision and consistency, and maintaining physical integrity throughout their shelf life. The pH of the preparations (1 to 6) has an average value of between 3.4 and 3.6. In terms of viscosity, by comparison, Ora Blend® has a higher viscosity than the preparations (1 to 6). The study of the release of sildenafil incorporated in Ora Blend shows that there is very little release in (SGF). In contrast, in (SIF), there is a release from 5 minutes, which increases to 60% after 60 minutes. Omeprazole incorporated into Ora Blend begins to release from 40 minutes in the SGF, and from the first few minutes in the SIF. These results contribute to the advancement of work on the formulation of oral suspension vehicles by providing in-depth knowledge and experimental results. These advances will stimulate innovation in the formulation and administration of paediatric medicines, thereby helping to improve patient care.

Keywords

Suspension, l'Ora Blend®, Sildénafil, Oméprazol

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1. Introduction

The pharmaceutical industry is the strategic economic sector that encompasses the research, manufacture and marketing of medicines for human and veterinary medicine. It is one of the most profitable and economically important industries in the world. So we can't talk about the importance of the pharmaceutical industry without mentioning its flagship sector, production. Pharmaceutical production covers all operations involved in transforming raw materials into finished products. Medicines come in several forms: solid forms (tablets, pills, lozenges, granules, powder, etc.); flexible forms (capsules, transdermal systems, etc.) and liquid forms (eye drops, syrups, elixirs, drops, embrocations, etc.) [1-4]. Unfortunately, only a third of these medicines are suitable for the paediatric population [5-7]. Healthcare professionals choose paediatric doses on the basis of the data available in adults for certain specialities that do not have forms suitable for paediatric use [8, 9]. Many paediatric medicines are also available only in powder and granule form. They must be reconstituted into oral liquids before administration. Drug suspension vehicles such as Ora Blend® can be used to dissolve these tablets, making them easier to administer to children and sometimes to patients who have difficulty swallowing. [8-12]; Unfortunately, these suspension vehicles are not available in Africa. This experimental study includes the manufacture of suspension vehicles, physicochemical characteristics and release of paediatric oral suspensions.

2. Materials and Methods

2.1. Materials

Saccharose, Glycérine, Sorbitol, Phosphate de sodium dibasique, Acide citrique, were obtained from Sigma-Aldrich. Méthyl parabène, Sorbate de potassium, were supplied by Gattefossé SA (Saint-Priest, France). Ultra-pure water was obtained from a Millipore Super-Q unit (Millipore, Illkirch, France). All chemicals were of analytical grade and used without further modification.

2.2. Methods

2.2.1. Preparation and Characterization of Suspension Agents

(i). Preparation

The method used to prepare the suspensions involves dissolving them. Various formulations were carried out. Table 1 below shows the ingredients used and their role in the formulation.

Table 1. *Ingredients used in the formulations.*

Excipients	Roles
Saccharose	Sweetener
Glycérine	Sweetener
Sorbitol	Sweetener
Phosphate de sodium dibasique	Antioxidant
Acide citrique	Curatorial agent
Méthyl parabène	Antimicrobial Fungicide
Sorbate de potassium	Curatorial agent
Eau distillée	Diluant

(ii). Characterization

With regard to organoleptic characteristics, flavour was determined by regularly tasting the preparations. The visual character was determined by observation in the light.

2.2.2. Physico-chemical Properties of Different Formulations

(i). pH

The principle of pH measurement using a pH meter is based on measuring the difference in electrical potential between a glass electrode and a reference electrode. We used the Fisher Scientific pH meter for the measurements. To measure the pH of our preparations with a pH meter, first calibrate the meter with buffer solutions of known pH (4 and 7), then dip the glass electrode and the reference electrode in the solution to be measured, wait for the measurement to stabilise and read the pH value on the pH meter display.

(ii). Viscosity

In the case of our study, we used the Brookfield LV digital viscometer, which is of the rotary type. For digital instruments, the synchronous motor has been replaced by a stepper motor. A torque transducer transforms the torsion of the spring into an electrical voltage, which can then be converted into viscosity by the electronic board. The Brookfield LV Digital viscometer measures viscosity using a rotating cylinder. The cylinder is immersed in the fluid and rotates at a constant speed. The force required to rotate the cylinder is measured and used to calculate the viscosity of the fluid. The viscosity is displayed on the viscometer's digital screen. In the case of our study, we took measurements at a speed of between 1 and 12 rpm/min.

2.2.3. In Vitro Release Study of Sildenafil and Omeprazole

A release study is a method used to measure the amount of active ingredient that is released from a pharmaceutical form,

and the rate at which it is released into the environment. This study can help determine how the drug is absorbed and distributed in the body. The results of the study can be used to optimise the formulation of drugs and improve their efficacy and safety.

(i). Preparation of Simulated Gastric and Intestinal Media

The simulated intestinal medium (SIF) was created by dissolving 6.8g of KH_2PO_4 and 1.52g of NaOH in 250ml of distilled water and adjusting to obtain 1L of solution. The pH was then measured at 7.4. The simulated gastric medium (SGF) was made by mixing 2g of NaCl in water with HCl; the pH was 1.4. The pH was then adjusted to 4 (with a NaOH solution), which is the gastric pH in children.

(ii). Release Method

Sildenafil and omeprazole were solubilised at 0.01g/ml and 0.03g/ml respectively after a few minutes using the Vortex mixer. In vitro release studies were performed by placing 5ml of each preparation with the different PAs (sildenafil and omeprazole) in the dialysate tube. The dialysis tube was introduced into the release medium 5 500ml, SGF, shaken at 100 rpm (using a magnetic stirrer) for 60 min. Aliquots of 5ml of the dialysate were collected and analysed by UV spectrometry (a Thermo scientific evolution 300UV-Vis spectrophotometer. The analysis was performed in a quartz cuvette, with light absorbance experiments performed at 294nm and 301nm for pH=4 and 7.4 for the different media). Release well conditions were maintained by replacing 5ml of release medium with fresh medium at each sampling point. The release profiles were determined at a fixed temperature and the entire experiments were reproduced.

3. Results

3.1. Formulation and Characterization of Paediatric Oral Suspensions

3.1.1. Formulation

The formulation study carried out enabled us to select 6 formulations. The composition of these is presented in Table 2 below.

Table 2. *Compositions of formulations 1 to 6.*

	Preparation 1	Preparation 2	Preparation 3	Preparation 4	Preparation 5	Preparation 6
Saccharose	40g	40g	40g	40g	40g	80g
Glycérine	2,5g	2,5g	2,5g	2,5g	4g	5g
Sorbitol	2,5g	3g	3g	3,5g	3,5g	5g
Phosphate de sodium dibasique	60mg	60mg	60mg	60mg	60mg	120mg
Acide citrique	100mg	100mg	100mg	100mg	100mg	200mg
Méthyl parabène	50mg	--	50mg	50mg	50mg	100mg
Sorbate de potassium	50mg	50mg	50mg	50mg	50mg	100mg
Eau distillée	50ml	50ml	50ml	50ml	50ml	100ml

3.1.2. Characterization

The flavour of the different formulations has been determined by regularly tasting the preparations. They tasted sweet. The preparations had an odour corresponding to that of flavourless syrups. Visual appearance was determined by regularly observing the preparations in the light over several days. The results obtained are presented in the following Supplementary information S0.

3.2. Physico-chemical Characterization of Paediatric Oral Suspensions

3.2.1. pH

Figure 1 below show the changes in pH of the different preparations (1 to 6) and ORABLEND over several days.

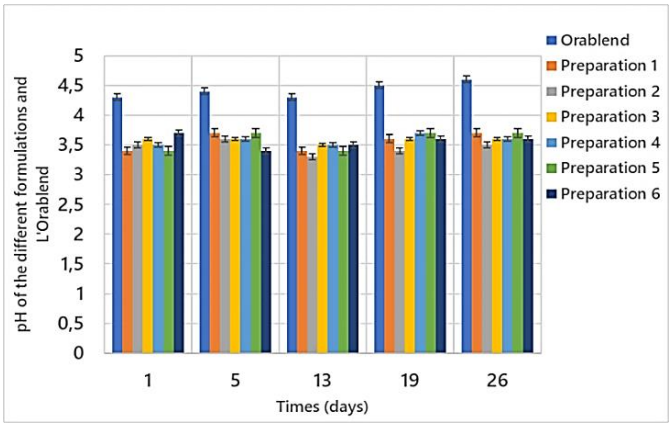

Figure 1. *pH of the different preparations over several days.*

3.2.2. Viscosity

The results of the viscosity measurements are shown in Table 3 and Figure 2 below. The viscosity of the different preparations was measured between 1 and 12 rpm/min. We can see the variation in viscosity as a function of speed.

Table 3. *Viscosity of preparations 1 to 6 and Ora Blend at 1-12 rpm/min.*

Rpm/min	ORABLEND	Pr ép aration 1	Pr ép aration 2	Pr ép aration 3	Pr ép aration 4	Pr ép aration 5	Pr ép aration6
1	168,6	70,5	55,5	61,6	22,4	50	14,4
1,5	137,1	69,3	52,3	61,2	19,8	49,4	13,3
2	119,1	64,4	49,8	55,5	18,8	48,4	12,7
2,5	106,3	65,5	49,3	54,3	18,8	47,7	12,8
3	95,5	64,8	49,2	53,8	18,7	46,4	12,2
4	76,3	63,5	48,5	-	19	46,2	12,5
5	60	61,8	48,4	-	19,1	45,9	12,4
6	49	51,3	48,3	-	18,8	45,8	12,4
10	28	29,9	30,4	-	18,8	-	12,1
12	-	22,3	24,6	-	18,7	-	12,1

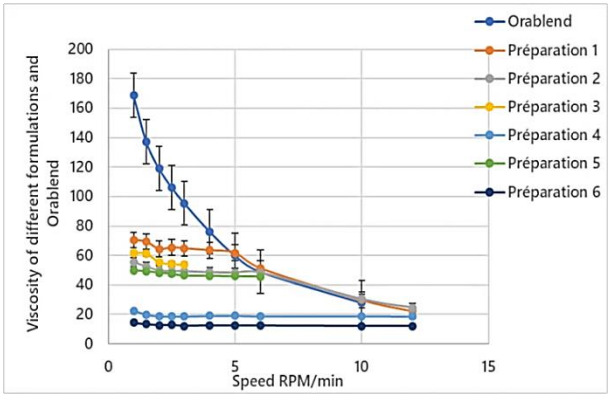

Figure 2. *Viscosity of preparations and ORABLEND.*

3.3. Release Study

We determined the wavelength of maximum absorption of sildenafil and omeprazole in the PBS buffer solution. Sildenafil absorbed most at 294nm and omeprazole at 301nm. Supplem show the absorption spectra of sildenafil and omeprazole and the calibration lines. After carrying out in vitro release studies of Sildenafil and Omeprazole in the different preparations, the release profiles are shown in the following Figures 3 and 4.

4. Discussion

The main results obtained with regard to characterisation

showed that physically all the preparations have a whitish colour, a homogeneous and stable appearance with no formation of deposits or phase separation on visual inspection throughout the shelf life, except for preparation 5, which begins to form deposits after D13. After shaking, the two phases mix again. Apart from this, the increase in Sorbitol to 4g in formulation 5 leads to an increase in the consistency of this preparation. This makes it possible to establish a link between the variation in the amount of Sorbitol (which is a sweetener half as sweet as sucrose) in the different formulations and their stability. Suspensions are dispersed systems that have physical stability problems [13-15]. An ideal suspension settles slowly and disperses easily when agitated [16]. During storage, suspensions can undergo sedimentation and aggregation (including the formation of deposits), leading to physical instability and variability in dosing. Inconsistent dosing can have serious consequences for patients, including drug toxicity and, suspensions is concerned, it is characteristic of flavourless syrups in general. Some oral vehicles are flavoured, while others are not, allowing the pharmacist to add flavours to suit the patient's preferences. Syrups have a high degree of sweetness, which may be attractive to children. Oral suspensions must be pleasant and well tolerated, provide precision and consistency, and maintain physical integrity throughout their shelf life [12, 17]. The main results obtained with regard to physico-chemical characteristics showed that the pH of the formulations (1 to 6) had an average value of between 3.4 and 3.6; there was also a slight variation of around 0.1 over the course of the days. It should be noted that many drugs are weak electrolytes (weak acids or weak bases), and the pH of the formulation affects drug ionisation, solubility and physico-chemical stability. Vehicles and formulations can be prepared with buffers to avoid sudden pH changes [18]. Most of the oral liquid vehicles described in this review have an acidic pH. In terms of viscosity, by comparison, Ora Blend® has a higher viscosity than the preparations (1 to 6). For ease of use, oral vehicles are permitted to be poured, measured, withdrawn into an oral syringe and instilled through an enteral feeding tube. Viscosity should be in a range high enough to maintain physical stability, but low enough to allow these procedures. For ease of use, the product should disperse easily on simple shaking [13]. Prolonged or vigorous agitation can be time-consuming or complicated for providers and patients.

In addition, patients, pharmacists and carers may have different interpretations of the ‘Shake well before usiong’ direction [16]. The study of the release of sildenafil incorporated into Ora Blend shows that there is very little release in the simulated gastric environment (SGF). In contrast, in the simulated intestinal environment (SIF), there is release from 5 minutes, increasing to 60% after 60 minutes. Most of the preparations (1 to 5) release into the simulated gastric environment (SGF) after 10 to 25 minutes; this release increases to over 60% after 60 minutes. These preparations begin to release into the intestinal tract after 20 minutes and reach their maximum release after 60 minutes. Omeprazole incorporated into Ora Blend starts to release from 40 minutes in the SGF, and from the first few minutes in the SIF. In comparison with preparations 1 to 6, it can be seen that there is little release (or even almost no release in preparation 5) in the SGF; whereas in the SIF there is release from the first few minutes and this increases to over 50% after 60min. This can be explained by the difference in pH between the two media (pH SGF=4 and pH SIF=7.2). In view of all this, preparations could be an alternative way of reformulating paediatric drug suspensions that appear to be similar to Ora Blend® in terms of behaviour in the gastric and intestinal environments. Most of the preparations (1 to 5) release into the simulated gastric environment (SGF) after 10 to 25 minutes; this release increases to over 60% after 60 minutes. These preparations begin to release into the intestinal tract after 20 minutes and reach their maximum release after 60 minutes. Omeprazole incorporated into Ora Blend starts to release from 40 minutes in the SGF, and from the first few minutes in the SIF. In comparison with preparations 1 to 6, it can be seen that there is little release (or even almost no release in preparation 5) in the SGF; whereas in the SIF there is release from the first few minutes and this increases to over 50% after 60min. This can be explained by the difference in pH between the two media (pH SGF=4 and pH SIF=7.2). In view of all this, preparations could be an alternative way of reformulating paediatric drug suspensions that appear to be similar to Ora Blend® in terms of behaviour in the gastric and intestinal environments.

5. Conclusions

Oral liquid medicines play an important role in meeting the unmet needs of special patient populations such as children, the elderly and patients with swallowing problems. Children have specific medical needs and metabolisms that differ from those of adults, making it essential to have pharmaceutical forms adapted to their age and physiological characteristics. Suspension vehicles such as Ora Blend are generally used to facilitate the preparation and administration of medicines to patients with specific physiological profiles. However, these suspension vehicles are often unavailable in the African medical system, making it difficult to customise formulations, ensure uniform dosages and solubilise active ingredients. As part of our study, we prepared six (6) different suspension vehicles using the same formulation excipients, while modifying the different proportions thereof. We evaluated the organoleptic properties, such as flavour, odour and physical appearance, as well as the physicochemical properties, i.e. pH and viscosity, of these different preparations. We then studied the ability of these suspensions to release an active ingredient incorporated into them. The active ingredients used are sildenafil, which is often used in paediatrics to treat pulmonary arterial hypertension in infants,

and omeprazole, which is used to treat inflammation of the oesophagus due to acid reflux. We found that our suspensions had much better properties than the Ora Blend suspension in terms of the release of active ingredients. This is probably due to the influence of the pH, which is more acidic in our preparations. We also note that our preparations are less viscous than Ora Blend suspension, which is important for facilitating administration and swallowing for children and patients with swallowing difficulties. This study has contributed to the advancement of work on the formulation of oral suspension vehicles by providing in-depth knowledge and experimental results. These advances will stimulate innovation in the formulation and administration of paediatric medicines, thereby helping to improve patient care. However, there are several parameters that could be studied to optimise this work. The remainder of this study could therefore be devoted to studying the sensitivity of the physico-chemical and organoleptic characteristics, the encapsulation of other active ingredients for therapeutic use and the study of the in vitro release of these active ingredients.

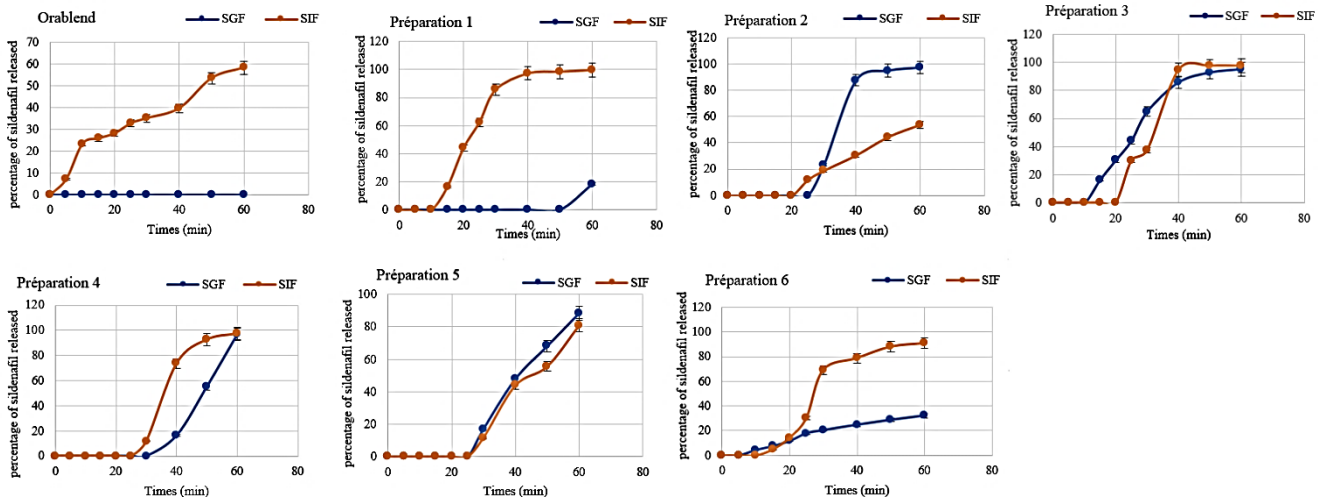

Figure 3. *Cumulative percentage of sildenafil incorporated into preparations released into the gastric and intestinal environment.*

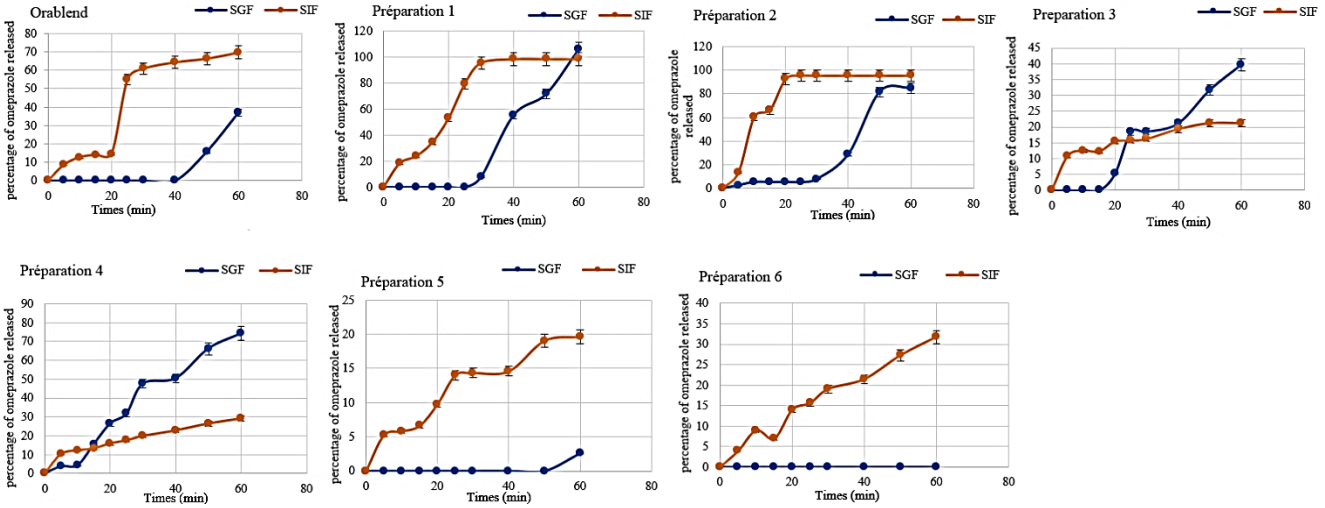

Figure 4. *Cumulative percentage of Omeprazole incorporated into preparations released into the gastric and intestinal environment.*

Abbreviations

SGF	Simulated Gastric Fluid (Medium)
SIF	Simulated Intestinal Fluid (Medium)

Author Contributions

Sidy Mouhamed Dieng: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review &

editing

Abdou Faye: Validation, Visualization, review & editing

Alphonse Rodrigue Djiboune: Validation, Visualization, review & editing

Djiby Faye: Validation, Visualization, review & editing

Moussa Diop: Validation, Visualization, review & editing

Viviane Yeto: Investigation, Methodology, Writing – original draft

Papa Mady Sy: Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

Louis Augustin Diaga Diouf: Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

Gora Mbaye: Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

Oumar Thioune: Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

Mounibe Diarra: Conceptualization, Formal Analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

Data Availability Statement

The data is available from the corresponding author upon reasonable request.

The data supporting the outcome of this research work has been reported in this manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

Appendix

Supplementary Information refer to the additional parts to a manuscript, Figures A1, A2 and A3.

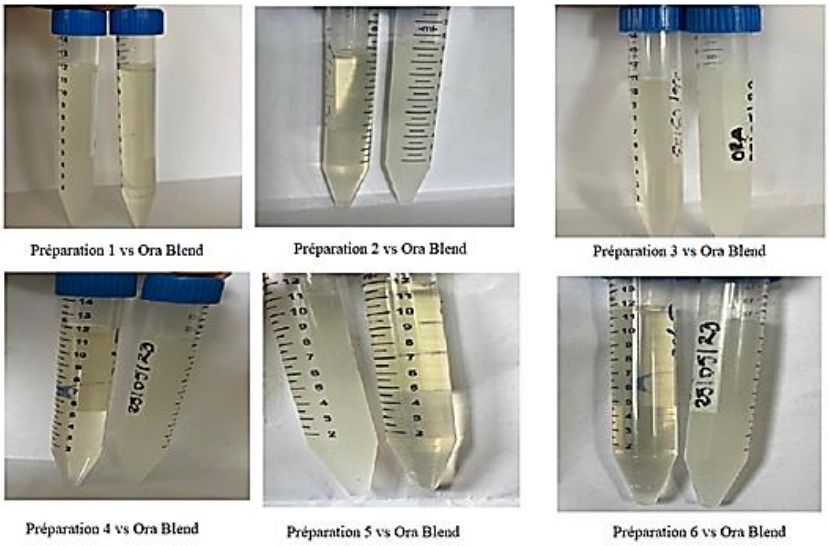

Figure A1. *Visual appearance preparation vs Ora Blend.*

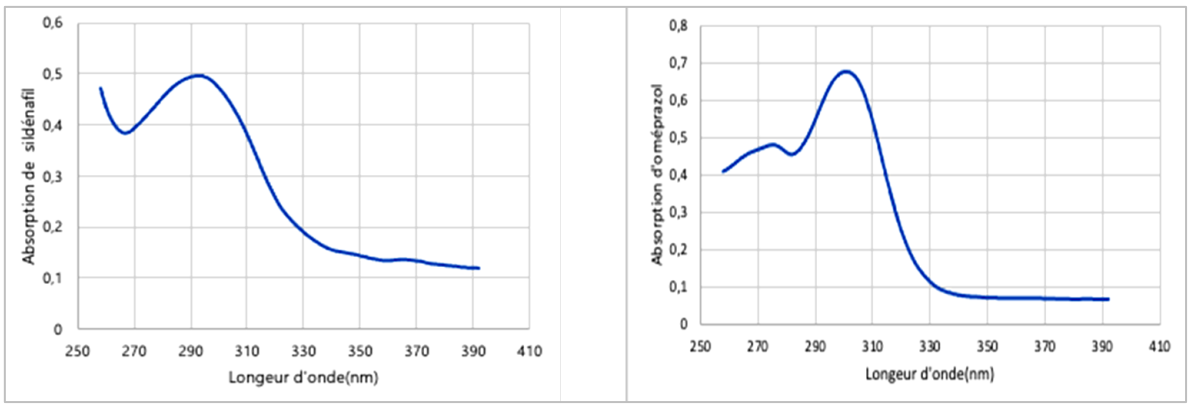

Figure A2. *Absorption spectrum of Sildenafil and Omeprazol.*

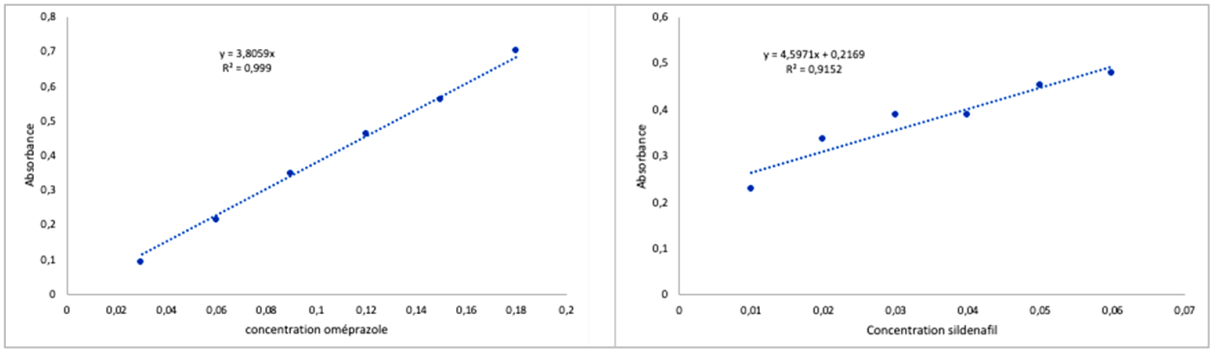

Figure A3. *Absorption spectrum of Sildenafil and Omeprazol.*

References

[1] F. Lagrange, «Deconditioning and stability of solid dry oral forms: state of knowledge », Ann. Pharm. Fr., vol. 68, no 6, p. 332-358, nov. 2010, https://doi.org/10.1016/j.pharma.2010.08.003

[2] G. Bardet, New remedies form. O. Doin, 1891.

[3] S. Ouedraogo et al., «Production of raw materials and manufacture of herbal medicines », Int. J. Biol. Chem. Sci., vol. 15, no 2, Art. no 2, juin 2021, https://doi.org/10.4314/ijbcs.v15i2.28

[4] Natou, 'potions', bp prepa pharma fact sheets. Accessed: 18 April 2023. [On line]. Available on: http://bpprepapharmafiches.over-blog.com/archive/2010-05/11

[5] F. Kaguelidou, «Optimising drug evaluation in neonatology: the example of anti-infective drugs », phdthesis, Université René Descartes - Paris V, 2012. Accessed: 19 July 2023. [Online]. Available from: https://theses.hal.science/tel-00717477

[6] F. Brion, S. Prot-Labarthe, A. Rouault, et O. Bourdon, « Medicines and paediatrics », 2018, p. 1119-1132. e1. https://doi.org/10.1016/B978-2-294-75077-9.00062-1

[7] T. B. Ernest, D. P. Elder, L. G. Martini, M. Roberts, et J. L. Ford, «Developing paediatric medicines: identifying the needs and recognizing the challenges », J. Pharm. Pharmacol., vol. 59, no 8, p. 1043-1055, août 2007, https://doi.org/10.1211/jpp.59.8.0001

[8] T. H. H. Thi, «Development and evaluation of medicinal products for paediatric use: taste masking of the active ingredient and manufacture of rapidly disintegrating minigranules », phdthesis, University of Law and Health - Lille II, 2012 https://doi.org/10/document

[9] J. F. Standing et C. Tuleu, «Paediatric formulations—Getting to the heart of the problem », Int. J. Pharm., vol. 300, no 1, p. 56-66, août 2005, https://doi.org/10.1016/j.ijpharm.2005.05.006

[10] D. S. Budnitz, M. C. Lovegrove, et K. O. Rose, «Adherence to Label and Device Recommendations for Over-the-Counter Pediatric Liquid Medications », Pediatrics, vol. 133, no 2, p. e283-e290, févr. 2014, https://doi.org/10.1542/peds.2013-2362

[11] B. Wansink et K. van Ittersum, «Spoons systematically bias dosing of liquid medicine », Ann. Intern. Med., vol. 152, no 1, p. 66-67, janv. 2010, https://doi.org/10.7326/0003-4819-152-1-201001050-00024

[12] V. Andrieu et J.-P. Reynier, «Galenics for safety in children 11 Oral presentation: Congress of the Société Française de Toxicologie organised in collaboration with the Société Française de Pharmacologie on 16 and 17 October 2003 », Therapies, vol. 59, no 6, p. 599-601, nov. 2004, https://doi.org/10.2515/therapie:2004103

[13] L. Allen et H. C. Ansel, Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. Lippincott Williams & Wilkins, 2013.

[14] M. Grillaud, D. Bandon, J. Nancy, Y. Delbos, et F. Vaysse, «[The polyols in pediatric dentistry: advantages of xylitol] », Arch. Pediatr., vol. 12, no 7, p. 1180-1186, juill. 2005, https://doi.org/10.1016/j.arcped.2005.01.032

[15] E. P. Halmos, «Role of FODMAP content in enteral nutrition-associated diarrhea », J. Gastroenterol. Hepatol., vol. 28, no S4, p. 25-28, 2013, https://doi.org/10.1111/jgh.12272

[16] M. Helin-Tanninen, K. Autio, P. Keski-Rahkonen, T. Naaranlahti, et K. Järvinen, «Comparison of six different suspension vehicles in compounding of oral extemporaneous nifedipine suspension for paediatric patients », Eur. J. Hosp. Pharm., vol. 19, no 5, p. 432-437, oct. 2012, https://doi.org/10.1136/ejhpharm-2012-000159

[17] S. Pawar et A. Kumar, «Issues in the Formulation of Drugs for Oral Use in Children », Pediatr. Drugs, vol. 4, no 6, p. 371-379, juin 2002, https://doi.org/10.2165/00128072-200204060-00004

[18] B. Sandmann, A. Dash, A. Al-Achi, et R. Greenwood, «Ionic Equilibria and Buffers », Appl. Phys. Pharm., janv. 2014, [En ligne]. Disponible sur: https://cufind.campbell.edu/pharmacy/599