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Medicines and Children: Parent Survey

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ABSTRACT

Objec ives: This survey was carried out to identify the problems encountered by parents when administering medicines and to consider ways to improve them.

Materials and methods: This study was conducted using questionnaires distributed to parents with children under 12 years old, *via* "Google Forms" software.

Results: Self-medication was a common practice in our sample. Syrups were the most commonly used and were considered to be the most suitable for the pediatric use. A significant portion of parents (78%) reported that they had been confronted with a refusal of treatment by their children. This refusal was mainly associated with the organoleptic characteristics of the medicines as well as difficulties related to administration. Besides, errors in the administration of medication, including dosing errors or forgetfulness, were mentioned by one third of respondents. To overcome acceptability problems, 68.11% of the parents used tricks to administer the medication to their children like co-administering it with food or drinks. Suggestions for improving the acceptability of drugs were mainly related to the palatability improvement, the reduction in the number of taken doses as well as the volume of liquid oral forms and the size of tablets or capsules.

Discussion: This survey showed that pediatric medicines did not necessary meet the needs of parents. Improvements could be made to raise acceptability and therefore ensure a better therapeutic adherence which is a key to the treatment efficacy.

Conclusion: This survey showed that pediatric drugs did not meet with parent's needs. Improvements should be made in order to ensure acceptability and therapeutic adherence which is key to the treatment effectiveness.

Keywords: Dosage forms; Pediatrics; Survey; Parents; Medicine

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INTRODUCTION

The study of medicines among pediatric patients has known a great progress worldwide since 1997 in response to the new legislation and regulations [1]. However, pediatric medicines remain underdeveloped. The lack of adequate drug formulations places health care professionals in an ethical dilemma. Many medicines currently available for adults are often used off-label in children [2]. The choice of a pharmaceutical formulation adapted to the child is a real challenge, both during drug development and clinical practice since it influences the safety of the drug, its acceptability, its administration and, consequently, its efficacy [3].

First, there are particularities in the physiological and biological characteristics of the pediatric population, which require a wide range of dosages. Second, the acceptability of a drug by the pediatric patient differs from the other population subgroups. Indeed, it is an essential aspect of drug development and prescription. However, there is little literature on the formulation factors that influences drug acceptability, particularly in the ambulatory setting. Other factors to be taken into consideration include the child's ability to use a dosage form, the ease of administration for both the child and the caregiver, the manipulations needed to prepare the doses to be administered, the stability of the dosage form, the special precautions, the type of pathology (chronic or acute), and the cultural environment.

Nevertheless, the available dosage forms do not always seem to be adequate for the use in children. Difficulties of administration as well as refusal by children lead parents or caregivers in general to mix medicines with drinks or food, and sometimes to grind or crush dry oral forms. However, any change in the dosage form can lead to dosing errors, ineffective treatment or even exposing patients to adverse effects. In this context, we chose to conduct a survey of parents, who are the main stakeholders in the care given to children.

MATERIALS AND METHODS

This was a descriptive cross-sectional study. It was a survey for parents with children under 12 years of age. The aim of this work was to understand the drug habits of the pediatric population, the problems encountered by the parents and to consider ways to improve the different dosage forms. Participants were required to anonymously complete a self-questionnaire developed and published online *via* "Google Forms" during the first semester of 2020.

The methodology for developing the set of questions was based on a review of the literature.

The questionnaire consisted of 16 questions that had the following objectives:

• To determine drug use patterns in the pediatric population and risky practices.

- To analyze the acceptability of medications by children and the problems encountered by parents with different types of medications.
- To study parents' expectations and to consider ways to improve the different dosage forms in order to promote the proper use of medication.

The statistical analysis was performed by the SPSS software in its 25th version with manual entry of the responses into a data table which was recoded with nominal and ordinal variables. A comparative study was based on the *Chi-squared* test, with a significance threshold set at 5%.

RESULTS

General Profile of the Survey Population

Our sample consisted of 323 parents with a female predominance (84.83%). The average age of the parents surveyed was 36, with extremes ranging from 23 to 57.

The majority of families in our panel (83.9%) had one or two children under the age of 12. In total, we had 574 children between the ages of 0 and 12, with an average of 1.78 children per family. Our pediatric population was almost symmetrical. The sex ratio of the children was 1, 09. Children aged 2 to 12 accounted for 79.21% (Figure 1).

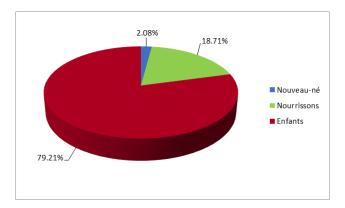


Figure 1: Classification according to the age of the children.

Habits of Drug Consumption

Self-medication: The drugs were consumed under medical prescription in 95.36% of cases (n=308). Self-medication was reported by 71.21% (n=230) of respondents, and 24.15% (n=78) reported giving a medication following pharmacist's advice. **Figure 2** illustrates the sources of information for self-medication. The use of the same prescription for two children was reported in 21.05% of cases (n=68). In our sample, 10.53% of the children were taking medication chronically. The rate of self-medication was lower in this population (47.06%) (p=0.001).

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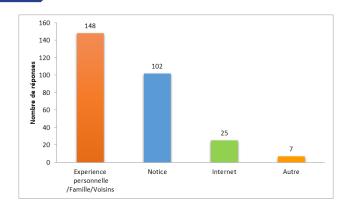


Figure 2: Sources of information for self-medication.

Preferred dosage forms: The most used dosage forms were syrups (94.33%), creams or ointments (89.28%), vaccines (86.67%), nasal forms (86.31%), oral forms for reconstitution (85.44%), suppositories (73.38%), and powders (64.86%) (**Figure 3**).

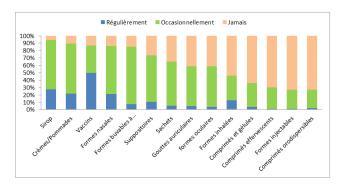


Figure 3: Frequency of use of dosage forms.

The Most Used Medicine Classes

We had 153 responses to this question. Almost 2/3 of the surveyed parents (62.09%) mentioned a paracetamol based drug as a syrup, suppository, or powders. The different classes are detailed in **Table 1**.

Table 1: Most commonly used medicine classes.

Drug class	Number of answers				
Drugs of respirator	Drugs of respiratory system				
Drugs used to treat asthma and chronic obstructive pulmonary disease	38				
Drugs used to treat cough	29				
Drugs used to treat rhinitis	54				
Anti-inflammatory, analgesic, and antipyretic drugs					
Analgesic and antipyretic drugs	96				
Nonsteroidal anti-inflammatory drugs	26				
Steroidal anti-inflammatory drugs	3				
Drugs of central nervous system					
Drugs used to treat epilepsy	2				
H1 antagonists	18				
Anti-infective d	rugs				
Antibacterial drugs	33				
Anthelmintic drugs	2				
Drugs of gastrointestinal tract					
Anti-diarrheal drugs	3				
Drugs used to treat constipation	2				
Others					
Enzymes	20				
Drugs for auricular use	4				

Acceptability and Compliance

In our sample, 86.07% of parents (n=278) reported that their

children had refused to take medication. The problems encountered by the parents are detailed by form (Table 2).

Table 2: Difficulties encountered with different dosage forms.

Category of the problem	Details of responses	Number of answers
	Details of problems encountered with oral liquid forms	
Taste	Bitter taste, strong taste, bad taste, overly sweet taste.	95
Smell	Unpleasant odor.	17
Couleur	Refusal due to dark color.	1
Administration	Refusal to take, especially antibiotics, difficulty swallowing syrup.	42
Intolerance	Vomiting	2
Texture	Diarrhea	2
	Non-homogeneous suspension, phase separation, difficult to dissolve, presence of granules, viscosity sticks to the bottom of the bottle.	38
Packaging	Difficulty in opening some vials.	2
Delivery devices	The pipette is inconvenient; hard the dosing devices of different drugs are mixed.	6
Administered volume	The spoon is not practical, the content spills.	2
	High volume to administer.	3
Conservation	Shelf life after opening the vial is not clear.	8
	Details of problems encountered with powders	
Taste and smell	Unpleasant taste and smell.	7
Administration	No pipette for babies Inability to administer the full dose.	2
	Details of problems encountered with tablets and capsules	
Administration	Refusal to take tablets and capsules Size, difficult to swallow. Or dispersible tablets are sometimes chewed or swallowed.	17
	Details of problems encountered with suppositories	
Administration	Often rejected pain, irritation, local discomfort.	14
Conservation	Melt with heat.	1
	Details of problems encountered with nasal forms	
Administrations	Difficult to administer discomfort.	9

Administration

Too long tube difficulty to inhale.

3

In case of refusal, 11.46% of the parents (n=37) reported stopping the treatment while the other 88.54% (n=286) requested the doctor's advice for treatment substitution.

Appropriate Use of Medicines

Mistakes committed by parents: In our sample, 33.43% of parents reported having made mistakes when administering

drugs to their children (n=108). Errors in the administered dose were the most frequent (44.44%), followed by errors related to omission and failure to comply with the frequency of administration (35.18%). **Table 3** details the errors as described by the parents.

Table 3: Mistakes committed by parents.

Categories of errors	Error details
Dose-related errors	Use of the teaspoon instead of the pipette, therefore administration of a lower dose. Giving a higher dose than necessary.
	Dose/weight: Ignorance of the exact weight of the child.
	Giving a false dose in self-medication.
	Both parents give the same medicine to the child (double dose).
Errors related to forgetting	Non-compliance with administration schedules.
	Failure to respect the duration of the treatment.
Errors related to administration	Non-compliance with the salt free diet with corticosteroids.
	Swallowing a sucking tablet (it was not mentioned on the box and the pharmacist did not specify it).
	Administration position especially for nasal wash solutions.
	Mix the drug with a large volume (bottle, water, yoghurt), in case of refusal to finish the whole volume, it is not known which dose has been administered.
	Giving a powder without having dissolved it in water, choking.
	Syrup spread on the skin instead of massage oil against bloating.
	Confusing antipyretic and anti-inflammatory to be given alternately.
	Giving iron and calcium based medications simultaneously.
Errors related to administration	Forgetting to keep the medication in a refrigerator.

Tricks used by parents: We obtained 220 answers to this question. The tips used are detailed in **Figure 4**. The

administration of drugs with juice was mentioned in 43.18% of cases, followed by yogurt (26.36%).

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Suggestions for improving the acceptability of drugs: We received 252 responses to this question detailed in **Table 4**. More than three quarters of the suggestions were related to taste (78.57%). Odor was in second place with 17.46% and then improvements in dosage form were cited in 15.48% of responses. Packaging was mentioned by 9.92% of the parents. Improvements in texture and color were cited in 4.36% and 3.57% of responses, respectively.

Figure 4: Medibottle.

Table 4: Suggestions for improving the acceptability of drugs.

tegories of answers	Details of answers	Number of answers	Total of answers	Percentage
Taste	Improve the taste, less bitter taste, children like sweet syrups candy/ fruity/strawberry/ chocolate taste. Diversify tastes (do not stay in the classic strawberry/banana).	183	198	78.57%
	Less sweet taste, no sugar added. Subtle, neutral taste, the overly sweet taste is unpleasant.	15		
Smell	Improve the smell. Aromatize the solutions, Add pleasant/natural aromas. Odorless tablets	44	44	17.46%
Texture	Improve texture/less concentrated/viscosity	8	11	4.37%
	Easier to aspirate through the pipette	1		
	Improve the solubility, less granules	2		
Aspect	Improve appearance, improve the color, no dark color.	9	9	3.57%
packaging	Beautiful packaging, attractive, with their favorite heroes. Bottle in the form of animals/toys give a puzzle piece with each dose or give a toy with the drug.	25	25	9. 92%
Dosage form	Develop the rectal route, develop suppository form for certain drugs that do	7	39	15.48%

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	not exist in this form (e.g. antitussives and corticosteroids).			
	Replace suppositories by other forms.	1		
	Develop the tablet form.	1		
	Drugs in the form of orodispersible granules.	3		
	Replace the tablets with a syrup, avoid tablets (before the age of 7 years).	4		
	Decrease the dose to be administered, more concentrated solutions Improve the size/reduce the size of the tablets. Coated tablets with acceptable taste.	12		
	Diversify the forms.	2		
	Injectable forms for antibiotics.	1		
	Develop drugs that can be safely mixed with juice or food.	1		
	Develop drug in the form of candy, juice, chocolate.	6		
	Make all medicines in cutaneous form, patches with drawings.	1		
Others	Prefer graduated pipettes for the administration of syrups for children under 2 years of age.	3	7	2.78%
	Attractive delivery devices.	1		
	Masks to facilitate the aspiration of liquids through the nose.	1		
	To note recommendations to mothers in the leaflet.	2		

DISCUSSION

Habits of Drug Consumption

Self-medication: The number of medical prescriptions for children seems to be high worldwide. In fact, more than half of the children in the United States receive one or more prescriptions each year [4]. In the United Kingdom, about 200 million prescriptions are dispensed each year to children and young people [5]. In 95% of cases, parents used medicines

prescribed by a doctor for their children. Only 32% of the cases mentioned the pharmacist's advice. Self-medication was cited in 71.20% of the questionnaires. The sources of information most frequently mentioned by parents were personal experience/family/neighbors (45.82%) and then the leaflet (31.58%). Parents whose children suffered from chronic diseases seemed to be more reserved regarding self-medication. The rate decreased from 72.20% to 47.05% for these parents (p=0.001<0.05), so there is a correlation between the type of pathology (chronic or acute) and the use of self-medication. Although it is becoming more and more

frequent, self-medication is not exempt from risks [6]. Selfdiagnosis, choice of medication, dosages and duration of treatment may be inappropriate and carry the risk of ineffectiveness and disease progression or, conversely, expose the patient to overdose. In addition, there is the risk of cumulating the same active ingredient present in different drugs which seems to be ignored by most parents. There is also the risk of drug interactions and undesirable effects that could be serious, such as laxative syndrome and convulsions under terpenes among infants. It is therefore necessary to highlight the role of health care professionals, especially the pharmacist who is the drug expert, in educating, alerting, and orientating. Also, the pharmaceutical industry must support this mission by organizing awareness actions around minor pathologies, to encourage patients to go to pharmacies or to their doctor's office to get the right advice. Some laboratories have provided pharmacists with digital and interactive tools to help them better advice and care for their patients.

Preferred dosage forms: Syrup was the most widely used dosage form. In fact, the liquid oral forms are the most suitable for pediatric use and they have always been the form of choice for pharmaceutical companies seeking to develop pediatric forms because they offer the advantage of dosing flexibility [7]. Drugs for the cutaneous route were in second place in frequency of use (89.28%). Nasal products were widely used (86.31%). Suppositories were used by 3/4 of the parents. The acceptability of the rectal route is culturally dependent [8]. A study carried out in the Netherlands in 2000 [9] evaluated the frequency of drug use according to the age group of children. About half (49.5%) of all prescriptions were for oral medicines. The main changes with age were for oral drugs: fewer prescriptions for oral solutions and more prescriptions for tablets/capsules. The change in other formulations was less important with age. Suppositories were less prescribed to children aged over 5 years (a decrease of 7%-1%). The proportions of other formulations were roughly constant, with about 10% of all prescriptions in all age groups for ear, nose, and eye forms and 19% for creams and ointments.

The most used medicine classes: Medications for pain and inflammation were the most cited (79.74%). Paracetamol was the most cited drug in 62.09% of cases and non-steroidal anti-inflammatory drugs in 16.99% of cases. A survey conducted in 2005 showed that the drugs available at home to treat fever in children were paracetamol in suppository form (71%) and in oral form (62%) and ibuprofen as an oral pediatric suspension (51%) [10]. Antibiotics were cited by 21.57% of parents. A study in Italy [11] showed that in 2015 antibiotic prescriptions were about 46% in the population of children fewer than 13 years of age.

Acceptability and Compliance

Medication refusal was reported by 86.07% of parents in our population. This result is higher than that obtained in a similar study conducted in 2015 by Venables, et al., in England, which showed that almost a third of the parents surveyed reported having experienced medication refusal at least once and that

the age of the child was a significant factor predicting refusal, with children aged 5 years to 11 years being the least likely to have refused medication.

Liquid oral forms: Oral forms presented the largest barriers to drug administration. The most frequently cited problems were related to taste, smell, and texture. Palatability is the most obvious and difficult challenge. It is defined as the overall appreciation of a drug by organoleptic properties such as the taste, aftertaste, flavor, odor, and texture of a drug to be administered by mouth or swallowed. It is essential for treatment compliance in the pediatric population and influences the choice and design of the dosage form. However, some generally acceptable medications are not tolerated by all children because of taste and other preferences. The concentration of medicines can also affect their acceptability. Acceptability studies in children in France showed that the preferred flavors are red fruits (strawberry, raspberry, wild berries), followed by banana, candy, and caramel. Flavors to avoid are mint and liquor ice [13]. The problem of texture is most often encountered with suspensions. A possible sedimentation is likely to generate an underdoes or on the contrary an overdose; moreover, a bad sensation in the mouth may occur [14,15]. Some parents mentioned the frequency of administration as a difficulty. Frequent dosing, i.e., more than twice a day, can have a negative impact on adherence to the dosing regimen and may conflict with the lifestyle of older children [16]. This problem is often encountered with liquid oral forms because it is difficult to obtain a prolonged release [17]. The volume to be swallowed per dose was also a limiting factor. When the volume of liquid exceeds a few milliliters, this can lead to spitting or vomiting. Smaller volumes are better tolerated, especially for preparations with known palatability problems, unless dilution provides better taste masking. Oral solutions containing paracetamol are an example of a problematic liquid form. The volume of the dose often becomes too large, even for infants [18].

Solid oral forms: Most of the answers concerned the dosage form. The main disadvantage was the difficulty in swallowing due to size. Indeed, the age at which most children acquire the skills necessary to swallow tablets and capsules safely was the subject of much debate. The early literature largely cites 6 years as the general age at which these dosage forms can be considered suitable for children. Recent evidence suggests that some children may have already acquired the ability to swallow tablets and capsules at an earlier age or, in some cases, may be trained through behavioral training interventions [19]. For example, Yeung and Wong [20] found that HIV-positive children as young as 3 years of age were prescribed solid oral Staudinger.

Oral dispersible tablets are difficult for some children to accept because of their texture and mouth sensation. A tablet that disperses in the mouth always tastes and feels like a lump remains in the mouth.

Inhaled forms: Problems related to delivery were reported with the inhaled forms. Breath actuated devices as well as dry powder inhalers require high breathing force and precise

coordination and are therefore difficult to use for young children. Aerosols also require hand lung synchronization. Although therapeutic education is being implemented, the difficulty of coordination limits the use of this form. However, it is possible that the pharmacist may offer an inhalation chamber to the parents to facilitate medication intake. Thus, for all devices concerning the inhalation route, learning is necessary since the risk of technical error is important.

Nasal forms: The nasal forms presented difficulties of delivery. Even though most young children are uncooperative during the administration of these forms, it is a relatively short procedure as the volume of the drug is less than 2 ml-3 ml.

Rectal forms: Most of the problems were related to the child himself, such as rejection of suppositories, refusal, and pain. Problems of melting with heat were reported also. In fact, rectal forms have several disadvantages, including decreased absorption when the rectum is not empty; involuntary expulsion of medication or during defecation; irritation caused by certain excipients; storage problems (suppositories melt at temperatures above 30°) and difficulties of administration and acceptability for sociocultural reasons.

Appropriate Use of Medicines

Mistakes committed by parents: Medication Error (ME) was defined in 2005 by the French society of clinical pharmacy as a "deviation from what should have been done during the patient's drug therapy management. It is the unintentional omission or unintentional execution of an act relating to a medicinal product, which may be the cause of a risk or an adverse event for the patient". It can be committed by a health care professional, a patient or a third party. In the case of pediatrics, the third party may concern the parents or the child's family and friends.

In our case, 33.43% of the parents had made a mistake when administering medication to their children.

The most frequent errors were those related to the dose administered (44.44%) and omission (35.18%). Other errors were mentioned such as delivery positions, delivery techniques or storage conditions. In view of the above, the reduction in the frequency of administration and the single dose formulation would reduce the risk of medication errors. Another important source of dosing error is the increasing diversity of available delivery devices.

Tricks used by parents: In our study, 68.11% of parents used tips to improve drug acceptability by their children. A similar study showed that nearly a third of the respondents reported handling formulations. The majority of the manipulations (79%) were done to make it easier to administer medicines. Children often have difficulty swallowing both liquid forms because of their unpleasant taste or smell, and solid forms because of their large size making them difficult to swallow whole. The medicine is often mixed with a suitable food or drink to mask the unpleasant taste or smell and make it easier to swallow. In our case, mixing medication with juice was mentioned in 43.18% of cases, followed by yogurt (26.36%).

Our results were consistent with those of a survey of nurses in the UK about the foods they used to administer medication to children, with juice and yoghurt being the most frequently used. Jams and milk were also commonly used. Although this practice is common among parents, several concerns have been raised about possible interactions between food and drugs. Indeed, mixing certain drugs with juice can change the pH, mixing with milk can induce binding to milk proteins and the formation of insoluble complexes, and grinding of tablets causes thermal degradation. Prolonging the contact time of a drug with a foodstuff may increase the binding capacity and thus reduce the bioavailability of the drug, which affects the therapeutic effect. In addition, powders dispersed in a liquid can be adsorbed on the walls of the container or sediment. Therefore, the dose error is increased when only part of the liquid is withdrawn and administered. In this context, FDA and EMA guidelines stipulate that the volume of the vehicles used should be small to ensure that the total dose of the drug is delivered, while facilitating swallowing and allowing acceptable taste masking. To guide parents in their choice of manufacturers must provide the necessary information in the leaflet. The FDA has published a guidance document on recommended approaches for determination of the appropriateness of vehicles for the coadministration of pediatric drugs. Guidance is provided on the selection of vehicles, description of standardized in vitro methods for assessing vehicle compatibility, and suggestions on product labelling to communicate their acceptability.

Suggestions for improving the acceptability of drugs: To ensure proper compliance, the discomfort experienced by children or their parents when administering the medication should be minimized. Children have a low tolerance for unpleasant tastes, 78.57% of parents cited improvements in taste. The use of tasteless or appetizing medications can minimize the risk of spills and/or spitting. New excipients can be sought to achieve this goal. It is important to note that the overuse of sugars and sweeteners can put children at risk for dental problems, obesity and type 2 diabetes. Electronic tongues can also be used to detect the bitterness of solutions before clinical trials set up. Their use would make it possible to avoid the development of drugs with low palatability. Smell was in second position (17.46%), improvements in dosage form were mentioned in 15.48% of responses. Improvements in texture and color were cited in 4.36% and 3.57% of responses, respectively. The reduction of the volume to be swallowed, the size of the tablets as well as the number of intakes were suggested by 11 parents. In this context, the development of sustained release drugs can be encouraged. Indeed, this type of formulation limits the number of doses taken and has a smaller impact on the patient's daily life. Although these techniques were long reserved for solid forms, a number of new approaches have been studied for the development of sustained release liquids, including ion exchange resins, coated micro particles in suspension or drug micro emulsions.

In addition, in order to reduce the size of tablets, innovative technologies are emerging such as the development of multiparticles, or dispersible films and mini-tablets with a diameter of 3mm to 4 mm. This allows the same flexibility of dosage and ease of ingestion that have traditionally made liquids the "gold standard" in pediatrics.

Tablet size and volume of solutions can be discussed according to the age of the child (Table 5).

Table 5: Proposed acceptable oral drugs parameters based on ages of pediatric populations.

Product attribute	Neonates (<1 month)	Infants (1 month–2 years)	Child (2-5 years)	Child (5–12 years)
Acceptable liquid volume	<5 ml	<2.5 ml	<2.5 ml	<10 ml
Acceptable tablet/ capsule size	<2 mm	<3 mm	<4 mm	<7 mm

The improvement in packaging was mentioned by 9.92% of the parents. The answers concerned the development of vials in the form of toys or secondary packaging featuring cartoon characters. New packaging approaches can be considered to improve acceptability but taking into account the risk of error by children. Indeed, the ANSM prohibits the affixing of a drawing, a fruit or an object on the packaging, reflecting the aroma, as it is not useful for the proper use of the drug and can be attractive and a source of serious intoxication for a child. However, mention of the name of the flavor (e.g. "strawberry flavor") on the packaging is considered sufficient to identify the medicine correctly.

Other responses (n=6) suggested making medicines in the form of candy, juice, or chocolate. In fact, pediatric tablets of different shapes (heart, ring, lion, bottle, etc.) printed in 3D and resembling candy was manufactured for the development of more appetizing dosage forms. *In vivo* evaluations showed excellent masking of the bitter taste of the active ingredient. However, the risk of accidental ingestion is significant with this type of medication. The drug must be differentiated from confectionery and toys in order to reduce the appeal of the product to children.

Recently, modified baby bottles such as Medibottle® have been developed. This is a traditional baby bottle with an oral dispenser that fits into the center sleeve of the feeding bottle. The bottle is filled with milk or another beverage and the dispenser is filled with the needed dose of medication and then inserted into the bottle. While the baby is drinking, the plunger of the dispenser is quickly depressed to deliver a squirt of drug with every few sips of milk or drink (Figure 5).



Figure 5: Baby medicine dispenser.

There are also some patents for modified teats and pacifiers in which the required dose of medication is placed in a container attached to a hollow nipple. The baby receives the medication either by sucking the nipple or by the caregiver compressing the reservoir to get the liquid into the baby's mouth. An example of a nipple is shown in **Figure 6**. Both devices are suitable for newborns and infants, but less so for older children. Although acceptability may be better, these devices are generally imprecise, as it is difficult to ensure that the entire dose has been delivered, and allow only very small volumes to be delivered.



Figure 6: Schematic illustration of the nipple shield device (left) and image of a prototype device including drug delivery insert (right).

In addition, the use of milk as a vehicle for drug administration has also led to the development of the "nipple shield" delivery system (Figure 7), which contains a drug loaded insert that delivers the active ingredient into the milk during breastfeeding of newborns.





Figure 7: Dose sipping technology: Prototype straw containing granulated product with removable cap (left) and without cap, ready to use in a glass of water (right).

Another example of a delivery device is a straw into which a granular drug has been inserted. By sipping through the straw, the granules reach the mouth with the liquid. This technique greatly increases children's compliance.

In addition, "pill swallowing cups" have been developed to help patients having difficulty in swallowing tablets. Users fill the cup halfway with a drink, place the lid on the cup and place the tablet in the spout. The flow of the liquid pushes the tablet towards the back of the throat allowing it to be swallowed easily.

CONCLUSION

Medication habits were different. Self-medication was widely practiced by many parents using multiple sources of information. Regarding consumption preferences, syrup was the most commonly used dosage form and considered by parents as suitable for pediatric use. The main problems encountered by parents when administering medicines to children were related to the organoleptic characteristics of the drug such as taste, smell, texture, and convenience for both the parents and the child. Parents often used coadministration of medication with food or drink. However, such practices can lead to altered bioavailability and adverse reactions due, for example, to chemical and physical instability. Several improvements were proposed by the parents to improve the acceptability of the drugs, they mainly concerned palatability, the reduction of the number of intakes as well as the volume of the liquid oral forms and the size of the tablets or capsules. As innovative technologies are expensive, the issue is: how to combine the accessibility of innovative drugs having a better acceptability with industrial interests? This is the new challenge for the pharmaceutical industry in the years to come.

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DECLARATION OF COMPETING 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

- Tuleu C (2017) Better medicines for children: Are we there yet? J Pharm Pharmacol. 69(4):349.
- Ivanovska V, Rademaker CMA, van Dijk L, Mantel-Teeuwisse AK (2014) Pediatric drug formulations: A review of challenges and progress. Pediatrics. 134(2): 361-372.
- 3. Lajoinie A, Henin E, Kassai B (2015) Choisir la forme pharmaceutique orale la plus adaptée à l'enfant. Arch Pediatr. 22:877-885.
- Chai G, Governale L, McMahon AW, Trinidad JP, Staffa J, et al. (2012) Trends of outpatient prescription drug utilization in US children, 2002-2010. Pediatrics. 130:23-31.
- Venables R, Batchelor H, Hodson J, Stirling H, Marriott J (2015) Determination of formulation factors that affect oral medicines acceptability in a domiciliary paediatric population. Int J Pharm. 480:55-62.
- Montastruc JL, Bondon-Guitton E, Abadie D, Lacroix I, Berreni A, et al. Pharmacovigilance: Risks and adverse effects of self-medication. Therapies. 71:249-255.
- 7. Meyers R (2020) A wish list for drug development in pediatrics. J Pharma Sci. 109:939-943.
- 8. Karunajeewa HA, Kemiki A, Alpers MP, Lorry K, Batty KT, et al. (2003) Safety and therapeutic efficacy of artesunate suppositories for treatment of malaria in children in Papua new guinea. Pediatr Infect Dis J. 22:251-255.
- Schirm E, Tobi H, Vries T, Choonara I, de Jong-van den Berg L (2007) Lack of appropriate formulations of medicines for children in the community. Acta Paediatrica. 92:1486-1489.
- Charkaluk ML, Kalach N, El Kohen R, Kremp O (2005) Family use of ibuprofen in the febrile child: A prospective emergency study in a lillois hospital. Arch Pediatr. 12:1209-1214.
- 11. Di Martino M, Lallo A, Kirchmayer U, Davoli M, Fusco D (2017) Prevalence of antibiotic prescription in pediatric outpatients in Italy: The role of local health districts and primary care physicians in determining variation. A multilevel design for healthcare decision support. BMC Public Health. 17:886.
- Martir J, Flanagan T, Mann J, Fotaki N (2017) Recommended strategies for the oral administration of pediatric medicines with food and drinks in the context of their biopharmaceutical properties: A review. J Pharm Pharmacol. 69:384-397.

- 13. Andrieu V, Reynier JP (2004) La galenique au service de la securite chez lenfant. Therapies. 59:599-601.
- van Riet-Nales DA, Schobben AF, Vromans H, Egberts TC, Rademaker CM (2016) Safe and effective pharmacotherapy in infants and preschool children: Importance of formulation aspects. Arch Dis Child. 101:662-669.
- 15. Kristensen HG (2012) WHO guideline development of pediatric medicines: Points to consider in pharmaceutical development. Int J Pharm. 435:134-135.
- 16. Lopez FL, Ernest TB, Tuleu C, Gul MO (2015) Formulation approaches to pediatric oral drug delivery: Benefits and limitations of current platforms. Expert Opin Drug Deliv. 12:1727-1740.
- 17. Rautamo M, Kvarnstrom K, Siven M, Airaksinen M, Lahdenne P, et al. (2020) A focus group study about oral drug administration practices at hospital wards: Aspects to consider in drug development of age appropriate formulations for children. Pharmaceutics. 12(2):109.

- 18. Mistry P, Batchelor H (2017) Evidence of acceptability of oral pediatric medicines: A review. J Pharm Pharmacol. 69:361-376.
- 19. Yeung VW, Wong IC (2005) When do children convert from liquid antiretroviral to solid formulations? Pharm World Sci. 27:399-402.
- 20. Rehn C, Odouard E, Poncet F, Cochat P, Breant V, et al. (2018) Factors influencing the acceptability of galeniques formulations in pediatrics-revue de la literature. Ann Pharm Fr. 76:163-171.

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