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Oral Suspension as Versatile Galenic Formulation in Pediatry

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Abstract

In the last years increased the prescription of drugs in pediatry as pharmaceutical form of oral suspension. The same in commerce there are various producer that provide specific ready for use excipeints to make more easy to prepare OS in the galenic laboratory. Aim of this work is to verify the advantages of this pharmaceutical form to cover pediatrics dosages vs other form and also to overcome shortcomings of some crucial registered drugs. In this work are reported also scientific literature relates some ready for use product as bases- veicle for suspension and some formulations of interest.

Keywords: Pediatric Galenic Formula, Magistral, Oral Suspension, Chemico-Physical Property Shortcomings, API, Excipients, Ready for Use Veicle, Innovations.

INTRODUCTION

Oral Suspension are liquid pharmaceutical form and are used when: there is not a suitable solvent available to dissolve a specific drug, when the API in solutions show reduced stability, when is needed an more gradual absorbtion of the API vs solutions.

When an API is insoluble in water with suspension is possible to reach more higher concentration vs the solutions.

OS are generally more stable vs oral solution in example for antibiotics. The OS can mask the taste of a drugs and in order to have control release of the API. Other use in shortcomings of registered drugs or due by instability problem of the API. The same oral suspension can be an alternative to solid oral form like cps or cp (more easy to subministrate in pediatry, better swallowing).

A dysperse sysrem is a two phase system in which an insoluble phase (solid particles, or liquid droplets) Is distribuited trought an a coninuous phase. The solids particle have not all the same size. This are dispersion of solid into an liquid, with diameter about 0,5-1 µm a 100µm and insoluble or partial soluble into the disperdant medium.

The disperdent phase can be acquous (for internal use) or oleous (for esternal use). The solid particle can have affinity or not with the liquid. The liofilic ones with affinity can produce stable suspension with easy re- dispersion after sedimentation.

Instead the liofobic produce instable suspension (are needed tensioactive to reduce the interface tension). The tensioactive used are adsorbed aroud the solid particle producinc a monolayer between the two phases facilitating the production of a suspension. (wetting property).

Generally are used viscose veicle to reduce the sedimentation viscosity. In normal galenic pharmacy practice are used API or as pharmaceutic powder or using in example cp or cps.

Api in suspension show an higher rate of bioavaiability ther other pahramaceutical form: Soluzion> oral suspension>cps, >tablets > coated tablets Related the divantages: physical stability, sedimentation

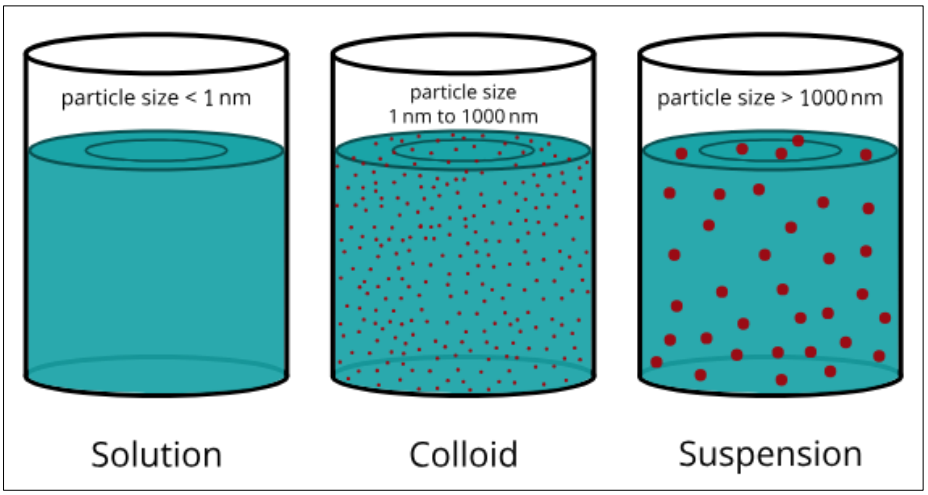

Fig. 1: solutions/ suspension particle size

The solid particle are interested int actractive forces like Van der Waals or repulsive (ions or electrical charges on their surface)

Between the formulation of interest are the suspending ages used excipients:

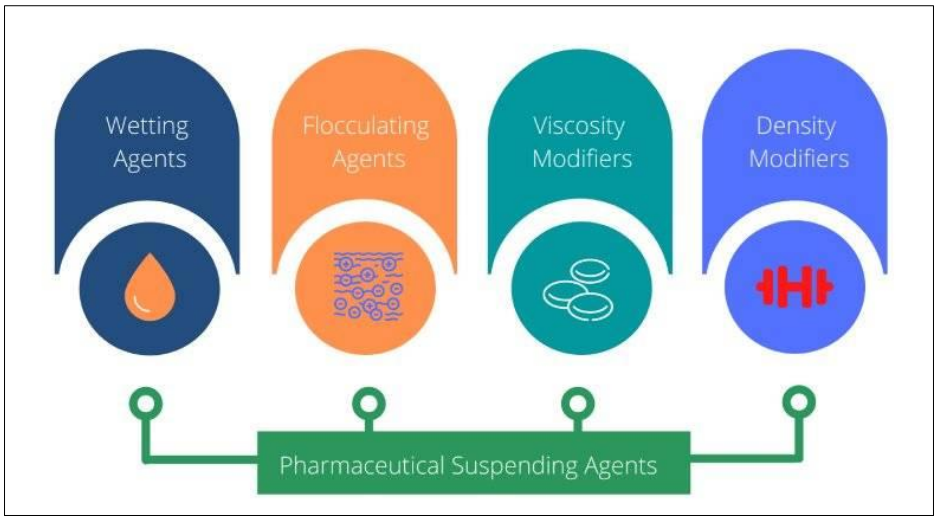

Fig. 2: https://pharmacentral.com/learning-hub/technical-guides/pharmaceutical-suspending-agents/ Pharmaceutical suspending agents

Suspending Agents: Idrophilic colloids that produces colloids dispersions, they acts on also on the viscosity: sodium alginate, metilcellulosae 1-2%, hydroxietilcellulose, hydroxypropyl cellulose, hydroxipropilmeticellulose.

Wetting Agents: surface active agents, hydrophilic collids, solvents

Flocculating Agents: electrolytes, ionic surfactants and polymer flocculating agents. (Starches Alginates, Cellulose ethers, Tragacanth gum, Carbomers, Aluminium silicate clays)

Viscosity Modifiers: polisaccarides like Acacia, Tragacanth gum, Sodium alginate, Starch and starch derivatives, Xanthan gum, Pectin

Water-Soluble Cellulose Ethers: To increase viscosity of aqueous systems in which they are dispersed: Methylcellulose Hydroxyethylcellulose, Sodium carboxymethylcellulose, and Microcrystalline cellulose, Hypromellose. (The viscosity-increasing properties of cellulose ethers depends on the molecular weight and degree level of substitution.)

Hydrated silicates are naturally-occurring siliceous clays that exist as colloids in water: Bentonite, Magnesium aluminium silicate Carbomers are high molecular weight cross-linked polyacrylic acid polymers that swell in water to produce viscous hydrogels depending on the degree of cross-linking.

Density Modifiers

From Stokes' law, it is clear that if the densities dispersed and dispersing medium are of the same magnitude sedimentation would be significantly slowed down.

So changing the density of the dispersing medium, in example, addition of glycerol, propylene glycol, polyethylene glycol or sucrose-based syrups, can significantly modify densities and leveraged to control the instability.

Other

Electrolites: Like alluminium clorure, allume that can induce negative charge on thse surphace of the solid particle increasing repulsion force.

buffers to contro le PH variation

Preservatives: for microbiological need (nipagin, k. sorbate, alcool)

Cosolvents: glycerol, sorbitol, propylen glicole

For the characteristics of the various excipents used it is possible to see HANDBOOK OF PHARMACEUTICAL EXCIPIENTS last version.

Stability of Oral Suspension:

Physical Stability: apparence, odour, taste PH, specific gravity, sedimentation, ZETA potential, compatibility with container, microscopic examination, cristal size, uniform drug distribution test.

Chemical Stability

API degradation change in viscosity

Antimicrobial property, incompatibility with preservant, degradation of preservant, adsorbion of the preservant on the API

Because often are water liquid formulation there is risk of microbial contamination.

The preservat agent used must to be compatible with the rest of the and API without interference with the stability of the suspension.

Because specific weight higer vs water phase it is clear that the particle will deposit also related size and other factors.

The sediment is tollerable if easily re-dispersible.

If it become compact, cake, with particle linked between them in various way, this particle will be re-dispersed in difficult way producing aggrgates with compromised disponibilirty of the API.

In magistral galenics the need to mix before the use contribute to reduce this phenomena. Instead in industrial product stoked for long time this risk can happen. To avoid this are used specific veicle with variou excipients.

Between physical factor that influence the stability it is possible to see: particle size, viscosity, electrical charge, suspensoid concentration, wetting agent and surfactants use.

According STOKES low sedimentation velocity is direclty proportional to the square of the particle diameter (too small or to large particle must to be avoided). Difference in density between the API and the suspension agents. (if API have a too much low density vs veicle it can float and can no to be produced good oral supension.

Browniam Movement:

Make possible to balance the gravity of the solid particle in the medium. ZETA potential related the particle charge; if the acctractive force exceed the repulsive it can happen the flocculation. In deflocculated system intead the repulsion forces are > the attraction. Flocculating agents can be electrolites like Nacl and phospate salts, tensioactives, gum, soluble cellulose derivates.

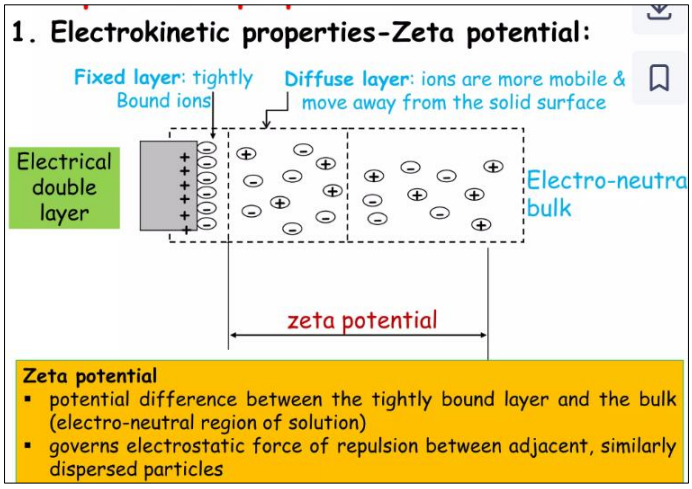

Fig. 3: form Hanieh: the ZETA potential

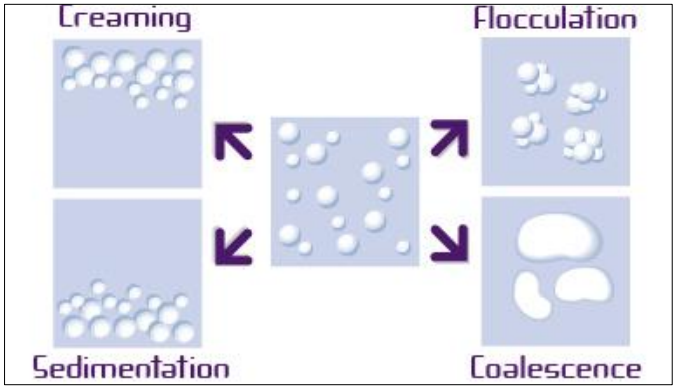

Fig. 4: destabilization process of liquid dispersion

Floculated Suspension:

are formed flocculi with liquid above the sediment re- dispersible usign light shaking. Deflocculated suspension: particle settle on the bottom linked more between them (cake), it is difficul to resuspend.

Fig. 5: from Sahib SUSPENSION deflocculated/ flocculated

According italian normative rules Legge 30 dicembre 2023, n. 214, articolo 16, “Preparazione dei farmaci galenici”, allow the use of pharmaceutical industry API in magistral formula.

And in a sentenza del Consiglio di Stato, (Sez. III, n. 4257/2015), it was recognized the legitimacy of the umpakaging of indsutria drugs in order to use the API in preparing a magistral formula - if not possible to proceed in other way, but clarifying that “it is needed to turn directly to the holder of the patent or to the distributor of the related drug.

Short Communication - (2024)
Enhancing Pediatric Care: The Importance of Oral Suspensions in Pediatric Drug Delivery
Samz Morg
27-Mar-2024, DOI: 10.21767/ipipr.8.01.009

"Pediatric oral suspensions are liquid dosage forms consisting of finely divided drug particles suspended in a liquid vehicle, typically water with additives such as suspending agents, flavoring agents, and sweeteners. Unlike solutions, which are homogeneous mixtures of drug molecules dissolved in a liquid, suspensions contain insoluble drug particles that settle over time and require shaking before administration to ensure uniform drug distribution."

And related the control in technical pharmaceutical for oral suspension:
check on suspension, granulometry, sedimentation and re -dispersibility, viscosity, density
accelerated aging, API title

Required by pharmacopeia in galenic lab.:
verify of the right procedure followed
check of the aspect
redisperibility of the phases
chek of the pakaging and its seal
right labeling also with conservation condition

But for this kind of galenic preparation is crucial also to consider the PH of the GI tract and its variation:
from J Fallingborg

"The intraluminal pH is rapidly changed from highly acid in the stomach to about pH 6 in the duodenum. The pH gradually increases in the small intestine from pH 6 to about pH 7.4 in the terminal ileum. The pH drops to 5.7 in the caecum, but again gradually increases, reaching pH 6.7 in the rectum."

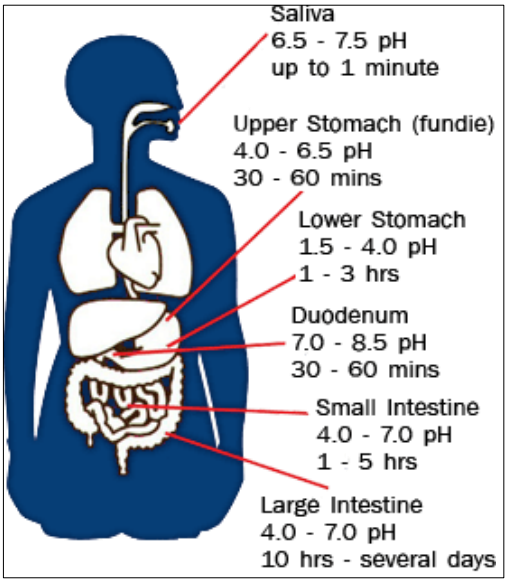

Fig. 6: from GI PH variation

The API can be in fact gastro sensible to the gastric acid fluids.

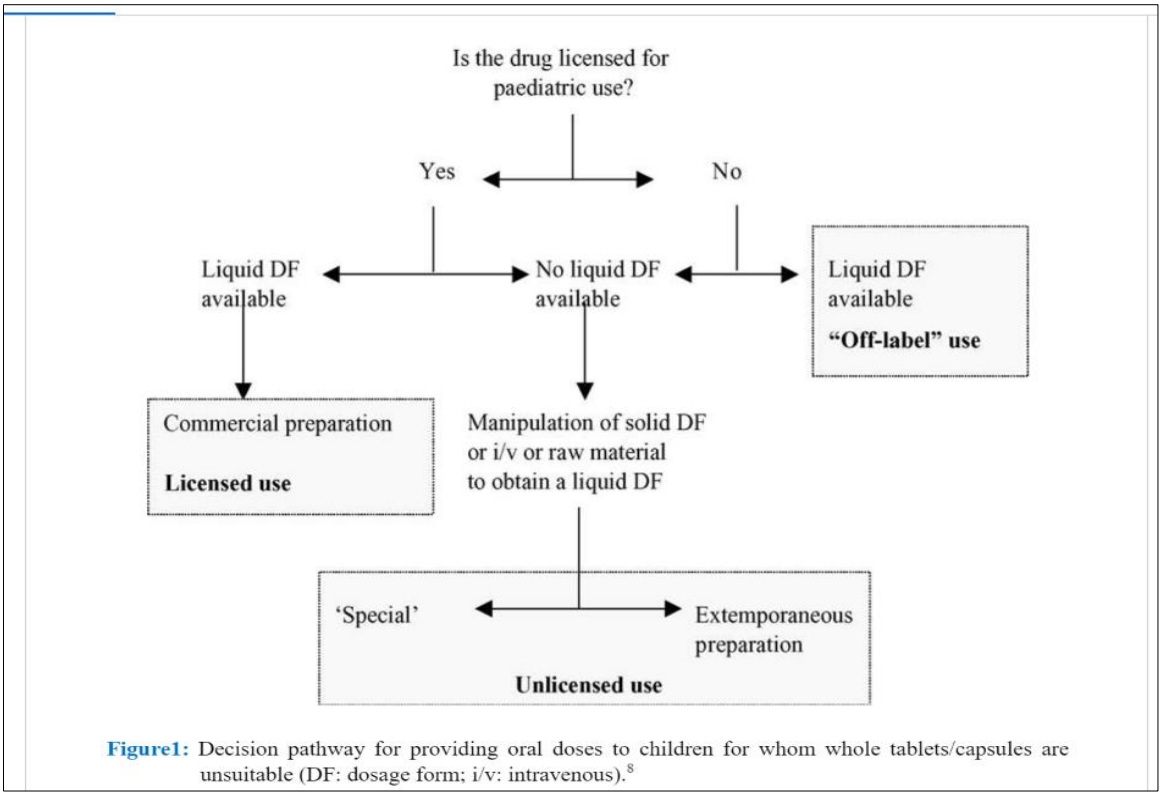

Figure1: Decision pathway for providing oral doses to children for whom whole tablets/capsules are unsuitable (DF: dosage form; i/v: intravenous).[8]

Fig. 7: from Pharmacophore EXTEMPORANEOUS DOSAGE FORM FOR ORAL LIQUIDS Vipul P. Patel, Tushar R. Desai, Bindi G. Chavda, Ridhi M. Katira

Pharmacy Services

COMPOUND EVALUATION FORM	
Compound Name: Captopril	**Container-closure system(s):** Amber Glass Bottle
Strength: 1 mg/mL	**Preservatives:** Ascorbic Acid
Dosage Form: Oral Solution	**Beyond Use Date (compound type):** 14 days (Room Temperature) or 56 days (Refrigerate)
Product Description: Solution	**Storage:** Refrigerate
Auxiliary Labels: Shake Well; Refrigerate	
Quality control procedures (ex: pH test, etc.): None	
Ingredients: Captopril 50 mg Tablets Ascorbic Acid (Vitamin C) 500 mg Tablets Sterile Water	

Fig. 8: from Nationwide Children's Hospital (using preservative: ascorbic acid)

From US PHARMACIST

Captopril 1 mg/mL Oral Solution

"Stability: The USP default beyond-use date for preserved aqueous oral liquids is 35 days. However, according to captopril stability studies, this formulation is stable for 14 days at controlled room temperature and for 56 days when refrigerated."

P T. 2018 May; 43(5): 258, 286.

Life-Threatening Errors with Flecainide Suspension in Children

Matthew Grissinger, RPh, FASCP

"Because it is available commercially only as 50-mg, 100-mg, and 150-mg tablets, it must be compounded into a suspension when needed for infants and small children. Unfortunately, errors during preparation and dosing of the suspension have occasionally led to serious overdoses that resulted in cardiac emergencies and required immediate therapeutic intervention. Overdoses can lead to seizures and cardiotoxicity, including ventricular tachycardia and fibrillation due to sodium-channel blockade. In hospitals, pharmacy labels should specify the dose in terms of both mg and mL, followed by the concentration, such as "Flecainide 5 mg (0.25 mL) 20 mg/mL suspension."

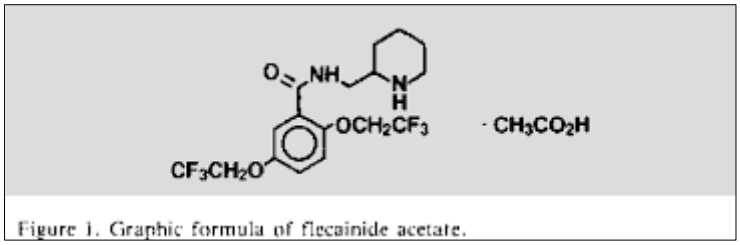

Figure 1. Graphic formula of flecainide acetate.

Fig. 9: flecainide acetate formula

Propranolol oral suspension 5mg/ml Procedure from Sickkids:

Equipment:

it is needed mortar and pestle glass stirring rod

graduated measure

Procedure:

Follow the Dept. procedures for risk assessment/training/PPE/equipment/facilities/NAPRA level

1. Crush tablets in the mortar to a fine powder with a pestle, or, soak tablets in a small amount of vehicle for at least 30 minutes.
2. Add a small amount of vehicle to powder and levigate to a smooth paste with a pestle. If soaked tablets, then levigate tablets into a smooth paste with a pestle. Continue to levigate as vehicle is added in small amounts until a liquid is formed.
3. Transfer liquid contents from mortar to graduate.
4. Use a small amount of vehicle to rinse mortar and add it to graduate.
5. Use vehicle to q.s.to the final volume. Stir well. Will be a very chunky suspension.
6. Transfer to amber bottle and label.
7. Let suspension sit for2-3 hours with intermittent shaking before using. Viscous chunks will fully dissolve into a smooth suspension.

SickKids®
THE HOSPITAL FOR SICK CHILDREN
Department of Pharmacy

propranolol 5 mg/mL Oral Suspension

Batch No: _____

Ingredients	Mfr	Lot #	Expiry Date	Quantity	Measured	Checked
propranolol HCL 40 mg tablets	APO/NOP			15		
ORA-Blend-SF	Perrigo			q.s.120 mL		

Fig. 10: Beyond-used date (BUD): 91 days at room temperature

From Preparation of extemporaneous oral liquid in the hospital pharmacy Márcio Robert Mattos da Silva, Letícia Pereira Dysars, Elisabete Pereira dos Santos, Eduardo Ricci Júnior Braz. J. Pharm. Sci. 2020; 56: e18358

"The stability of an extemporaneous suspension of 1.5 mg/mL propafenone was determined.

To prepare the suspension, 150 mg of propafenone tablet was triturated to a fine powder in a mortar, and then 100 mL of pomegranate syrup was added. The suspension was placed in an amber glass flask, where one flask was stored at 3-5 °C and the other at 15 ± 5 °C. In both storage conditions, the suspension remained stable for 90 days".

FORMULA

Sildenafil Citrate 2.5 mg/mL Oral Liquid

Rx (for 100 mL):	*Ingredient*		
	Sildenafil citrate		*250 mg*
	Ora-Plus:Ora-Sweet (1:1)	*qs*	*100 mL*

Fig. 11: US PHARMACIST sildenafil **oral liquid 2,5mg/ml formulation**

New Zealand standardised oral formulation batch sheet

Hydrocortisone suspension 1 mg/mL (100 mL)

Patient's name		**Storage condition**	**In a refrigerator**	**At room temperature**
NHI		Temperature	2-8°C	≤ 25°C
Date compounded		Shelf life	30 days	30 days
Batch number		Recommended storage	☑	May be stored at room temperature if this is more practical and temperatures greater than 25°C are avoided

Ingredients required and formula:

Ingredient	Supplier	Batch number	Expiry date	Standard formula	Quantity dispensed	Dispensed by	Checked by
Hydrocortisone 20 mg tablets				5 tablets			
Ora-Blend®	Perrigo			to 100 mL			
OR							
Ora-Plus®	Perrigo			50 mL			
Ora-Sweet®	Perrigo			50 mL			
Ora-Blend SF® or Ora-Sweet SF® (sugar free) can be substituted?				Yes			

Fig. 12: pharmaceutical society of New Zeland (Special instructions:1. Shake well before use.

2. Store in a refrigerator)

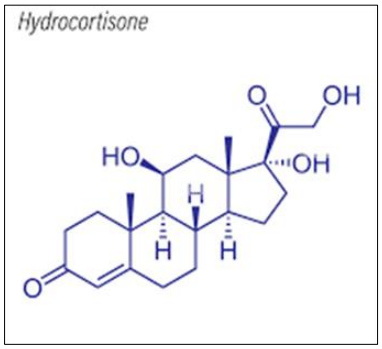

Fig. 13

Budesonide 2 mg/10 ml Oral Suspension is a homogeneous liquid medication, formulated to treat conditions such as asthma, allergic rhinitis, Crohn's disease, ulcerative colitis, and eosinophilic esophagitis.

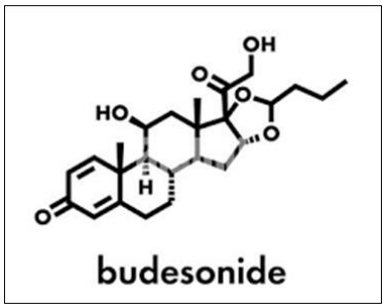

Fig. 14: budesonide

Budesonide oral suspension for eosifilic esofagitis: example of formulation:
Budesonide 200mg

Excipients:

Alcool 2ml, Saccarose 50g, Glicerol 10g, Sodio saccarinate 80mg, Carbossimetilcellulosa sodica 40mg, Sodio fosfato bibasico 735mg, Nipagina 100mg, Nipasolo 20mg, Aroma 0,2mg, water qb a100ml.

Int J Pharm Compd. 2020 May-Jun;24(3):246-251.
Alcohol-free Extemporaneous Formulations of Furosemide Are Chemically and Physically Stable in Ora-Blend Products for 30 Days

Darren Svirskis, Johaina Jaffer, Priyanka Agarwal, Ayeshah Khan, Jaskarn Kaur, Alan Cheng, Sara Hanning "Formulations containing 2 mg/mL furosemide were prepared by crushing furosemide tablets and mixing with commercial vehicles Ora-Blend, Ora-Blend SF, or SyrSpend-SF Alka."

From Bayview Pharmacy:
"Aspirin 20 mg/ml Oral Suspension is a liquid dosage form that contains aspirin uniformly dispersed throughout a liquid medium."

From UTIFAR technical italian union of pharmacist: oral suspension NIAPRAZINE 3MG/ ML
NIAPRAZINA 3 mg/mL
NIAPRAZINA 300 mg
BASE L. x SOSP. pH 4 ml 500 CILIEGIA qb a 100.0 Ml
(expiration data: 90 days if used this ready for use exipients formulation)

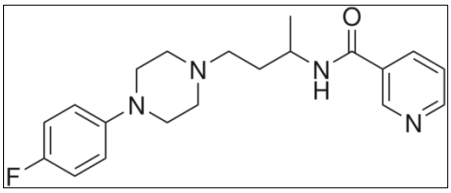

Fig. 15: NIAPRAZIN chemical formula

From Secundum artem vol 14 n.3 STABILITY OF EXTEMPORANEOUSLY PREPARED

ORAL LIQUID FORMULATIONS

"The Ursodiol 25 mg/mL oral liquid was prepared by counting out ten 300 mg ursodiol capsules.

The contents of the capsules were emptied into a glass mortar and comminuted well. Ten mL of glycerin was added and the mixture levigated to form a smooth paste. Sixty mL of Ora-Plus was added geometrically with mixing until a smooth mixture was obtained. The mixture was transferred to a calibrated 120 mL amber bottle. A small quantity of orange syrup was added to the mortar to rinse the remaining drug mixture and added to the bottle. Sufficient orange syrup was added to volume and mixed well.

From the results of this study, a beyond-use date of up to 60 days can be used for this preparation. The initial and final pH values for both temperatures did not vary outside the range of pH 3.5 to pH 3.7.13"

From SIFAP italian society of preparatory pharmacist galenic procedure:

5. FORMULAZIONE

5.1 Allestimento a partire dalla materia prima

Forma farmaceutica: Sospensione orale Amoxicillina (250 mg/5 mL)
Composizione quali-quantitativa

Ingredienti	**quantità**	
Amoxicillina triidrata	5,74 (equivalente a AMOXICILLINA 5 g)	g
Aroma ciliegia (o altro)	0,2	g
Destrosio monoidrato	30	g
Idrossipropilmetilcellulosa	0,8	g
Acqua purificata	q.b. 100	mL

Fig. 16: Amoxicillin oral suspension 250mg/5ml

From UTIFAR

example of one basis for supension ready for use in commerce: advantages for galenic pharmacist.

- it simplify the work of API slightly soluble in water;
- it make possible to prepare pfarmaceutical form safe, stable and easy to be also for patients with difficulty in swallow
- it make possible to personalyze the therapy and dosing for a wider target of patiens (pediatric-geriatric);
- it improve the reologic property of the preparation helping in preventing the sedimentation of the API, and making more easy the omogeneization of all components to assure maxim accurancy of the dosage;
- they have a pleasante taste good palatability and high masking power.
- withuot glutine, lattose and other allergizant
- without sugar and etanolo, heavy metals, solvents

Recently, USP pharmacopeia prioritized a list of formulations for development of CPMs for pediatric patients:
Aspirin compounded oral suspension 230 mg/ml Captopril, carvedilol, hydrocortison, bosentan, nadolol and other

Preparation of magistral oral suspension

It Must to be used mortar and pestel to treat and triturate the solid powders API and and the idrocolloide Then necessary to use the sift, then must to be added the wetting excipients mixing, add the preserved water since at final volume. If present tensioactive it must be dissolved before in a little amount of preserved water.

If used gum or cellulose derivates: the API is mixed in mortar and worked whit pestel with this mucillagin adding little portion of preserved water, with other water solution of the other component since total final volume requested.

In order to favor the preparation The polisaccaride can be wetting with idrofile liquids like glicerol, alcool, sorbitol (all excipient and its concentrations must to be present like the formulation requested).

From SIFAP procedure IBUPROFEN oral susp 100mg/ 5ml:

"The pharmacists can evaluate for the preparationof ibuprofen oral suspension the use of ready for use bases like: Base liquida per sospensione Acef; Base per sospensione orale Galeno; Fast Oral Solution Wagner – Farmalabor, SyrSpend SF PH4 Fagron; or other similar".

MATERIAL AND METHODS

Whit an observational point of view some relevant literature is reported as well as some formulations and some commercial product like ready for use basis. The figure reported (1-18) help in clarify some concepts.

An experimental project hypotesis is submitted After all this an global conclusioni s reported related the topic of this work.

RESULTS

From Literature

International Journal of PharmaceuticsVolume 657, 25 May 2024, 124169. Exploring paediatric oral suspension development: Challenges, requirements, and formulation advancements Sachin S. Gaikwad *et al*., https://doi.org/10.1016/j.ijpharm.2024.124169

"The main reason for the development of pharmaceutical suspensions PS is because of drug poor water solubility. Additionally, suspensions also aim to prevent the bitter taste of the API -therapeutic ingredients, and increase the oral absorption and bioavailability, as well as the drug stability." (1)

Hosp Pharm. 2020 Oct; 55(5): 314–322.
Oriana Boscolo *et al*.,

"It is well known that the chemical stability of OMZ omeprazole is a function of pH. OMZ is rapidly degraded at pH value below 7.4, but it is stable at alkaline condition (pH 9.5).4 For this r, OMZ is commercialized as oral dosage form like enteric-coated tablets ECT or extended-release capsules containing enteric-coated granules or pellets. The enteric coating protects OMZ from acid degradation in the stomach." (2)

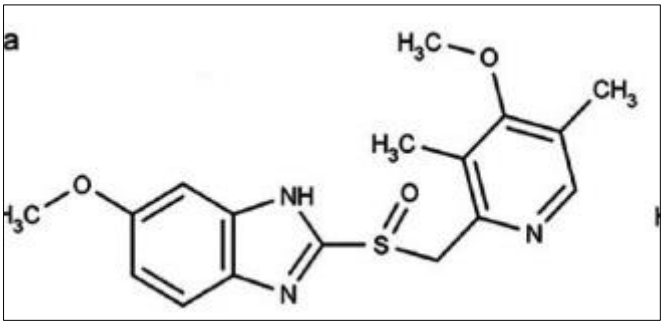

Fig. 17: Omeprazole

Paul A Whaley *et al*.,

"Omeprazole OMZ is available in both tablet and capsule form, with varying strengths of each. The need for other administration options for those patients who cannot take tablets or capsules has led compounding pharmacies to seek other alternatives. One alternative is the use of a suspending agent to create an oral solution or suspension OS. In the past, this has been accomplished using a sodium bicarbonate solution as the vehicle. Sodium bicarbonate/omeprazole OMZ combination imparts a bitter and unpleasant taste. SyrSpend SF Alka (reconstituted) is a vehicle for making a suspension which has a pleasant taste, thus increasing palpability and compliance." (3)

Christine M Geiger *et al*.,

"The API was considered stable if the suspension retained 90% to 110% of the initial concentration. Furosemide was stable for at least 14 days in the SyrSpend SF Alka at refrigerated conditions. Prednisolone sodium phosphate in the SyrSpend SF PH4 was stable for at least 30 days at room temperature and refrigerated conditions. Ranitidine hydrochloride suspensions in the SyrSpend SF PH4 at room temperature and refrigerated conditions were stable for at least 30 days and 58 days, respectively. Hydrocortisone hemisuccinate and sodium phosphate retained greater than 90% for at least 60 days at both room temperature and refrigerated samples in the SyrSpend SF PH4. Amiodarone hydrochloride and nifedipine suspensions at both room temperature and refrigerated conditions retained greater than 90% of the initial concentrations for at least 90 days in SyrSpend SF PH4. Refrigerated samples of simvastatin in SyrSpend SF PH4 were stable for at least 90 days. Spironolactone in the SyrSpend SF PH4 at room temperature retained more than 90% of the initial concentration for at least 90 days. Phenobarbital in the SyrSpend SF PH4 retained above 90% of initial concentration for at least 154 days at room temperature. (4)

Mercedeh Mansourian *et al*.,

"The stability of amoxicillin trihydrate oral suspension in SyrSpend® SF PH4 was investigated under storage conditions of 2–8 °C and 25 °C for 30 days. The results demonstrated that the formulation remained stable throughout the study duration in both the temperature conditions. At 25 °C, a decline of 5.62% was observed after 30 days, although no accompanying physical changes were noted." (5)

Marianne Bobillot *et al*.,

"In pediatric and neonatal units, oral liquid forms OLF are widely used, as solid forms are

contraindicated before the age of 6 due to anatomical and neurological immaturity. (7)

Khadija Rouaz *et al.*,

"The most toxic excipients in neonates are known to be Na benzoate, propylene glycol, methyl para hydroxybenzoate, propyl, sodium saccharine, benzyl alcohol, benzalkonium chloride, polysorbate 80 and ethanol. These excipients are used in formulations according to the study conducted" (8)

by Antonio Spennacchio *et al*.,

"To provide appropriate therapeutic care for pediatric patients, BU could be extemporaneously formulated as viscous oral suspensions VOS. The main limit of this therapy is the low residence time of the formulation on the esophageal mucosa that is not sufficient for the drug, which is suspended in a liquid vehicle, to solubilize and diffuse into the mucosa exerting its local anti-inflammatory action. This limitation is even more pronounced because of BU's low water solubility. To overcome this kind of problem, a new ready-to-use mucoadhesive viscous liquid vehicle, named Fast Oral Solution Wagner (B1), has been used. Utilizing ready-to-use liquid vehicles is a valuable strategy for creating extemporaneous formulations" (9)

EXPERIMENTAL PROJECT

In a public hospital (PC area) of about 700 beds and with pediatric wards and neonatal pathology
Time of observation 6 month from Jan. to June 2024
All pediatric request for oral solution or suspension (classic formula vs ready for use bases use)
Proportion of amount of prepared Oral solution/ suspension: 1/5

Total preparation = 100 (captopril, propranolol, flecainide, furosemide, sulfadiazin, Pirimetamin, niaprazin, hydrocortison)

Collection Of Data: by the galenic pharmacist

Evaluation Method: verify all written makjor non conformity related prepared orals suspension or solution

Results: No report of written mayor non conformity for both of this preparation in the same galenic lab.

One signal of not complete dissolution for an oral solution with an API whit a low water solubility (Sulfadiazin) and one Related a break of an oral suspension produced using a ready for use bases in proximity with expiration data (pirimetamin).

Note: The collection of the written non conformity is an admitted procedure in hospital settings

DISCUSSION

It's clear that the oral suspension in galenic practice are a real versatile kind of pharmaceutical form. Easy to be taken for children, are available varius ready for use excipient and easily prepared in the galenic labs.

It is clear also that the capsules preparation are a more complex procedure and take more time then the oral suspension. As innvoation are available ready for use bases that make possible to produce in more easy way this oral suspension. Necessary to verify the compatibility of the basis with the API: gastrosensible or not.

The chemico-physical global compatibility and microbilogical stability. The same it is necessary to verify the possibility of use or not specific excipient and their concentration related the age of the patients.

In every way It is mandatory in the label to write the concentration in mg / ml to avoir errors in subministration. To be added the label Narcotics if used relard API. It is needed to verify the dose related age or body weight in the prescription to avoid dangerous overdosage (expecially for API with strictly terapeutic index like Flecainide or other).

The final bottle must to be in preference way of dark glass in order to avoid light inactivation of some API.

Expiry Data:

30 days, but this limits can to be reduced or increased if are adopted specific measure for microbial protection and related the stability of the oral suspension.

The producers of ready for use vehicle provide generally written information about this:
In example 14 days for captopril without ascorbic acid as antioxidant, or 30 -60 -90 days for other API related a specific ready for use base. Temperature of conservation: can be at 2-8 grades for some API and room temperature for other based on the global stability.

In order to guarantee the right dosing, it is Needed to add the label on the bottle: NEEDED TO BE MIXED BEFORE THE USE.

Fig: 18

Special Instructions:

1. Shake well before use (before take the right dose with graduated siringe). 2. Store at adeguate temperature, keep out of reach of children.

Is needed a specific safety closing system to protect the children.
Mandatory to label with the conservation modality (temperature, light)
Needed to provide siringe dispensere graduated in order to make possible to measure the amount to be subministrated.

Expiry Data:

verify the indication of the producer of the ready for use bases related the specific API used or pharmacopea prescription for this kind of liquid preparations.

CONCLUSION

OS Because are versatile kind of galenic preparation: the pediatry can ask the preparation of oral suspension vs cps when possible.

This make possible to reduce the complexity in galenic lab reducing time and costs. This also because into the commerce there are various ready for use basis for many API. (Also for gastro sensible).

But it is mandatory verify the compatibility of this bases with the ready for use product or to ask to the pediatry. A classic oral solution formula with all excipients written into the prescription.

Related the Local Practical Experience Submitted: no difference in report of major non conformity between the classic formula and with ready for use bases.

As Conclusion: The pharmacist can use ready for use bases for oral suspension verifying the compatibility and safety with the specific API in order to simplify the procedure for OS.

Conflict of Interests: no

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