PHYSICOCHEMICAL CHARACTERIZATION OF LIQUID ORAL FORMULATIONS AND REVIEW OF THE LITERATURE FOR SAFE AND EFFECTIVE ADMINISTRATION BY ENTERAL FEEDING TUBES

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BACKGROUND AND IMPORTANCE

Although the choice of oral liquid forms facilitates administration in patients with enteral feeding tubes, it can cause adverse effects such as diarrhoea, vomiting or additional gastrointestinal intolerance associated with an osmolarity >500 mOsm/L, pH <3.5 and high sorbitol content of these preparations.

AIM AND OBJECTIVE

The objective of the study is to obtain updated data on physicochemical and gastrointestinal absorption properties from the main drugs marketed as oral liquid forms in order to establish practical instructions to increase the safety and efficacy of their administration by transpyloric tube.

MATERIALS AND METHODS

45 formulations were analyzed for which the pH, osmolality and density were experimentally determined in triplicate. In addition, the sorbitol content was reviewed from the descriptions of the technical data sheet. The pH was measured with a pH meter (Crison-2006, Hach-Lange-Spain, S.L.U., Spain). Osmolarity was determined using the Micro-Osmometer-Fiske Model 210 apparatus (John-Morris-Scientific Pty Ltd., Australia). The osmolality data provided (mOsm/kg), is multiplied by the density of the solution (g/ml) to obtain the osmolarity (mOsm/L). The density data was obtained with two Nahita densimeters with ranges of 1000-1200 mg/ml and 1200-1400 mg/ml.

RESULTS

Formulas tested with good bioavailability

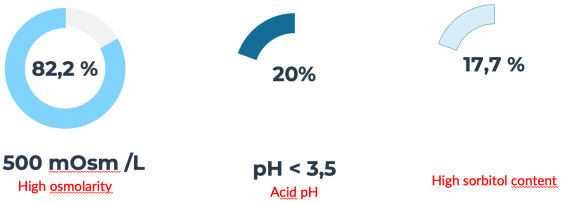
- Acetazolamide 25 mg/ml
- Allopurinol 20 mg/ml
- Amiodarone 5 mg/ml*
- Amlodipine 1 mg/ml
- Amoxicillin 50 mg/ml
- Amoxicillin clavulanic acid 100/12,5 mg/ml
- Atenolol 2 mg/ml
- Azithromycin 40 mg/ml*
- Caffeine 5 mg/ml
- Captopril 1 mg/ml
- Carvedilol 0,5 mg/ml
- Cefuroxime 50 mg/ml
- Cyclosporine 100 mg/ml
- Clonidine 20 mcg/ml
- Cotrimoxazole 8/40 mg/ml
- Dexamethasone 1 mg/ml
- Dexchlorpheniramine 0,4 mg/ml
- Digoxin 0,05 mg/ml
- Domperidone 1 mg/ml *
- Enalapril 1 mg/ml
- Spironolactone 10 mg/ml
- Phenobarbital 5 mg/ml
- Fosfomycin 50 mg/ml
- Furosemide 2 mg/ml
- Hydralazine 10 mg/ml
- Hydrochlorothiazide 2 mg/ml
- Ibuprofen 20 mg/ml
- Levetiracetam 100 mg/ml
- Levofloxacin 5 mg/ml
- Methadone 1 mg/ml
- Mycophenolate mofetil 200 mg/ml
- Midazolam 2 mg/ml
- Morphine hydrochloride 2 mg/ml
- Ondansetron 0,8 mg/ml
- Paracetamol 100 mg/ml
- Propranolol 1 mg/ml
- Sildenafil 2,5 mg/ml
- Sodium Valproate 200 mg/ml
- Tacrolimus 0,5 mg/ml
- Ursodeoxycholic acid
- Valganciclovir
- Voriconazole

Transduodenal and transjejunal
Transduodenal only
No information
Not recommended
*Recommended to increase the dose

Table 1. Physicochemical properties.

• High osmolarity	Acetazolamide, Allopurinol, Amiodarone, Amlodipine, Amoxicillin, Azithromycin, Caffein, Captopril, Carvedilol, Cyclosporine, Clonidine, Cotrimoxazole, Dexamethasone, Dexchlorpheniramine, Digoxin, Domperidone, Enalapril, Spironolactone, Phenobarbital, Fosfomycin, Hydralazine, Hydrochlorothiazide, Ibuprofen, Levetiracetam, Levofloxacin, Mycophenolate mofetil, Midazolam , Morphine hydrochloride, Ondansetron, Paracetamol, Propranolol, Sodium Valproate, Tacrolimus, Ursodeoxycholic acid, Valganciclovir, Voriconazole.
Acid pH	Captopril, Enalapril, Hydrochlorothiazide, Methadone, Midazolam, Propranolol, Valganciclovir.
High sorbitol	Captopril, Carvedilol, Dexchlorpheniramine, Domperidone, Phenobarbital, Hydralazine, Levofloxacin, Ondansetron.

Figure 1. Physicochemical properties:



CONCLUSION AND RELEVANCE

In most of the active ingredients studied, the gastrointestinal absorption of the drug is not sufficiently characterized, which generates uncertainty in its bioavailability when administered by transpyloric tube.
Most formulations have a high osmolarity, so prior dilution is necessary. The pH values of some of them can be an added factor for the development of digestive intolerances.

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