

EXTEMPORANEOUS FORMULATIONS FOR PEDIATRICS AND GERIATRICS

Presented by

Ayman Alameddine, RPh, Pharm.D

OPL 24th CONGRESS 19-11-2016

CONTENT

1. Introduction
2. Alternatives to formulation of oral liquids
3. Preparation of Oral liquids; Practices and Problems
4. Conclusions

مدة الانقطاع عن العمل:	مدة الانقطاع عن العمل:	Durée estimée du traitement :	المدة المقدرة للعلاج:
من	من	de	من
إلى	إلى	à	إلى
نوع العمل الطبي	نوع العمل الطبي	Traitements effectués par le médecin :	للمعاملات التي جراها الطبيب:
بدل الأتعاب	بدل الأتعاب	Ordonnance médicale Nbre	سلفة بية عدد
نفقات انتقال	نفقات انتقال	Une entente préalable	أفقة بقة

* الأدوية والعلاجات والفحوص الموصوفة

* Médicaments, traitements et examens médicaux prescrits

- Lasix (1cp = 40g)
- تذويت ربع حبة في ٥ ملل من الماء
- وارتظار ٥ دقائق ثلاث مرات يوميا
- Aldactone (1cp = 25mg)
- تذويت نصف حبة في ٥ ملل
- من الماء وارتظار ٥ ملل
- مرة يوميا

Nom et prénom du patient

Date de Naissance

C.17

* الأدوية والعلاجات والفحوص الموصوفة

* Médicaments, traitements et examens médicaux ordonnés

Inderal.

WT 4kg.

age 1 month

0,5 mg/Kg/day

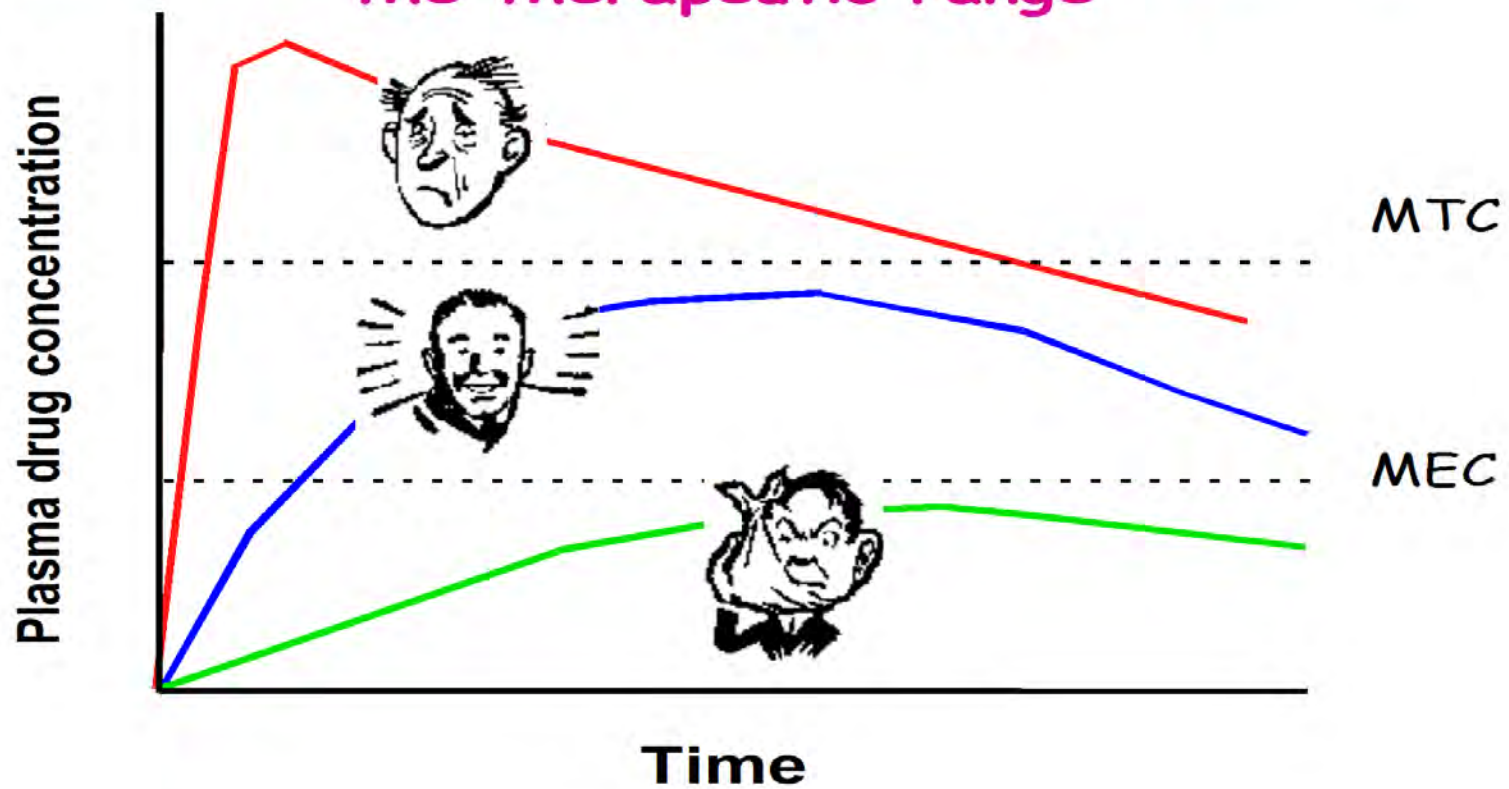
divided to 3 doses.

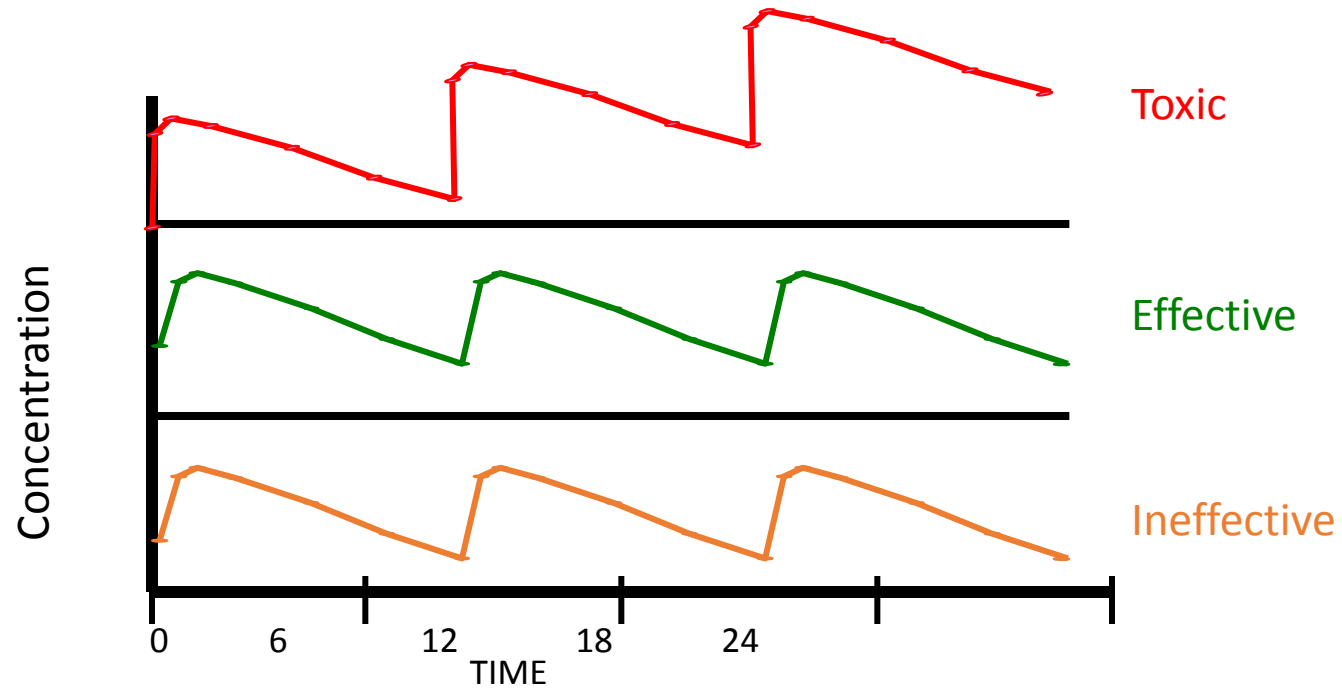
up

day



Need to keep concentration of drug within the therapeutic range





Propranolol 1mg/ml Suspension

MFG BY CHK BY

- Propranolol 40 mg tablets 3
- Water 2.4 mL
- Citric Acid 25% solution 0.5 mL
- Simple Syrup qs to 120 mL

• EQUIPMENT

- • Mortar and pestle
- • Graduated cylinder

- **PROPRANOLOL 1 mg/mL SUSPENSION**
- Refrigerate. Shake well.
- Date Prepared: Date Expired:
- **STABILITY**
- 45 days in fridge.
- **REFERENCE(S)**

- **MASTER FORMULA SHEET(LABEL) – NON-STERILE MANUFACTURING**
- **NAME OF THE PATIENT (KG?)**
- **PRODUCT: PROPRANOLOL 1mg/mL SUSPENSION**
- **POSODOLOGY: MG/KG/DAY ..ML/DAY(ACCORDING TO THE PRESCRIPTION**
- **Date Prepared: _____ FINAL**
PRODUCT CHECKED BY: _____
- **EXPIRY DATE: _____**
- **REF(2-8C)**
- **SHAKE BEFORE USE**

Introduction

- Pharmacists and Pediatricians are often faced with the problem of modifying an oral dose form intended for adult use into a suitable form for pediatric administration.
- The range of commercially available pediatric oral liquids and tablets is narrow because the relatively specialized use of these products makes industrial product development, manufacture and registration financially unattractive.



In the absence of a ready-made product a frequent approach by pharmacists is to prepare an oral liquid from tablets , capsules or powdered drug dispersed or dissolved in a suitable base.

Frequent problems are unpleasant taste, achieving dose uniformity and a lack of chemical and physical stability data.

Alternatives to formulation of oral liquids

- Tablet dispersion:

The practice of crushing tablets or opening capsules and adding the powder to a drink or sprinkling into solid food is a time-honored alternative , but there are few circumstances when this method is appropriate or necessary. It is difficult to ensure that a complete dose has been taken and the practice of nurses or carers handling powdered drug may present health concerns.

- If the tablet disperses readily and the drug is soluble , dispersing the tablet in a known volume of water allows a fractional dose to be accurately measured with a syringe as in the case of Captopril.
- In case of an insoluble drug , the measurement of a fractional dose by taking an aliquot from a suspension formed in this way cannot be recommended due to probable rapid sedimentation of insoluble drug and resultant dosage inaccuracy(e.g. Furosemide).

Oral administration of the injection

- This is possible for some drugs but there are important factors which must be considered when evaluating whether the injection is suitable for oral use. This can be illustrated with some examples.
- 1- If the injectable form of the drug is the same as the oral form (for example labetalol hydrochloride, ondansetron hydrochloride) it can be assumed that the drug will be absorbed from the injectable formulation.

- 2- The injectable form of drugs which are chemically degraded by gastric acid(for example omeprazole) are unsuitable for oral administration.
- 3- Drugs like cefuroxime and enalaprilat which are administered orally as pro-drugs (cefuroxime axetil and enalapril maleate) have relatively poor bioavailability and are not suitable for oral administration.
- 4- Injections may contain excipients and adjuvants that are undesirable in some patients. For example Ethanol, Propylene glycol.
- 5- the cost of using the injectable form orally is approximately 50 times the cost of using the oral form.

Preparation of Oral Liquids; Practices and Problems.

Issues Affecting Extemporaneous Preparations

- Stability
- Bioavailability
- Homogeneous mixture

- The expiry date or “Shelf-life” of an extemporaneously prepared oral liquid is assigned empirically or based on published information on a particular formulation.
- Therefore many references opinion that extemporaneously prepared oral liquids should only be used for a maximum of one month from the date of preparation to minimize any unrecognized product deterioration.

Microbiological Instability

- Microbial growth in an oral liquid may cause foul odor and turbidity.
- By-products of microbial metabolism may cause a change in the PH of the preparation and reduce the chemical stability or solubility of the drug.
- Microbial contamination during preparation must be minimized by using clean equipment , sterile water(Water for irrigation) and avoiding contaminated raw materials and containers.
- If sodium benzoate or benzoic acid are used as antimicrobial preservatives the final Ph must be less than 5 so that the active unionized form is predominant. Consequently the drug must also be stable at this pH.

Physical Instability

- Refrigeration, whilst usually desirable to maximize chemical stability and reduce microbial growth, can also increase the viscosity of a suspension making re-suspension more difficult or cause the precipitation of active drug or preservatives.
- It is important to consider the effect on PH of all components of the formulation and the possible impact on stability.

Chemical instability

- The most common reactions are hydrolysis , oxidation and reduction.
- The rate of chemical degradation usually increases with temperature , a factor which is the basis for accelerated stability trials of pharmaceutical formulations.
- Preparations made from tablets containing excipients may reduce chemical stability by changing the pH to a value at which more rapid degradation occurs.

- Deterioration of an oral liquid may be due to chemical , physical or microbiological instability which can lead to a sub-therapeutic dose of drug, exposure to toxic degradation products or ingestion of unacceptable numbers of micro-organisms.
- It is important for pharmacists and clinicians to be aware of potential problems caused by instability to ensure that drug therapy is effective and safe.

Conclusions

- Consider an alternative drug
- Consider an alternative method , for example, tablet dispersion or oral administration of the injection
- Consult the latest information data-bases and publications. Prepare a formulation according to a published study and follow the conditions of this study as closely as possible.
- A maximum expiry date of one month from preparation is recommended and liquids without an antimicrobial preservative should be given a shorter expiry date

- If there are no data from a published study consult pharmaceutical manufacturers, other pediatric hospitals and research centers.
- It may be possible to adapt existing information from drug stability texts(e.g. solubility, PH stability profile) or from the formulation details of the injection or oral liquid available elsewhere.
- Monitor use of the product and observe for any signs of physical instability such as color change or difficulty in re-suspension.
- Provide information to patients to ensure correct use of the product (e.g. storage conditions, use of an oral syringe , shaking before administration).

The 5 Rs

- Right drug
- Right route
- Right time
- Right dose
- Right patient



THANK YOU