

Literature review on swallowability of oral solid dosage forms in children

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# Overview

- Outcomes of a systematic literature review on swallowability of oral solid dosage forms in children
- > Analysis in recently approved paediatric products



# Search strategy

- Databases: Pubmed, Scopus, and Embase
- Keywords: ("paediatric" OR "pediatric" OR "children" OR "infant" OR "newborn" OR "adolescent" OR "teens" OR "youth" OR "teenagers") AND ("oral formulation" OR "oral dosage form") AND ("Satisfaction" OR "acceptance" OR "preference" OR "approval" "acceptability" OR "swallow" OR "palatability")
- Date: From the start of the source to May 2016
- Study selection: English, paediatric population, swallowing related



### Search results

- A total of 13 studies were identified on swallowability of oral solid dosage forms in children:
- Tablet (> 5 mm): 3
- Mini-tablet (1-4 mm): 7
- Capsules: 3



### Search results - tablets

	Formulation factors							
Formul -ations	Size	Shape	Coating	Drug content	Age	Disease status	Methodology	Reference
Tablet	7mm	Round	Uncoated	Ketoprofen 25 mg	1-9 years	Post-surgery	Questionnaire	(Kokki, Nikanne et al. 2000)
	5mm and 8mm	Round	Film coated	Levamisole 5, 10, 25 or 50 mg	2-11 years	Healthy	Observation	(Kreeftmeijer- Vegter, de Meijer et al. 2013)
	7mm	Cylinder	Wax coated	placebo tablets	6-11 years	Healthy or had dermatologic and/or respirat- ory diseases	Observation	(Meltzer, Welch et al. 2006)



# Search results – mini-tablets

	Formulation factors							
Formul- ations	Size	Shape	Coating	Drug content	Age	Disease status	Methodology	Reference
Mini- tablet	3mm	Round	uncoated	Placebo (single tablet)	2-6 years	Attend outpatient clinic	Observation	(Thomson <i>,</i> Tuleu et al. 2009)
	2mm	Round	Uncoated	Placebo (single tablet)	6 months – 6 years	Attended hospital	Observation	(Spomer, Klingmann et al. 2012)
	2mm	Round	Coated and uncoated	Placebo (single tablet)	6 months – 6 years	Attended hospital	Observation	(Klingmann, Spomer et al. 2013)
	2mm	Not specifie- d	Enteric coated	Pancrelipas-e	6-30 months	With cystic fibrosis	Questionnaire	(Van de Vijver, Desager et al. 2011)
	4mm	Round	Uncoated	Placebo (single tablet)	1-4 years	Healthy	Observation	(van Riet-Nales, de Neef et al. 2013)
	2mm	Round	Uncoated	Placebo (single tablet)	2-28 days	Attended hospital	Observation	(Klingmann, Seitz et al. 2015)
	2mm and 3mm	Round	Uncoated	Placebo (5-10 tablets with jelly)	2-3 years	Attended health clinics	Observation	(Kluk, Sznitowska et al. 2015)

# Search results – capsules

Formul- ations	Formulation factors							
	Size	Shape	Coating	Drug content	Age	Disease status	Methodology	Reference
Capsule	Increasing sizes	Gelatin capsule	Uncoated	Placebo	3-13 years	HIV infection	Observation (training effects)	(Czyzewski, Runyan et al. 2000)
	Increasing sizes	Gelatin capsule	Uncoated	Placebo	4-21 years	HIV infection	Observation (training effects)	(Garvie, Lensing et al. 2007)
	#4	Gelatin capsule	Enteric coated	Typhoid vaccine	4-12 years	Healthy	Observation	(Mekmullica and Pancharoen 2003)



# Challenges in assessment methodology

- Study design
- Population
- Formulation factors
- Swallowability criteria



# Study design

- Questionnaires
- Interviews
- Clinical trials
- Observational study





# Population

#### > Age groups

Preterm newborn infants	Term newborn infants	Infants and toddlers (1m- 2y)	Pre-school children	School children	Adolescents (12-18y)
0 -28 days	0 -28 days	1 months – 2 years	2- 5 years	6 – 11 years	12 – 18 years

 $\succ$  Healthy *v*s with particular diseases



### **Formulation factors**

- > Size
- > Shape
- Coating
- Taste/smell
- Mouth feel
- > Number



### Swallowability criteria

- Do we need a set criteria?
- How can we vary the criteria for different cases, e.g. particular diseases, different formulations?
- > Chewing
- Risk of choking/coughing



### An analysis on recently approved paediatric products

- A database search on EMA approved pharmaceutical products was conducted
- Date: Jan 2007 to May 2016
- All approved products for oral use in paediatric populations (0 18 years) were selected
- Different dose strengths were treated as separate products



#### Number of products

# Minimum age approved

Number of products Newborn 1 m - 2 y 6-11 y 2-5 y 12-18 y total

\* Newborn: include products for paediatric use but no age specification



# Products for newborns





### Products for 1 month – 2 years



#### **Tablet shapes**



#### Tablet sizes (oblong types)

Min length: 14.2 mm Max length: 17.6 mm



### Products for 2 - 5 years

Number of products



#### **Tablet shapes**



Tablet sizes (round)

Diameter: 7 mm

Tablet sizes (oblong types) Min length: 9.3 mm Max length: 19.6 mm



### Products for 5-11 years



#### Tablet shapes (include MR)



#### Tablet sizes (round)

Diameter: 7 mm

Tablet sizes (oblong types) Min length: 12.3 mm Max length: 16.5 mm



### Products for 12-18 years



#### Tablet shapes (include MR)



#### Tablet sizes (round)

Min diameter: 6 mm Max diameter: 10 mm

Tablet sizes (oblong types)

Min length: 8.1 mm Max length: 22 mm



# Thank you!

