Self-emulsifying drug delivery systems loaded with apple peel extract for the prevention of intestinal inflammatory disease in children

Greta Cucci[1], Chiara Migone, Anna Maria Piras, Ylenia Zambito, Angela Fabiano

Deparment of Pharmacy, University of Pisa

g.cucci@studenti.unipi.it

Introduction

Apple peel extract contains polyphenols that have potent anti-inflammatory properties useful against intestinal inflammatory diseases [1]. However, the bioavailability of polyphenols after oral administration is really low. An efficent drug delivery system form could be represented by self-emulsifying drug delivery systems (SEDDS). These systems are composed of active ingredients, oils/lipids, co-solvents, and surfactants, which, once they reach the gastrointestinal lumen, form a finely dispersed emulsion, increasing the absorption of the active ingredients and protecting them from the intestinal environment. Thus, the aim of this study was to prepare SEDDS containing Annurca apple peel extract (APE) to prevent inflammatory intestinal diseases in childhood.

Methods & Results

1. Characterization of APE

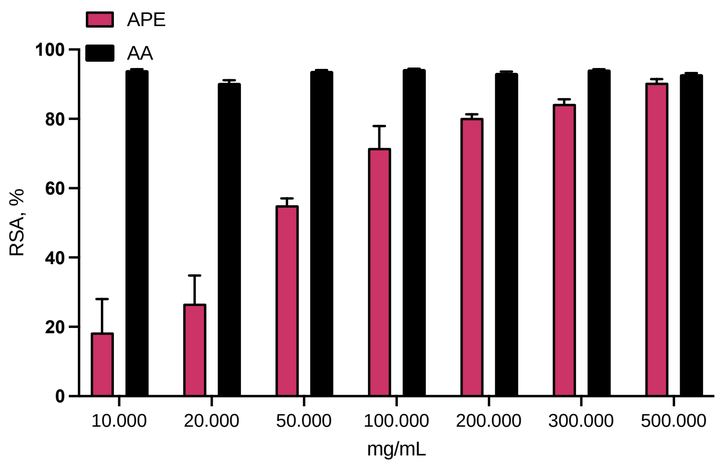
The total polyphenols content was determinated by the **Folin-Ciocalteau** cholorimetric method and by **High Pressure Liquid Cromatography**.
The antioxidant capacity was determinated using the DPPH assay. The absorbance was measured at 517 nm.

$$\% \text{ inhibition} = \frac{Abs_{control} - Abs_{sample}}{Abs_{control}} \times 100$$

The IC_{50} (concentration scavenging 50% of radicals) was 43.68 mg/mL, points out a good antioxidant activity of APE.

TPC	Chlorogenic acid	Quercetin	Catechin	Epicatechin
0.29± 0.01	0.66 ± 0.11	0.1± 0.03	0.04± 0.01	0.02± 0.01

Composition of APE



Scavenging activities of different concentrations of APE on the DPPH radical

2. Preparation and characterization of SEDDS

The APE (400 µl) was mixed with glycerin in ratio 2:3 and added under stirring to a mixture of Tween® 80 and Capmul in ratio of 5:1.

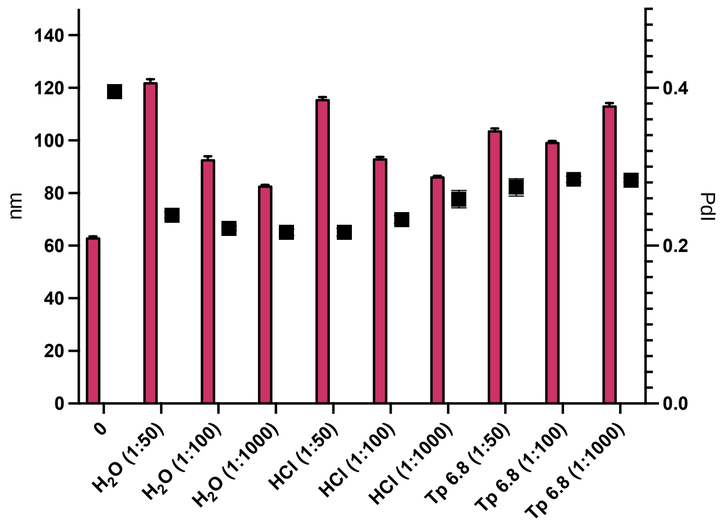
Size, nm	PdI	ζ, mV
63.25 ± 0.29	0.39 ± 0.11	-7.23 ± 0.94

Characteristics of SEDDS-APE

The PdI values as well as ζ-potential values pointed out that SEDDS-APE had good uniformity in distribution and good stability.

Robustness to dilution and pH

This study was carried out to investigate the effect of dilution and pH on SEDDS-APE following oral administration.

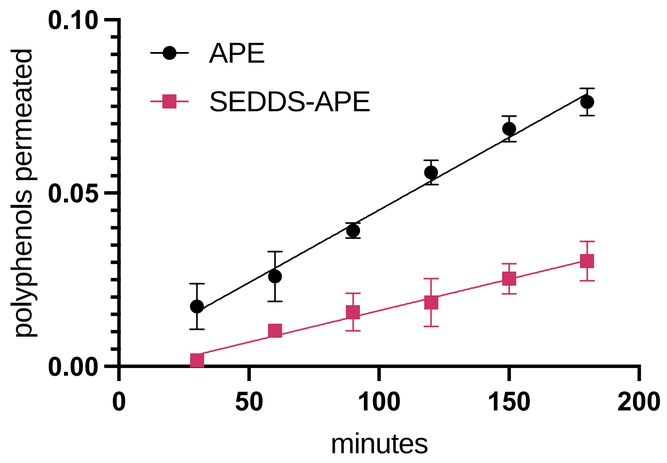


Effect of dilution in different media of SEDDS-APE.

An increasing in sizes was observed already after 50-fold dilution in water. However, this increase does not exceed the limit for reconstitution of emulsion into gastrointestinal fluids and indicated the stability of SNEDDS upon change in the volume and pH of gastrointestinal tract that reflects a decrease in PdI values.

3. Ex-vivo permeation study

The intestinal mucosa was excised from non-fasting male Wistar rats weighing 250–300 g. The excised intestine was cut into strips and mounted in Ussing-type chambers without stripping off the underlying muscle layer.
The apical to basolateral transport of polyphenols was investigated.



SEDDS-APE are able to increase the gastrointestinal residence time of polyphenols contained, suggesting their potential use in gastrointestinal inflammatory diseases.

Formulation	Flux 10^4 (mg cm^{-2} min^{-1})	P_{app} 10^3 (cm sec^{-1})	EPR	T_{4h} (mg cm^{-2})
APE	4.19 ± 0.21	1.50 ± 0.08	2.30	7.63 ± 0.40
SEDDS-APE	1.82 ± 0.18	0.65 ± 0.06	-	3.04 ± 0.57

Data on polyphenols apparent permeation across excise rat intestine

Conclusions

APE had a good content of polyphenols and a high antioxidant ability. When APE is encapsulated in SEDDS forms droplet with size less than 200 nm, which may be easily reconstitured upon contact with gastrointestinal fluid. Studies of polyphenols intestinal permeation indicate that SEDDS-APE increase the intestinal residence time of polyphenols contained suggesting their potential ability to protect the intestine from invasive bacteria, thus fortifying the intestinal mucosa. [2]

Reference

[1]Lamperi, Lavinia, et al. "Polyphenol levels and free radical scavenging activities of four apple cultivars from integrated and organic farming in different Italian areas." Journal of Agricultural and Food Chemistry 56.15 (2008): 6536-6546.
[2]Lee, Jin-Hyung, et al. "Apple flavonoid phloretin inhibits Escherichia coli O157: H7 biofilm formation and ameliorates colon inflammation in rats." Infection and immunity 79.12 (2011): 4819-4827.

Acknowledgments

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AZIENDA AGRICOLA "LA GALLUCCIO" DAL 1997 DI ANTONIO GALLUCCIO

Author reference: Greta Cucci; g.cucci@studenti.unipi.it