

Investigation and development of propranolol hydrochloride oral solid formulations designed for paediatric patients

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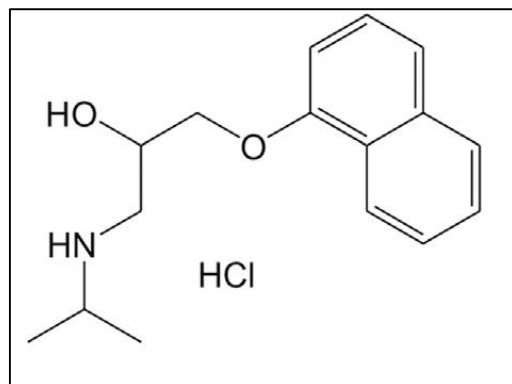


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SUMMARY OF THE STUDY

ACTIVE PHARMACEUTICAL INGREDIENT PROPRANOLOL HCl

THERAPY



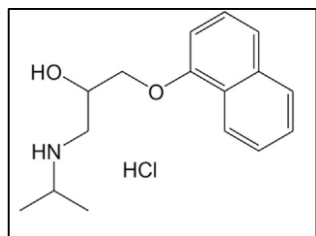
DOSAGE FORM



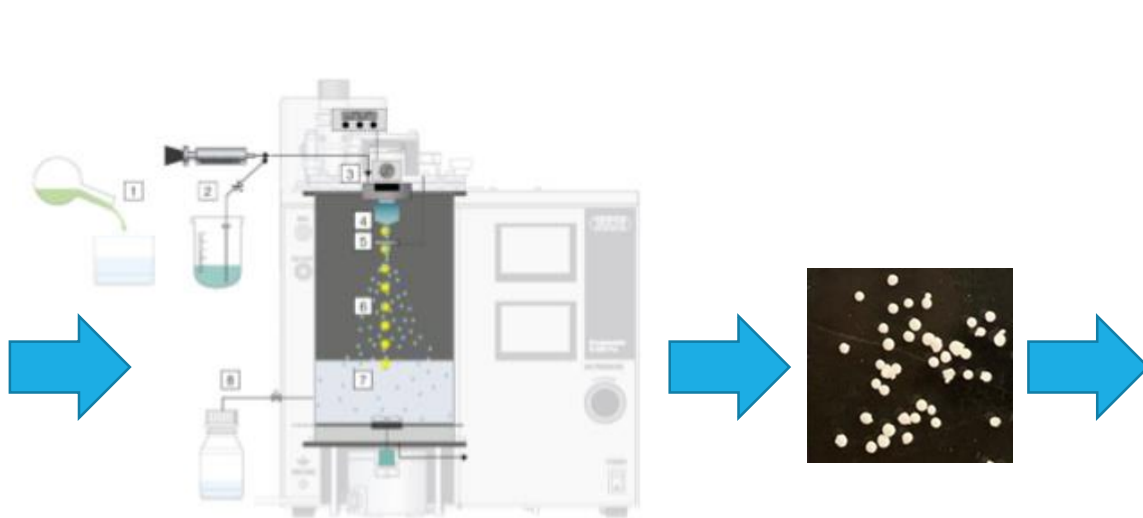
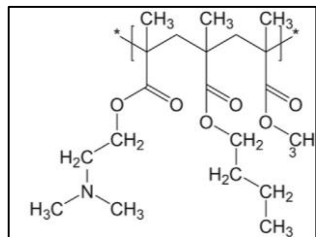
ORAL MULTIPLE-UNIT
DOSAGE FORM DESIGNED
FOR CHILDREN

OBJECTIVE

PROPRANOLOL HCl



EUDRAGIT® E PO



PRILLING TECHNIQUE
(ENCAPSULATOR)

MICROBEADS

DRUG
LOADING

MORPHOLOGY
(SEM)

RELEASE
STUDY

E-TONGUE

STABILITY



METHODS

Parameters used for the preparation of the microbeads by prilling.

Sample code*	Ratio PR/matrix (w/w)	PR (mg)	Volume processed (mL)	Nozzle size (µm)	Frequency (Hz)	Flow rate (mL/min)	Electrode potential (V)
F ₁	1:25	214.4	50	300	1500	23	2500
F _{1n}	1:25	214.4	50	450	1500	20	2500
F _{2n}	1:15**	357.3	50	450	1500	21	2500
F _{2t}	1:15	357.3	50	300	1000	14	1500
F _{2nt}	1:15	357.3	50	450	1000	12	1500
F _{3t}	1:10	536.0	50	300	1000	12	1500
F _{3nt}	1:10	536.0	50	450	1000	10	1500
A	–	–	50	300	1500	17	2500
A _n	–	–	50	450	1500	14	2500

* The codes (n) and (t) indicate a nozzle diameter of 450 µm and a feed in the vehicle water:tert-butyl alcohol (1:0.85 v:v) respectively.

** Theoretical ratio.

HPLC

Drug loading, encapsulation efficiency and stability

SEM

Morphology and inner structure

FT-IR and DSC

Drug/polymer compatibility and stability

Paddle Apparatus (2)

Drug release

Electronic Tongue

Bitterness

RESULTS

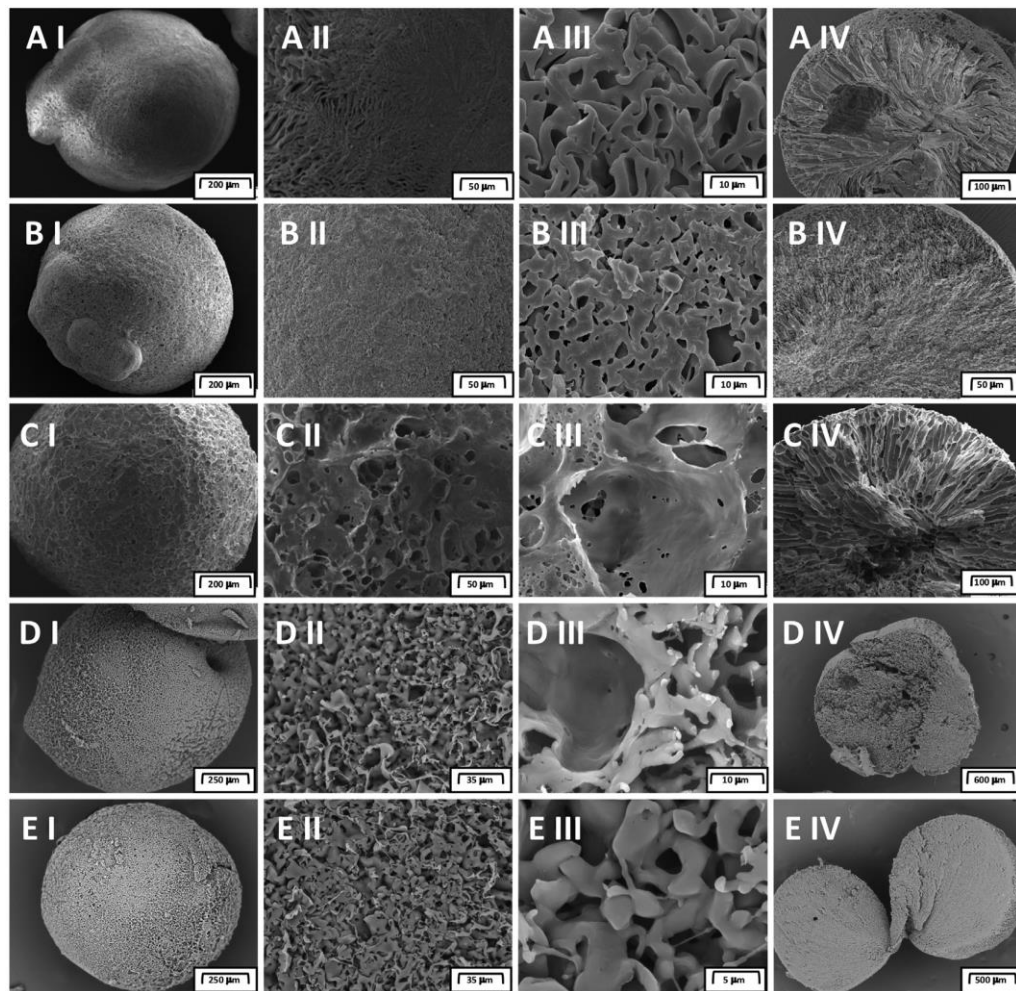
DL, EE % and percent of the yield of production, size of microbeads. Data are reported as mean of three results \pm SD.

Sample	Ratio PR/ matrix	DL*	EE %	Yield %	Size (μm)
F ₁	1:25	38.4 \pm 1.8	100.0 \pm 1.6	87.0 \pm 1.7	356.8 \pm 19
F _{1n}	1:25	38.4 \pm 1.5	100.0 \pm 1.2	89.0 \pm 1.5	663.5 \pm 38
F _{2n}	1:15**	22.0 \pm 1.6	22.4 \pm 1.8	18.0 \pm 0.8	699.8 \pm 25
F _{2t}	1:15	60.0 \pm 2.6	96.0 \pm 2.2	71.6 \pm 2.4	333.5 \pm 13
F _{2nt}	1:15	59.4 \pm 4.0	95.1 \pm 2.6	84.3 \pm 1.2	654.3 \pm 37
F _{3t}	1:10	76.5 \pm 1.9	84.0 \pm 1.8	90.2 \pm 2.0	354.2 \pm 22
F _{3nt}	1:10	74.3 \pm 5.6	81.6 \pm 4.4	80.2 \pm 2.4	648.6 \pm 24
A	–	–	–	98.2 \pm 2.1	327.5 \pm 29
A _n	–	–	–	99.1 \pm 1.8	663.6 \pm 38

* DL is expressed as mg of PR per g of microbeads.

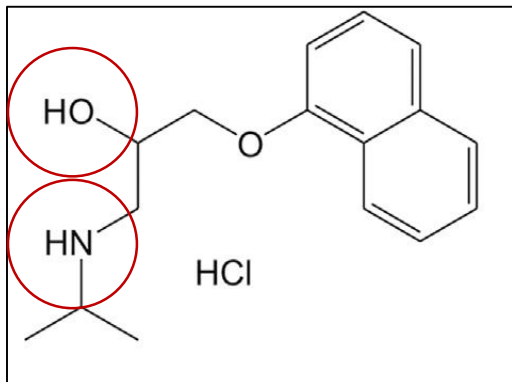
** Theoretical ratio, the effective ratio drug/matrix was 1:10.

RESULTS

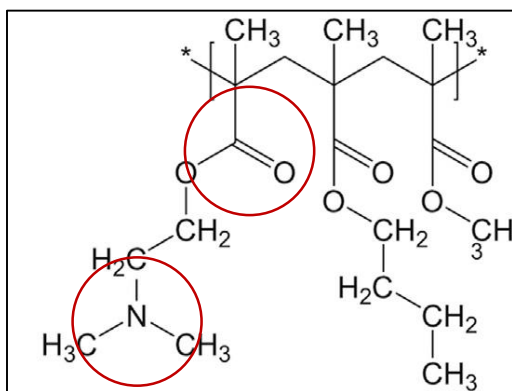


RESULTS

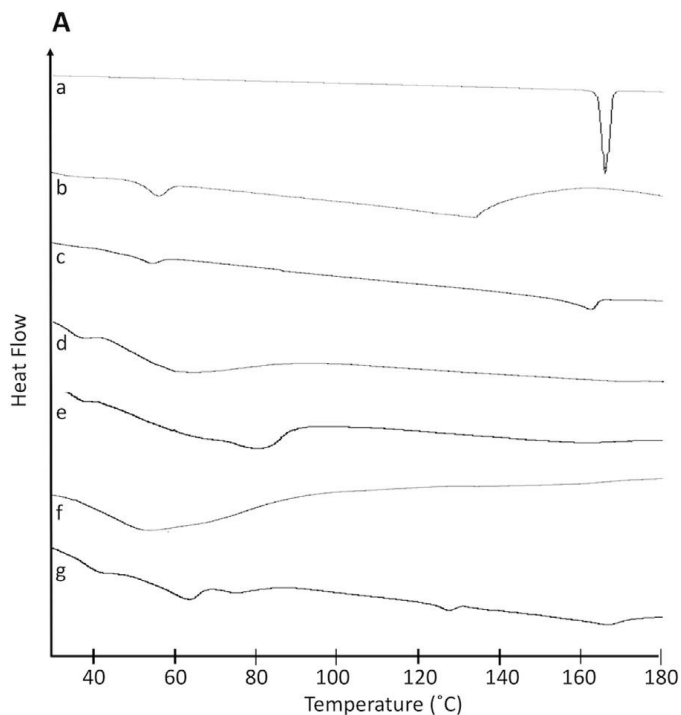
PROPRANOLOL HCl



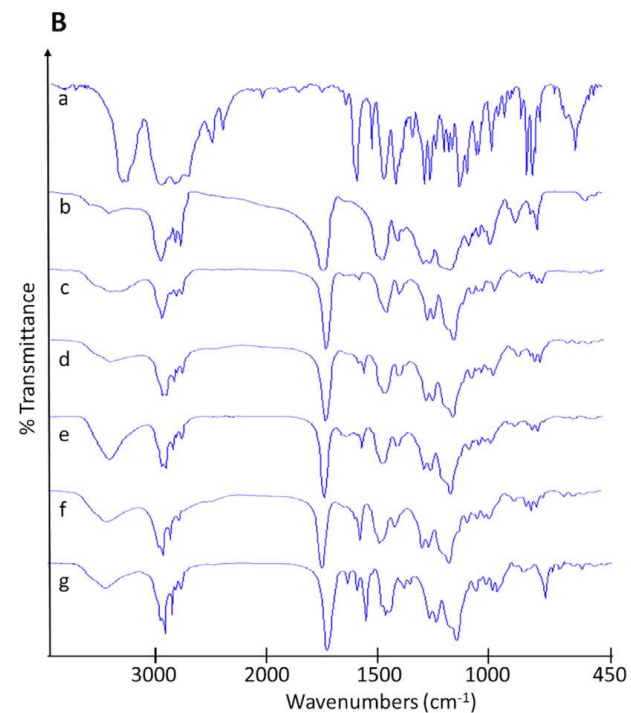
EUDRAGIT® E PO



DSC



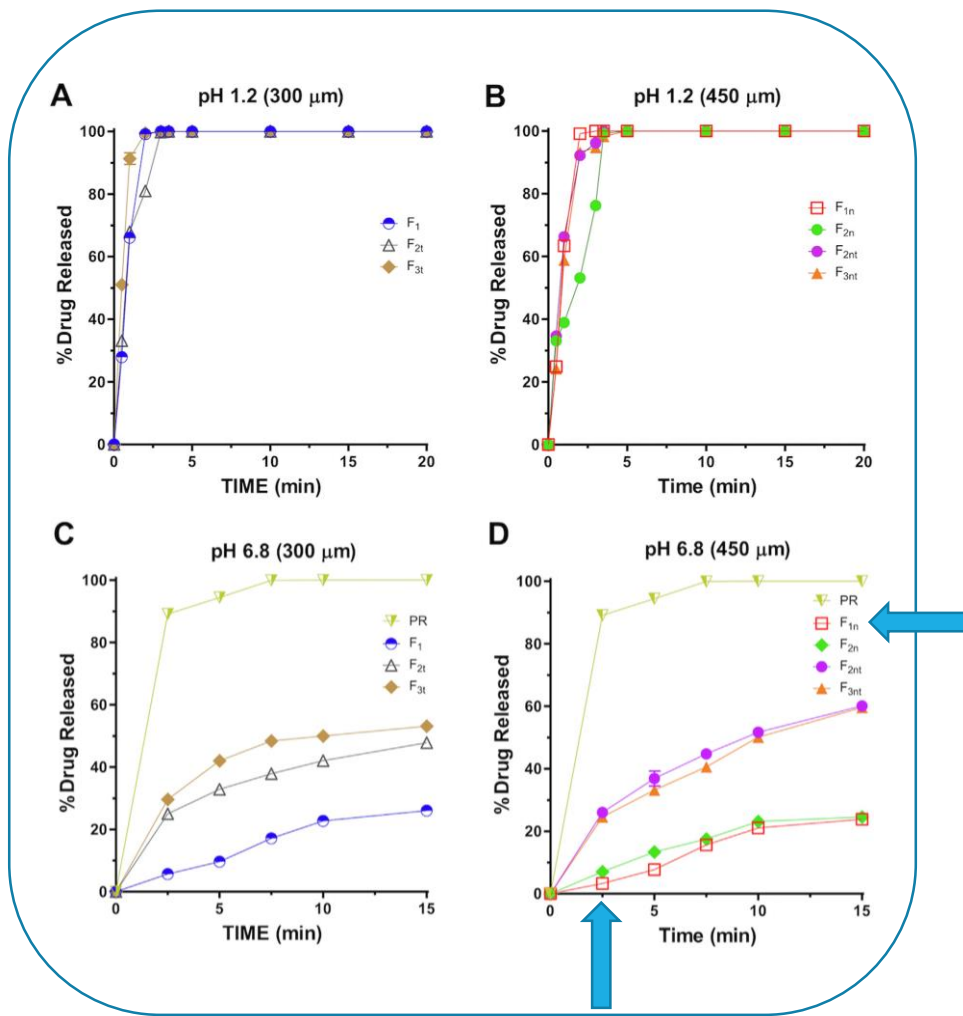
FT-IR



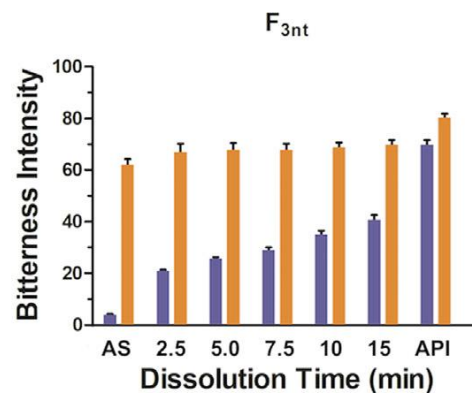
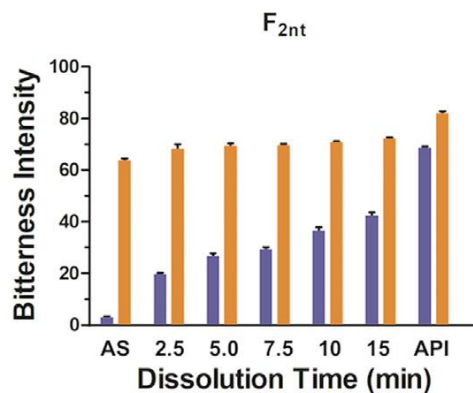
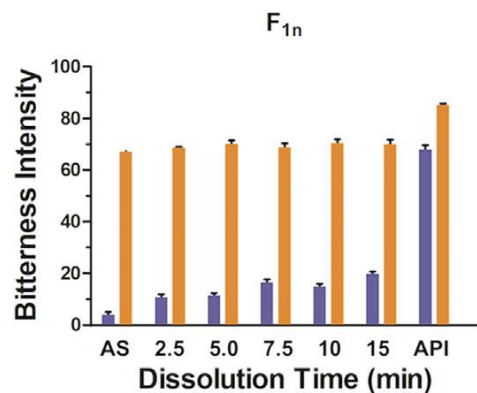
RESULTS

SIMULATED GASTRIC MEDIA

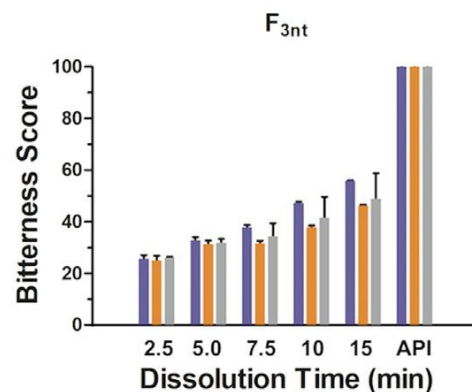
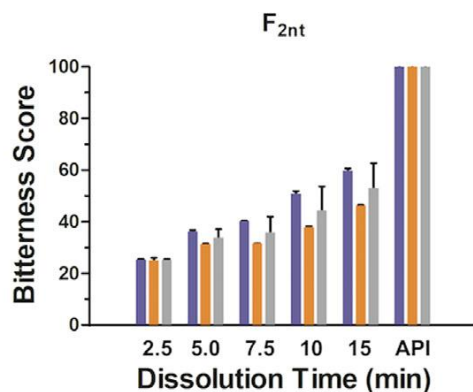
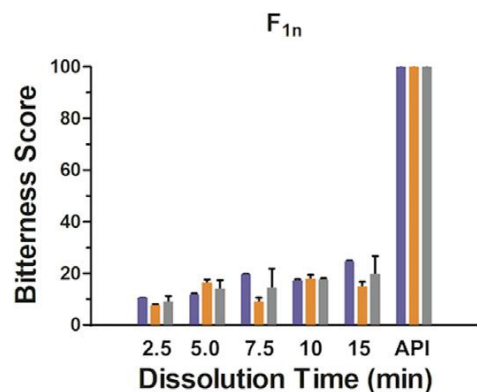
ARTIFICIAL SALIVA



RESULTS



■ Bitterness Intensity 1
■ Bitterness Intensity 2



■ Bitterness Score 1
■ Bitterness Score 2
■ Total Bitterness Score

CONCLUSIONS

PROPANOLOL HCl LOADED EUDRAGIT®
E PO MICROBEADS



Pediatric Dosage
Form



Flexible Dosing



Patient
Compliance by
Masking
Unpleasant Taste
and
Swallowability



Drug and
Formulation
Stability

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