Co-axially electrospun chlorpheniramine maleate fibres for paediatric drug delivery

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Objectives

- The aim of this study was to manufacture co-axial taste-masked fibres as a novel approach for paediatric drug delivery.
- **Eudragit E PO (EPO**), and **Kollicoat Smartseal 30D (KCT),** both taste masking polymers, were co-axially electrospun [Figure 1] with the bitter antihistamine Chlorpheniramine Maleate (CPM).
- The fibres produced were physically characterized and their functionality evaluated using an electronic taste sensing system (E-tongue) along the drug loading.

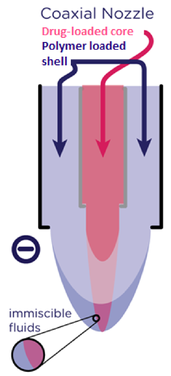

Figure 1. The co-axial nozzle. Adapted from www.spraybase.com

Experimental

Spraybase® electrospinning apparatus was used to co-axially manufacture CPM fibres. [Table 1] Applied voltage ranged between 15 and 20kV, gap distance between 12.5 and 17.5cm, and flow rate between 0.5 and 1 mL/h; these conditions were optimized in a previous study. EPO concentration was set at 35% w/v and KCT at 7.5% w/v; all systems contained 3.5% w/v CPM in the core of the fibres.

Table 1. The structure of the co-axial systems tested

Co-axial Sample	Core	Shell	Theoretical DL (%)	Actual DL (%)	Mean ± SD Diameter (nm)
1	KCT	EPO	Placebo	N/A	1220 ± 501
2	KCT	EPO	7.6	10.3 ± 0.9	795 ± 505
3	EPO	EPO	4.76	5.3 ± 0.2	616 ± 228
4	KCT	KCT	18.9	17.8 ± 3.6	967 ± 262
5	EPO	KCT	7.6	7.0 ± 1.6	633 ± 271

The core solutions were dyed with Rhodamine B and viewed under Texas Red light on an EVOS FL imaging system. To complement, SEM and TEM images were taken to assess fibre morphology and diameter distribution. XRD and DSC characterization of the fibres were completed to ascertain their solid-state. FTIR was completed to complement the solid-state characterization. Drug loading of CPM was assessed using UV spectroscopy. The co-axially electrospun fibres were taste-assessed using an Insent E-tongue.

Results

Figure 2 details the E-tongue mean sensor response; the lower the response the better the taste-masking.

- Sample 5 (KCT in the shell, EPO in the core) showed the best taste-masking efficiency. It had the same theoretical drug load as sample 2 (EPO in the shell, KCT in the core) , but with KCT on the surface of the fibre, as opposed to EPO for sample 2. KCT alone appears to show superior taste-masking to EPO.
- Sample 1 (EPO in the shell, KCT in the core), a placebo co-axial system shows a smaller response than EPO or KCT placebo fibres alone, which suggests an enhanced taste-masking response when both polymers are combined together.

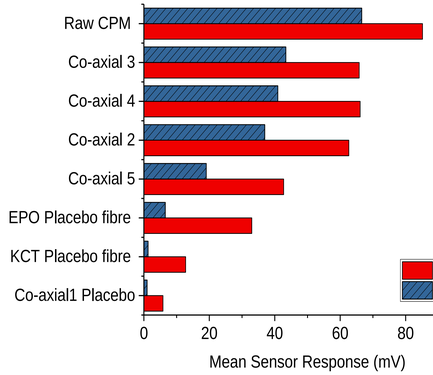

Figure 2. Mean sensor response of fibres to E-tongue. AC0 and AN0 represent two basic bitterness sensors.

The X-ray diffraction patterns [Figure 3] show diffraction peaks for the crystalline CPM alone, and a halo for the amorphous EPO.

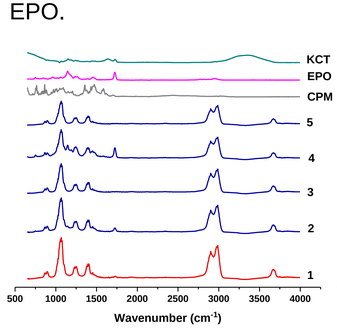

Figure 4. FTIR spectra of pure CPM, raw EPO, Kollicoat, and the 5 co-axial systems electrospun

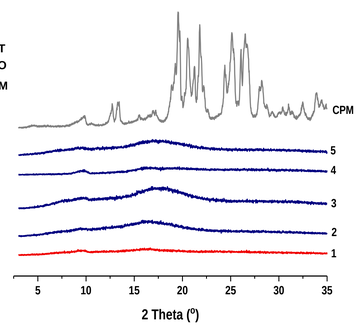

Figure 3. XRD diffraction pattern of pure CPM and the 5 co-axial systems electrospun

The drug loaded fibres showed no crystalline peaks suggesting a molecular dispersion of the drug in the polymer matrix. The DSC data showed complementary results. This is further consolidated by the FTIR spectroscopy [Figure 4]. Peaks confirm presence of the three components (EPO, KCT and CPM) in the co-axial system

As mentioned, sample 5 (KCT in the shell, EPO in the core) showed the most promising taste-masking results. The SEM, TEM, and FL microscopy images of the co-axial fibres in addition to the diameter distribution of the fibres are shown in Figure 5. The drug is present throughout the fibres as shown by the FL microscopy image.

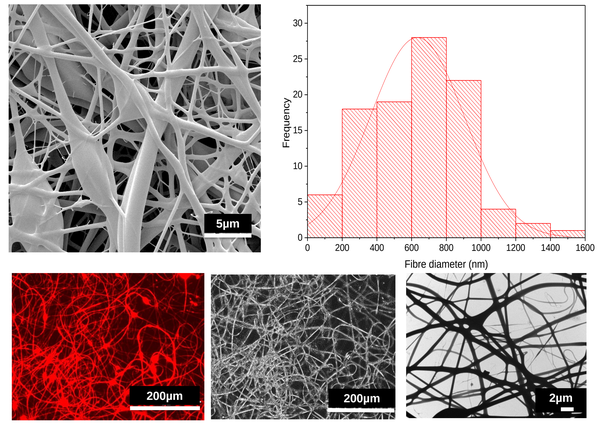

Figure 5. Clockwise: An SEM image of formulation 5; diameter distribution frequency histogram ; TEM image; optical microscopy and fluorescent microscopy images dyed with Rhodamine B and viewed under Texas Red filter

Conclusions

Co-axially electrospun fibres showed an improved taste response compared to raw drug, and is therefore a promising technique. Furthermore, as hypothesized co-axial electrospinning is an effective method of taste-masking. Combining two taste-masking polymers, EPO and KCT, improve the taste-masking effect as shown by the E-tongue.

Acknowledgements

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Pfizer