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Research Article

EVALUATING POLARCRILEX RESIN AS DIRECT COMPRESSION FILLER FOR THEOPHYLLINE TABLETS

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ABSTRACT

This work was aimed to evaluate theophylline tablets using polarcrilex (PLC) in comparison with microcrystalline cellulose (MCC) as direct compression filler. The results revealed that the morphology of tablet surfaces was affected by the type of direct compression fillers and content of theophylline. The diameter of theophylline tablets made from PLC and MCC was comparable, dispersing in the range from 9.53 to 9.55 mm. However, the tablets made from PLC had a larger thickness (3.11-3.60 mm) than that those using MCC (2.95-3.01 mm). At 0, 10 and 100 mg of theophyline, the hardness of tablets made from PLC i.e. > 50, 46.4 and 38.4 kg was higher than that made from MCC i.e. 41.7, 34.4 and 32.6 kg, respectively. However, they decreased to the comparable strength (27-28 kg) at 200 mg of theophylline. The PLC tablets containing 0, 10, 100 and 200 mg of theophylline completely disintegrated at 7.95, 6.25, 3.47 and 2.12, respectively, but MCC tablets did not within 60 min, thus exhibiting the faster drug release. The drug release from tablets made from PLC as well as MCC decreased as the theophylline content in the tablets was increased. In conclusion, PLC was a potential candidate for use as alternative direct compression filler for fast released tablets.

Keywords: Polarcrilex, Direct compression filler, Theophylline.

INTRODUCTION

Tablets are one of preferably used dosage forms because of easy preparation, convenient administration, accurate dosing, good stability, low price, etc[1]. Generally, they are prepared by either granulations or direct compression. The direct compression method receives increasing interest since it requires fewer relevant steps, instruments and time compared with the other method. Moreover, this method is suitable for drug substances that are particularly heat and moisture labile. Nonetheless, a sufficient hardness may not be obtained by the direct compression if the tablet contains a high amount of excipients and drug substances that have poor compressibility. According to this, direct compression fillers are developed specially for tablets prepared by the direct compression. They can be chemically classified into following categories namely cellulose (e.g. microcrystalline cellulose), starch (e.g. corn and rice starches), polyol (e.g. sorbitol), lactose, inorganic salt (e.g. dicalcium phosphate dihydrate), which may be used in a native, modified, physically mixed or co-processed form.

A number of researches have been conducted to find alternative direct compression fillers which are highly compressible or have multifunction[2-5]. For example, Kumar and Medina developed and evaluated modified cellulose II as multifunctional direct compression fillers for direct compression tablets. The ibuprofen tablets prepared by the modified cellulose II achieved the accepted disintegration and dissolution qualities without the addition of a disintegrant[4,5]. Polarcrilex (PLC) is a water insoluble crosslinked copolymer of methacrylic acid and divinylbenzene resin (Fig. 1)[6].

The resin possesses a weakly cationic exchange property, which is reported to have several pharmaceutical applications e.g. drug carrier, taste masker and disintegrant[6,7]. In this work, tablets containing theophylline and the resin were prepared by direct compression and evaluated, which was conducted in comparison with those using microcrystalline cellulose (MCC) as direct compression filler. The obtained result would inform the feasibility of PLC for additional application as alternative direct compression filler.

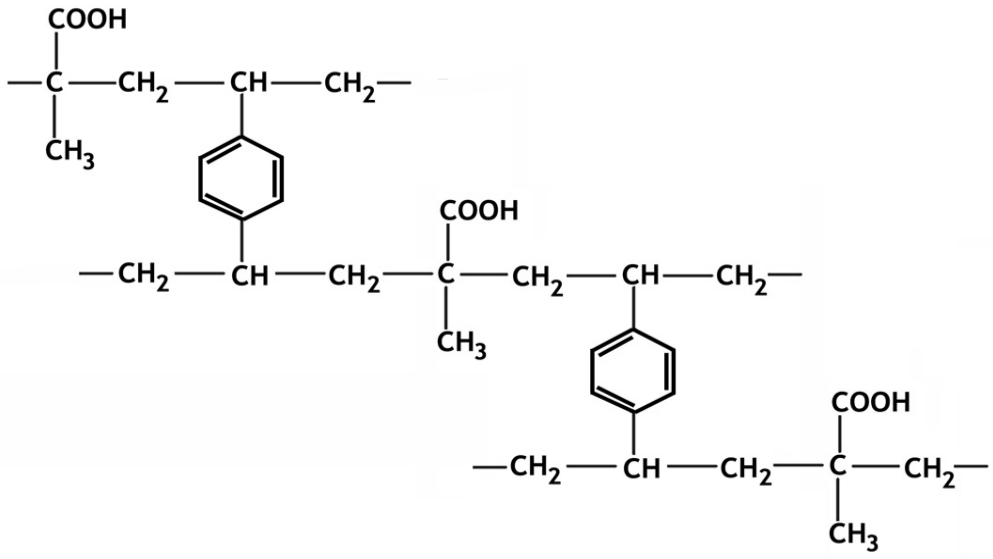


Fig. 1: The chemical structure of polarcrilex (PLC)

MATERIALS AND METHODS

Polarcrilex (Amberlite IRP 64®, Sigma Chemical Company Ltd., USA), microcrystalline cellulose (Avicel PH 102®, FMC Corporation, USA) and theophylline (Jilin Shulan Synthetic Pharmaceutical Company Ltd., China) were purchased and used as received.

Tablet preparation

Tablets containing the mixture of theophylline and PLC or MCC were prepared by direct compression on a hydraulic hand press machine (Specac P/N 15011/25011, UK). The total weight of each tablet was fixed at 300 mg, comprising 0, 10, 100 and 200 mg of the drug and a direct compression filler used (PLC or MCC). The mixture was blended for 10 min prior to compression using stainless steel flat-faced cylindrical punches (9.35 mm in diameter) at a constant pressure of 5 tons and dwelling time of 10 sec. Produced tablets were kept in sealed containers until evaluations.

Tablet evaluation

The thickness and diameter of ten tablets from each batch were measured by a dial caliper (Peacock G, Japan). The morphology of tablet surfaces as well as employed fillers was determined at a fixed magnification (× 500) by using a scanning electron microscope (SEM, CamScan MX 2000, UK). Before testing, the samples were fixed on stubs and sputter coated with gold in a vacuum evaporator (Cressington Sputter Coater 108, UK).

The hardness was determined by a texture analyzer (Stable Micro Systems TA.XT plus, UK). In this testing, ten tablets from each batch were individually pressed by a stainless steel flat-faced (6 mm in diameter) cylindrical probe moving at a constant speed (0.1 mm/s). The hardness was expressed in terms of the weight that caused a diametrical break in the tablet. The friability was tested by a Roche friabilator as follows. Ten tablets from each batch were weighed (m_0) and placed in the friabilator operating at 25 rev/min for 4 min. After removal of fines, the tablets were re-weighed (m_1), and the friability (%) was calculated by $100\times(m_0-m_1)/m_0$[8].

A USP disintegration tester (Sotax DT 3, Switzerland) was employed to determine the disintegration time of tablets[8]. In each run, six tablets from each batch were tested in deionized water maintained at 37±1°C. The disintegration time, at which the tablets disintegrated and passed through the assembly screen, was recorded.

The drug release of six tablets from each batch was determined by a USP basket dissolution apparatus (Dissolutest Prolabo, France). The measurement was conducted in 900 ml of deionized water maintained at 37±1°C, and the basket was rotated at 50 rev/min[8]. The test medium withdrawn at the interval times of 5, 15, 30 and 60 min was assayed by an ultraviolet spectrophotometer (UV, Agilent 8453 E, USA) at 272 nm. The percent of drug release was calculated by 100×released drug/assayed drug content. The drug content was assayed by the following procedure. Five tablets from each batch were crushed in a mortar. Thereafter, three portions of the crushed powder were weighed and separately placed in 250 volumetric flasks, and deionized water was added to adjust the volume. The slurry was stirred on a magnetic stirrer for 30 min, and the drug content was assayed by the UV method. The employed assay procedure was proven to exhibit > 98 % recovery.

Water uptake

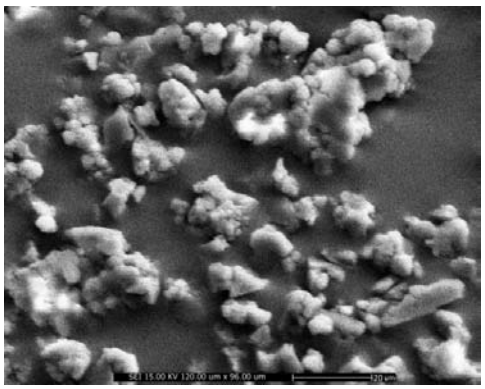
The water uptake of PLC and MCC was determined in triplicate by placing one gram of samples (w_0) on a wetted filter paper of which weight was recorded. Then, an excess of deionized water was added and left for 2 h to attain the equilibrium of water uptake. Thereafter, the excessive water was gravimetrically drained off, and the weight of water adsorbed sample was calculated (w_1) by subtracting the final from initial weight of the wetted filter paper. The degree of water uptake (%) was calculated by $100\times(w_1-w_0)/w_0$[9].

RESULTS AND DISCUSSION

Similar to using MCC as direct compression filler, the tablets containing 0-200 mg of theophylline were successfully prepared from PLC without capping. The diameter of these tablets dispersed in the range from 9.53 to 9.55 mm. The thickness of PLC tablets containing 0, 10, 100 and 200 mg of theophylline was 3.60±0.03, 3.49±0.06, 3.32±0.02, 3.11±0.02 mm, respectively. It was considerably thicker than that of MCC tablets, which was 2.95±0.03, 3.01±0.02, 2.97±0.01 and 2.95±0.02 mm for the tablets containing 0, 10, 100 and 200 mg of theophylline, respectively. The results additionally demonstrated that the thickness of tablets particularly made from PLC tended to decrease with increasing the containment of theophylline in the tablet.

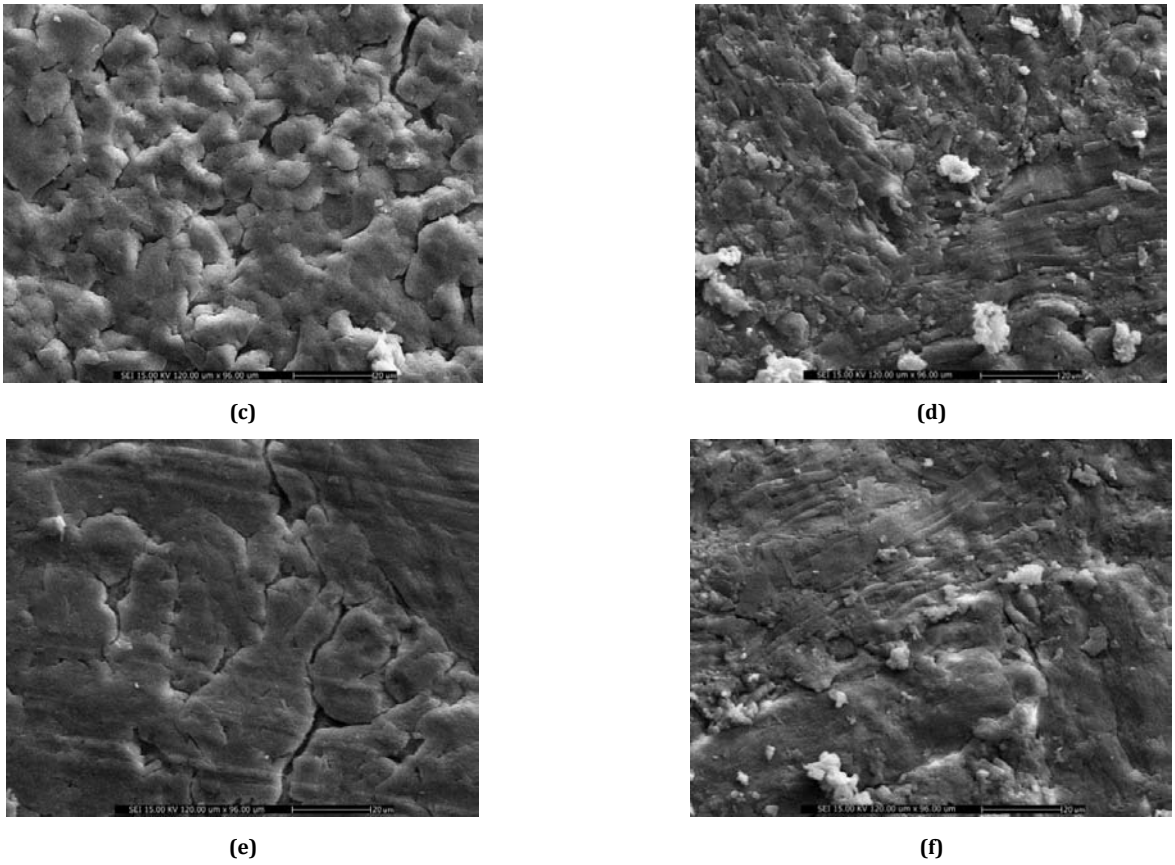
From SEM figures as shown in Fig. 2, the morphology of tablet surfaces was affected by the type of direct compression fillers and content of theophylline. At the low content (10 mg) of theophylline, the surface morphology of tablets using PLC and MCC was considerably different, somewhat depending on the starting morphology of direct compression fillers. The drug tablets made from PLC seemed to have rougher and greater porous surfaces than that made from MCC. However, an increase in the theophylline content enhanced the smoothness of tablet surfaces for PLC as well as MCC, which finally appeared similar due to prevalent proportion of the drug (200 mg).

The hardness of obtained tablets is illustrated in Fig. 3. The neat MCC tablet (41.7±1.0 kg) was softer than that of the neat PLC tablet of which the hardness was so high that the hardness tester could not measure (> 50 kg). At 10 and 100 mg of the drug, the tablets made from MCC were also softer than those made from PLC. Nonetheless, the MCC and PLC tablets containing 200 mg of theophylline exhibited the similar hardness (27-28 kg). The findings additionally demonstrated that the tablet hardness from both direct compression fillers decreased as the content of theophylline was increased. It might postulate that the apparent compressibility of theophylline was lower than MCC and PLC, respectively. It was also found that the decrease of hardness with increasing the theophylline content for the tablets made from PLC was more pronounced than MCC. This might inform that the dilution potential of PLC was inferior to MCC.



(a)

(b)



(c) **(d)**

(e) **(f)**

Fig. 2: The morphology of (a) PLC, (b) MCC, and the surfaces of (c, d) PLC and (e, f) MCC tablets containing 10 and 200 mg of theophylline

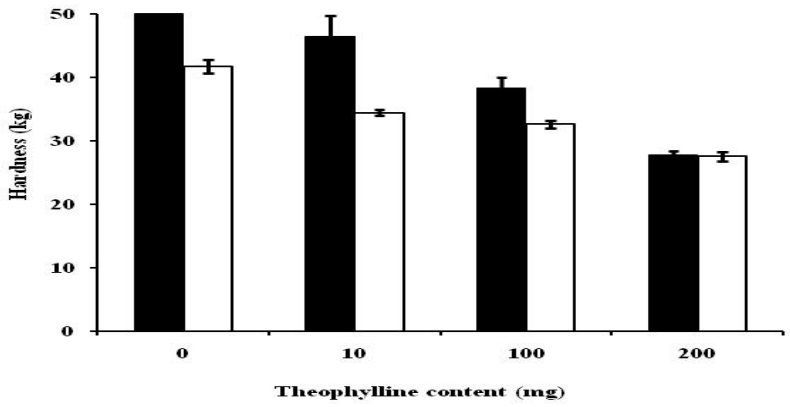


Fig. 3: The hardness of theophylline tablets made from (filled bar) PLC and (empty bar) MCC

The friability of 0, 10, 100 and 200 mg theophylline tablets using PLC was 0.02, 0.01, 0.23 and 0.47, while that using MCC was 0.02, 0.04, 0.07 and 0.42 %, respectively. It demonstrated that the friability tended to increase as the thephylline content increased, which corresponded to the decreased hardness of tablets (Fig. 3). However, the friability of all tablets was less than 1 %, which was acceptable according to the friability criteria set for USP pharmaceutical tablets[8].

The PLC tablets containing 0, 10, 100 and 200 mg disintegrated completely at 7.95±1.17, 6.25±1.02, 3.47±1.04 and 2.12±0.11 min, respectively. The decreased disintegration times with increasing the drug content well correlated to the decreased hardness of resultant tablets. This relationship could be found in published reports[10,11]. On the other hand, the tablets using MCC at all theophylline contents did not completely disintegrate within 60 min. An explanation for this might probably be due to the attribution that the carboxyl group (-COOH) of the resin was more dissociable, and thus had a higher affinity for water than the hydroxyl group (-OH) in MCC[1]. This consequently led PLC to exert a greater disintegrating action. To verify this, the water uptake of PLC and MCC was experimentally conducted. It was found that the degree of water uptake for PLC (155.6±2.9 %) was approximately twice greater than MCC (82.3±2.6 %), thus supporting the proposed explanation.

The release profiles of theophylline from the obtained tablets are shown in Fig. 4. The drug release of all theophylline tablets made from PLC was substantially faster than that made from MCC. This finding well coincided with the fact that the theophylline tablets made from PLC completely disintegrated, but those made from MCC did not. Disintegration brought about the tablet into finer pieces with increased surface area, thus promoting the drug release[12].

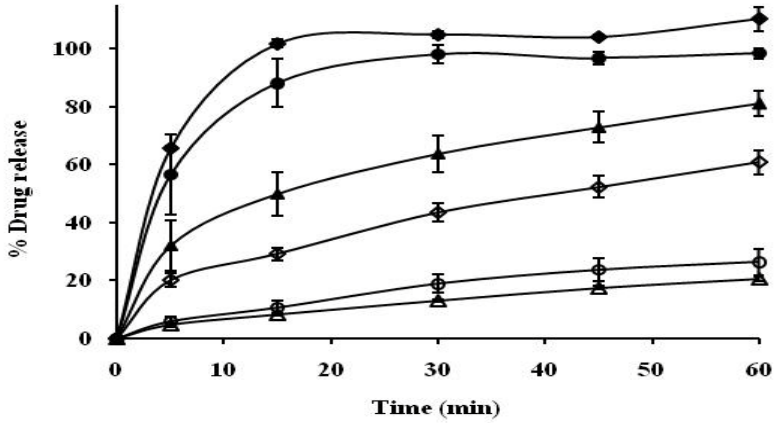


Fig. 4: Release profiles of (filled symbol) PLC and (empty symbol) MCC tablets containing (◊) 10, (○) 100 and (Δ) 200 mg of theophylline

Moreover, Fig. 4 revealed that the drug release was dependent on the theophylline content in the tablet. The PLC tablet containing 200 mg had a substantially slower release of drug than that containing 100 and 10 mg of theophylline, respectively, which was contrary to the shorter disintegration times observed. This might postulate that the effect of theophylline content on the release was primarily governed by the rate of drug dissolution rather than tablet disintegration. According to the Noyes-Whiney equation, the dissolution rate is proportional to the gradient between the drug solubility (C_s) and concentration (C_b) in the dissolution medium i.e. (C_s-C_b)[13]. It was usual that the tablet with the higher drug content would yield the higher concentration of drug dissolved in the constant volume of dissolution medium. Since the drug solubility was the constant parameter, this in turn reduced the gradient and hence rate of dissolution, thus resulting in the slower release for tablets containing the higher content of drug. Interestingly, this effect was also observed for the theophylline tablets made from MCC, which did not completely disintegrate. The assayed content of theophylline in the tablets made from PLC and MCC was found to be 9.57±0.08, 102.20±0.68 203.58±0.91, 8.91±0.02, 97.57±1.61 and 198.69±4.52 mg, which was close to 10, 100 and 200 mg of required contents, respectively.

CONCLUSION

Theophylline tablets using PLC as direct compression filler could be successfully prepared, which possessed high hardness and low friability (< 1 %). Furthermore, without the addition of a disintegrant, they exhibited faster disintegration and hence release of the drug as compared with those made from MCC. PLC was a potential candidate for use as alternative direct compression filler for fast released tablets although more assessments with other drug substances should be verified.

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