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Design and Fabrication of a Special Punch for Buccoadhesive Core-in-Cup Tablets

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A special punch was designed and fabricated to prepare buccoadhesive core-in-cup tablets by making protrusion in the 11 mm upper flat-faced punch. The buccoadhesive cups were prepared by direct compression method using polymers like carbopol 934P and hydroxy propyl methylcellulose on a Cadmach single station tableting machine. The cups were evaluated for uniformity of weight, depth and thickness.

Absorption of therapeutic agents from the oral mucosa overcomes premature drug degradation within the gastrointestinal tract, as well as active drug loss due to first-pass hepatic metabolism that may be associated with other route of administration. The oral cavity has a number of features that make it a desirable site for drug delivery, including a rich blood supply that drains directly into the jugular vein bypassing the liver and thereby sparing the drug from first-pass metabolism. Successful buccal delivery requires atleast three things, (a) a bioadhesive to retain the drug in the oral cavity and maximize the intimacy of contact with mucosa, (b) a vehicle that releases the drug at an appropriate rate under the conditions prevailing in the mouth and (c) strategies for overcoming the low permeability of the oral mucosa¹.

Buccoadhesive tablets consist of three layers, the core layer, the peripheral layer, and a backing layer, usually prepared by direct compression method as follows. The core layer is first compressed and is placed in a die cavity of higher diameter, then the peripheral layer material is added and compressed. Next the upper punch is raised; the backing layer material is added and compressed to get a buccoadhesive tablet². The tablets prepared by this method have certain drawbacks like more number of compressions (three times), non-uniformity in peripheral layer thickness and multidirectional release of the drug.

Agarwal and Mishra have prepared buccoadhesive compacts of pentazocine using 7 mm and 11 mm flat faced punches to prepare core layer and peripheral layer, respectively by compressing three times². Dinsheet *et al.* have prepared mucoadhesive buccal tablets of hydralazine hydrochloride using 9.6 mm and 13.6 mm flat faced punches to

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prepare core and peripheral layer respectively, by compressing three times³. Yukimatsu *et al.* have prepared transmucosal controlled release device of isosorbide dinitrate, which is a tablet shaped mucoadhesive system formulated without the peripheral layer and composed of two layers. The upper layer is a fast-release layer and the lower layer is a sustained-release layer, which is designed for placing between buccal and gingival mucosae⁴. Danckwerts has prepared core-in-cup tablets of theophylline and caffeine for oral route and showed that zero order release can be obtained from core-in-cup tablets⁵.

The buccoadhesive tablets prepared by the above methods have certain drawbacks like more number of compressions (three times) and non-uniformity in peripheral layer thickness. Due to this nonuniformity in peripheral layer thickness, drug release may not be unidirectional. Hence there is a need for a special punch, which reduces the number of compressions from three to two and avoids non-uniformity in peripheral layer thickness. To overcome the above said draw backs, a special punch was designed and fabricated to prepare buccoadhesive core-in-cup tablets. In the newly designed punches, the 11 mm upper punch has protrusion as shown in the diagram (fig. 1) and the 11 mm lower punch remained flat faced.

The buccoadhesive cup layer is prepared by using a mixture of bioadhesive polymers, Carbopol 934 P and HPMC K4 M in the ratio mentioned in Table 1. The cups were first prepared by placing the polymer mixture in the 11 mm die

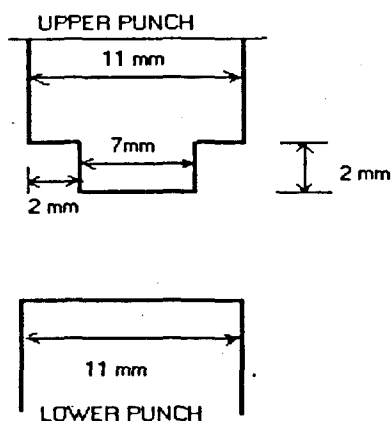


Fig. 1: Cross sectional view of the specially designed and fabricated punch.

The figure shows 11 mm upper punch with a protrusion of 2 mm and 11 mm flat-faced lower punch.

TABLE 1: COMPOSITION OF BUCCOADHESIVE CUPS.

Ingredients	Quantity per cup (mg) Carbopol: HPMC ratio			
	1:0	1:1	1:2	0:1
Carbopol-934P	145.5	72.5	48.5	0.0
HPMC K4M	0.0	72.5	97.0	145.5
Magnesium stearate (3%)	4.5	4.5	4.5	4.5

Powder equal to 150 mg was compressed into cup with different ratios of carbopol and HPMC K4M viz., 1:0, 1:1, 1:2 and 0:1, respectively with the specially designed upper punch in 11 mm die cavity and flat faced lower punch on a Cadmach single station tablet press.

cavity and compressing with the specially designed 11 mm upper punch. The polymer type, quantity and their ratio may be varied to optimize the bioadhesive strength of the cups. The buccoadhesive core-in-cup tablets were prepared by placing the core materials in the cup and compressed with a flat-faced 11 mm punch. The prepared buccoadhesive core-in-cup tablets had a uniform peripheral layer thickness.

The prepared buccoadhesive cups were evaluated for uniformity of weight, thickness, depth of the core, hardness, friability, and bioadhesive strength (Table 2). The thickness was measured by Vernier callipers. The mucoadhesive strength of buccoadhesive cup was measured by a modified two-arm balance using porcine buccal mucosa and rabbit buccal mucosa. The porcine buccal mucosa and rabbit mucosa were obtained from local slaughterhouse and stored in Krebs buffer and studies were done within 3 h of the procurement. The weight required to separate the sample system from a model substrate was measured by using a modified two-arm balance. Coloring and flavoring agent may be added to the buccoadhesive cups to improve the patient compliance. The depth of the buccoadhesive cups can be varied by changing the protrusion length in the punch but the quantity of the bioadhesive polymers required to form cups increases with the thickness and weight of the cups, which is not desirable. Cup with thickness of 2.5 mm and depth 2.0 mm is more suitable as it requires only about 150 mg of the bioadhesive polymers. About 100 mg of the core material can be filled into the cups. Magnesium stearate used in the preparation of cups acts as a barrier for multidirectional release of the drug from the core-in-cup tablets.

TABLE 2: EVALUATION OF PHYSICAL PROPERTIES OF BUCCOADHESIVE CUPS.

Formulation	Weight variation* (%)	Thickness* (mm)	Depth of the core* (mm)	Hardness* kg/cm ²	Friability* %	Bioadhesive strength* (g)
A	0.79±0.18	1.93±0.05	1.80±0.04	6.93±0.25	0.40±0.05	22.22±2.81
B	0.77±0.10	2.50±0.05	2.00±0.08	9.20±0.16	0.31±0.06	44.76±3.66
C	0.80±0.25	2.06±0.48	1.92±0.24	10.00±0.17	0.25±0.05	39.76±1.98
D	0.79±0.13	2.00±0.00	1.90±0.36	7.86±0.09	0.38±0.03	23.29±4.73

* indicates mean of three estimations with standard deviation. Table summarizes the evaluation of the cups prepared with different ratios of carbopol and HPMC K4M viz., 1:0, 1:1, 1:2 and 0:1, respectively which are indexed as formulations A, B, C and D.

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In vitro Permeation of Verapamil Hydrochloride From Polymeric Membrane Systems Across Rat and Human Cadaver Skin

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In this article various polymeric membrane systems of poly vinyl pyrrolidone, ethyl cellulose, Eudragit RS100 and ethylene vinyl acetate, containing verapamil hydrochloride, along with glycerol and dibutyl phthalate as plasticizers have been fabricated for transdermal use. Both monolithic and membrane controlled systems were prepared by the method of casting on mercury surface and evaluated for thickness uniformity, drug content uniformity, tensile strength, Percentage of elongation and skin irritation. *In vitro* drug permeation through rat abdominal skin and human cadaver skin was performed using Keshary-Chien diffusion cells. Results indicated that, the order of permeation of the drug from different polymeric membranes was poly vinyl

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