reproducibility and accuracy of the methods. The absorbance difference between two points on the mixture spectra is directly proportional to the concentration of the component of interest, independent of the interfering component is the basic principle underlying the two wavelength method of analysis.

In the second method employing derivative spectroscopy, first, second, third and fourth order derivative spectra of both the drugs were observed and fourth order spectra was selected keeping in view the resolution and sensitivity of the instrument used. Both the drugs did not interfere at the wavelengths used.

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Mucoadhesive Formulations of Theophylline

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Accepted 25 March 1998
Received 19 April 1997

Buccal mucoadhesive films and mucoadhesive gels of theophylline were prepared using Hydroxy Propyl Methyl Cellulose (HPMC), Ethyl cellulose (EC), and Carbopol. The drug release pattern and stability of these formulations were studied. The *in vitro* drug release and *in situ* intestinal drug absorption were higher with formulations containing Carbopol.

ONE of the significant approaches in the modern drug delivery systems is to target the drug to particular site of the body. In the living body, mucosal surfaces are available in the gastrointestinal tract, urogenital tract, air ways, nose, ear and eye. Nagai et al.[1] utilized the combination of HPMC and Carbopol 934 to prepare oral bioadhesive tablets for the administration of insulin. Studies using benzydamine and lidocaine employing carbopol have been reported[2]. Buccal mucoadhesive films of theophylline were prepared to avoid the gastrointestinal irritation commonly experienced on oral administration.

The films were prepared by a method employed by Roopa et al.[3] The composition of the films were as follows, Drug:Polymer-1:10, HPMC:EC-3:1, Carbopol -0.0%, 3.0% w/w. Drug was dissolved in ethanol. HPMC 15 cps, EC and Carbopol (940NE) were separately dissolved in ethanol. The two were mixed and the resulting mass was sonicated and poured on to specially designed rectangular glass mould (3X5 cm)lined with aluminum foils. It was

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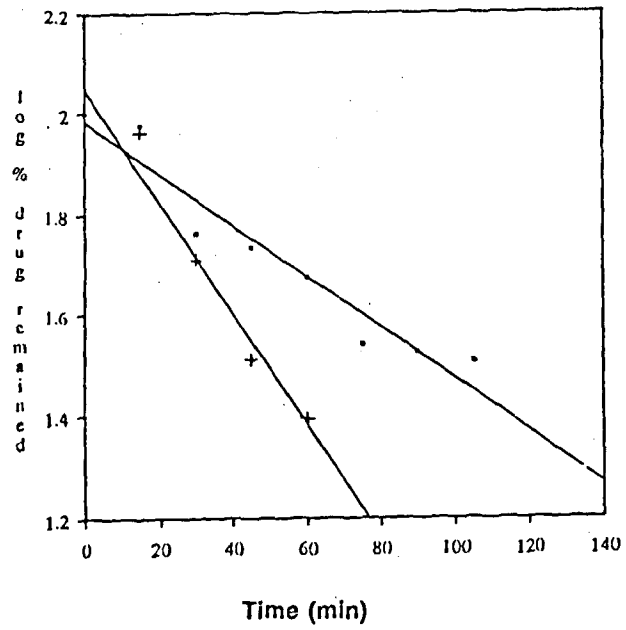
Table 1
COMPOSITION OF MUCOADHESIVE GELS

Ingredients	Formulation I	Formulation II
HPMX (50 cps)	1.00 g	1.00 g
Carbopol	-	0.03 g
Glycerin	0.50 g	0.50 g
Theophylline	0.05 g	0.05 g
Dist. Water up to	10.00 g	10.00 g

allowed to dry overnight at ambient temperature. The films obtained were cut into 0.5x0.5 cm strips, each containing 1 mg of drug.

In vitro drug release form buccal mucoadhesive films were performed using a fabricated model[4], which was a modification of a flow-through diffusion cell[5]. The lower chamber of the apparatus had a small volume compartment (1.5 ml) and the medium was stirred using a teflon coated magnetic bead on a magnetic stirrer (300 rpm). Phosphate buffer of pH 6.2 (simulating the salivary pH) was continuously pumped through the apparatus at a flow rate of 0.65 ml/min. The flow rate chosen corresponded to the mean resting saliva flow rate[6].

Fig. 1: *In vitro* drug release from films through Fabricated apparatus
▪ without corbopol + with corbopol



A piece of intestinal mucosal membrane was tied to the lower surface of the upper compartment, instead of mucosal membrane of fresh bovine cheek pouch with the mucosal side towards the lower compartment. The buccal mucoadhesive films were stuck to the mucosal surface. Fractional samples from the outflow were collected at 15 minutes interval. The samples were analyzed spectrophotometrically at a wavelength maxima of 271 nm.

Mucoadhesive gels were prepared using HPMC and Carbopol (Table 1). Weighed quantity of HPMC was transferred to a beaker containing half the quantity of water. Theophylline and glycerin were added and mixed well to ensure uniform distribution. The gels prepared were stored in collapsible tubes.

The modified Doluisio technique was used to study *in situ* intestinal absorption[7]. Healthy albino rats weighing 200-250 g were selected for the studies. The rats were fasted for 24 h but had free access to drinking water. They were anesthetized with pentobarbitone sodium (6 mg/100 g body weight i.p.). A midline abdominal incision was made and the intestine was exposed. Two L-shaped cannulae were inserted through small slits in the duodenal and ileal end of rat intestine. Two hypodermic syringes of 10 ml volume, fitted with three way stop cock were attached to each cannulae. Air was pumped slowly through the syringe of duodenal end such that the intestinal contents can be sampled from ileal end. The gel formulations were pushed through the syringe into the intestine. Samples were collected at every 10 minutes time interval and the remaining fluid was returned to the intestine. Samples were analysed spectrophotometrically at a wavelength maxima of 271 nm against a blank of intestinal fluid.

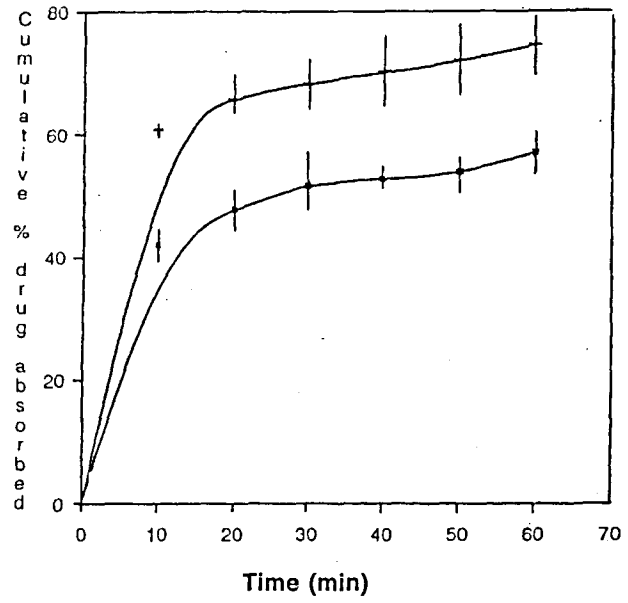
The films were stored at room temperature, 37°, 82.5% relative humidity (R.H.) and exposed to light (L.E.). At specific time intervals (7th, 14th, 21st, and 28th day) samples were withdrawn and analyzed for drug content.

The index for *in vitro* drug release was based on drug loss from formulation. The drug loss from formulations containing 3.0 % w/w Carbopol was higher than the formulations without Carbopol. The higher slope (Fig. 1) of plot of formulation containing 3.0 % w/w Carbopol clearly indicated the greater drug loss with time. This may be due to

Table 2
K VALUES FOR THE SAMPLES OF FORMULATION STORED AT DIFFERENT CONDITIONS

Formulation	Rate of drug degradation K ($days^{-1}$)			
	R.T	37°	82.5% R.H	L.E
Films:				
(0.0% Carbopol)	$5.5x10^{-3}$	$12.3x10^{-3}$	$15.2x10^{-3}$	$14.6x10^{-3}$
(3.0% Carbopol)	$6.2x10^{-3}$	$13.0x10^{-3}$	$15.7x10^{-3}$	$13.8x10^{-3}$
Gels				
Formulation I	$6.2x10^{-3}$	$12.3x10^{-3}$	—	—
Formulation II	$7.1x10^{-3}$	$9.2x10^{-3}$	—	—

Fig. 2: Intestinal absorption of Theophylline from gel formulations
■ gel without carbopol + gel with carbopol



the increase in the mucoadhesion of the formulation on addition of Carbopol. Similar results using atropine sulfate were reported by Baun and Walker[8].

The intestine absorption study showed that there was an increase in the total amount of theophylline absorbed from formulation II containing Carbopol compared to Formulation I (fig, 2). The stability studies indicated that there was no significant degradation of drug. But upon light exposure, the rate of degradation had slightly accelerated (table 2). The stability of films was found to be in the following order:

Room temperature> 37°> 82.5% R. H.> L. E.

The stability studies of gels indicated that the rate of degradation of gels stored at 37° was more as compared to that stored at room temperature. Mucoadhesive gel formulated with Carbopol was very useful to enhance the absorption of theophylline, thus justifying its promising utility in the treatment of asthma.

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