Formulation and *In-vitro* Evaluation of Celecoxib Buccoadhesive Tablets

Sayed M. Ahmed, Eman M. Samy, Mahrous O. Ahmed, Niveen G. El-gendy

Department of Industrial Pharmacy, Faculty of Pharmacy, Assiut University, Egypt.
Email: dr.niveenelgendy@hotmail.com

Abstract: Celecoxib, a non-steroidal anti-inflammatory drug (NSAID), is a selective inhibitor of cyclooxygenase enzyme type II (COX-2 inhibitor) and commonly prescribed in dental practice for management of pain, swellings and inflammation. Recently, celecoxib showed a promising anticancer activity in different tumor types. It has a poor aqueous solubility and release rate that limits its absorption and bioavailability. The aim of the work is to enhance the solubility and dissolution rate of Celecoxib using dimethyl beta cyclodextrine (DM-β-CD) and to develop bioadhesivebuccal tablets using various suitable bioadhesive polymers to reduce dose dependent side effects and frequency of administration of the drug. Physical mixtures, coevaporates and cogroundmixtures of clecoxib with DM-β-CD (1:1 molar ratio) were prepared and Characterization of the prepared systems were performed using Differential Scanning Calorimetry (DSC), Powder X-ray Diffractometry (P-XR) and Fourier Transform Infrared Spectroscopy (FT-IR). Controlled-release buccoadhesive tablets were prepared by adding of different types of bioadhesive polymers to Celecoxib / DM-β-CD coevaporate system (which gave the highest release rate of the drug) using direct compression technique. Different water soluble polymers carbopol974P (CP974), hydroxyl propyl methyl cellulose 15000 (HPM 15000), sodium alginate (NaAlg) and sodium carboxy methyl cellulose (SCMC)) or their combinations were used. The prepared celecoxibbuccoadhesive tablets had acceptable physical parameters, such as hardness, swelling behavior, bioadhesive strength and surface pH. The buccoadhesive tablet containing celecoxib / DM-β-CD coevaporates with polymer mixture of; HPMC: SCMC (1:3 weight ratio) showed the most suitable release rate and properties for adhesion to the buccal mucosal membrane.
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Key words: Celecoxib, Buccoadhesive tablets, DM-β-CD, Cp974P, HPMC, SCMC

1. Introduction:

Cyclodextrins are widely used as "molecular cages" in pharmaceutical formulations (Roux et al., 2007). They are used as complexing agents to increase the aqueous solubility of poorly water-soluble drugs and to increase their bioavailability and stability (Loftsson and Duchene, 2007). Cyclodextrins have been extensively applied to enhance the bioavailability of sterols, cardiac glycosides, non-steroidal anti-inflammatory drugs (Uekama and Otagiri, 1987). The potential uses of cyclodextrins for the development of new formulations of new drugs that are difficult to be formulated and delivered are increasing (Irie and Uekama, 1997 and Agu et al., 2000).

Bioadhesive delivery of a desired drug using mucoadhesive polymers has been accepted as a promising strategy to prolong the residence time and to improve the specific localization of drug delivery systems on various membranes (Khairnar and Sayad, 2010).

An ideal buccal delivery system must possess three characteristics: a) Remains in the oral cavity for a few hours to maximize the proximity of contact with mucosa; b) Releases the drug in a controlled fashion under the conditions dominant in the mouth; and c) Overcomes the low permeability of the oral mucosa (Remunan-Lopez et al., 1998).

With regard to the first requirement, strong adhesion of the system to the buccal mucosa can be achieved by using appropriate combinations of mucoadhesive polymers. If these mucoadhesive polymers would be able to control drug release, the second requirement is also achieved. Therefore, the first step in the development of a buccal delivery system is the selection of appropriate adhesives. The third requirement may be fulfilled by preparation of a system having uniform adhesives (Emami et al., 2008 and Salamat-Miller et al., 2005). Advantages of buccal drug delivery systems are: 1-The richly vascularized mucosa enhances the absorption of buccal dosage forms. 2-Buccal drug delivery has a high patient acceptability compared to other non-oral routes of drug administration. 4-Avoidance of acid hydrolysis in gastrointestinal tract and by passing the first pass effect. 5- Moreover, rapid cellular recovery and achievement of a localized site on the smooth surface of the buccal mucosa (Yajaman and Bandyopadhyay, 2006).

The buccal delivery of NSAIDs avoids the direct contact with gastric mucosa, hence reduces the possibility of gastrointestinal ulceration associated

with its administration (Doshi et al., 2011 and Brahmareddy et al., 2015).

The aim of this study was toenhance dissolution rate of Celecoxib using DM-β-CD and the use of the prepared mixture that gave the highest release rate of the drug with different water soluble polymers in an attempt to prepare buccal tablets of celecoxib in order to enhance the rate of drug release, make more sustaining of the drug action, reduce frequency of administration and reduce dose dependent side effects.

2. Materials and Methods:

Materials

Celecoxib was obtained as a gift from Sedico Company (Egypt). Heptakis-(2,6-di-O-methyl)-β-cyclodextrin (DM-β-CD) was supplied from Toshin Chemicals Company, Japan. Carbapol 974P (Cp974P), hydroxyl propyl methylcellulose 15000 (HPMC 15000) and anhydrous lactose was supplied from El-Gomhouria Co., Cairo, Egypt. Sodium alginate (NaAlg) was applied from the General Chemical and Pharmaceutical Co., Ltd., Sudbury Middlesex, England. Sodiumcarboxy methylcellulose (SCMC) was supplied from El-Nile Co. for Pharmaceutical and Chemical Industry, Egypt. All other reagents and solvents were of analytical grade and were used as received.

Methods

1) Preparation of Physical Mixtures, Coevaporates and Coground Mixtures of Clecoxib with DM-β-CD:

Physical mixtures of celecoxib with DM-β-CD were prepared by simple mixing of equimolar amounts (1:1 molar ratio) of the drug: DM-β-CD, using mortar and pestle. Coevaporates of celecoxib with DM-β-CD (1:1 M) were prepared by dissolving equimolar amounts of celecoxib and DM-β-CD in a small volume of methanol. The solvent was evaporated in a vacuum oven at 40°C until complete drying. Coground mixtures were prepared by grinding equimolar amounts of celecoxib and DM-β-CD using the vibrational uniball mill for about 15 minutes. The obtained powders were sieved to obtain a particle size range of 125-250 µm. The obtained samples were stored in a desiccator over calcium chloride till investigated.

2) Characterization of Celecoxib-DM-β-CD prepared systems using Differential Scanning Calorimetry (DSC), Powder X-ray Diffractometry (P-XR) and Fourier Transform Infrared Spectroscopy (FT-IR).

3) Dissolution Studies:

Dissolution studies were done for celecoxib, the physical mixtures, coevaporates and coground mixtures with DM-β-CD using USP dissolution apparatus type II.

4) Formulation of Celecoxib Buccoadhesive Tablets:

4.1) Preparation of Celecoxib Buccoadhesive Tablets:

Controlled-release buccoadhesive tablets containing Celecoxib / DM-β-CD coevaporate system (1:1 M), equivelant to 50mg celecoxib, were prepared by the direct compression technique. Different weight ratios of Cp974P, HPMC 15000, NaAlg and SCMC or their combinations were used. Anhydrous lactose was added as a diluent to obtain the desired weight of each tablet (250 mg). MgSt (2 mg) was added as a lubricant. These ingredients were passed through a No. 100 sieve and then, mixed by trituration in a glass mortar with pestle to obtain uniform mixture. The blended powders were compressed into tablets on a single punch tablet machine using a flat-faced non-beveled punch and die set of 8 mm diameter.

4.2) Physical Evaluation of the Formulated Buccoadhesive Tablets:

Uniformity of Weight (British Pharmacopeia, 2009):

Twenty tablets were individually weighed. The average weight was determined and the standard deviation was calculated.

Uniformity of Drug Content (British Pharmacopeia, 2009):

Ten tablets were randomly selected from each formula and assayed individually. A p reweight tablet was powdered and transferred into a 100 ml volumetric flask containing 50 ml of phosphate buffer solution of pH 6.8 and was stirred continuously on a magnetic stirrer. The volume was made up to 100 ml with the buffer solution and filtered, and then the solution was assayed spectrophotometrically at 250 nm against phosphate buffer solution (pH 6.8) as a blank.

Thickness and Diameter of the Prepared Tablet (Kane et al., 1993):

The average thickness and diameter were determined using a micrometer.

Tablet Hardness (Kane et al., 1993):

Determined by means of the Erweka hardness tester. For each batch, the hardness of 10 tablets was determined and the mean was calculated.

Tablet Friability (British Pharmacopeia, 2009):

Tablet Friability was evaluated by calculating the percentage loss in the weight of 20 tablets from each formula after the revolution in a friabilator, at 25 r.p.m., for 4 minutes. The percentage loss was calculated using the following equation: % loss= (weight before – weight after) / weight before x 100.

Swelling of Buccoadhesive Tablets using Agar-Gel Plate (Agarwal and Mishra, 1999 and Ismail, 2004):

The swelling procedure was evaluated using agar-gel (1% w/v of agar in phosphate buffer pH 6.8). Thirty two tablets were used. The average weight of each four tablets was calculated (W_1). The tablets were placed on the gel surface in eight Petri dishes (each containing four tablets) which were placed in an incubator at 37°C. Four tablets were removed at time intervals of 0.5, 1, 2, 3, 4, 5, 6 and 8 hrs; excess water on the surface was carefully removed using filter paper, and the swollen tablets were weighed. The average weight (W_2) was calculated and then the swelling index was calculated by the following formula:

$$\text{Swelling index} = \frac{W_2 - W_1}{W_1}$$

W_1 and W_2 are the weights of dry and swollen tablets at different time intervals.

5) Surface pH of the Tablets:

Buccoadhesive tablets were allowed to swell by keeping them in contact with (1% w/v) of agar gel in phosphate buffer (pH 6.8) for 8 hours at temperature 37°C (Ismail, 2004). The surface pH was measured by placing the electrode in contact with the surface of the swollen tablet (Mahrous, 2006).

***6) In-vitro* Bioadhesion Test:**

The mucoadhesive strength of the buccoadhesive tablets was determined by measuring the force required to detach the tablet formula from a mucin tablet using a modified balance method (El-Kamel, 2002 and Desai and Kumar, 2004).

7) In-vitro Drug Release (Abdel-Aal, 2003**):**

The drug release from the prepared buccoadhesive tablets was determined using USP apparatus II (paddle method). Phosphate buffer solution of pH 6.8 (500 ml) was used as the dissolution medium which was maintained at 37±0.5°C and stirred at a rate of 50 rpm. Aliquots (5 ml each) were withdrawn after 30, 60, 90, 120, 180, 240, 300, 360, 420 and 480 minutes and the sample volume was replaced with an equal volume of the fresh dissolution medium at the same temperature. The samples were filtered and the drug content was determined spectrophotometrically at λ_{max} 250 nm. Three tablets were examined at the same time and the mean was considered.

3. Results and Discussion:

1) Characterization of Celecoxib-DM-β-CD prepared systems:

1.1. Differential Scanning Calorimetry (DSC):

Figure1: showed the DSC thermogram of pure celecoxib with an endothermic peak at 165°c corresponding to the melting point of the drug (trace A). The DSC thermogram of DM-β-CD showed a broad endothermic peak at 70-90°c which may attributed to evaporation of water (trace B). DSC thermogram of coevaporate of celecoxib with DM-β-CD showed the disappearance of the drug melting peak (trace C) which indicated the formation of partial inclusion complex.

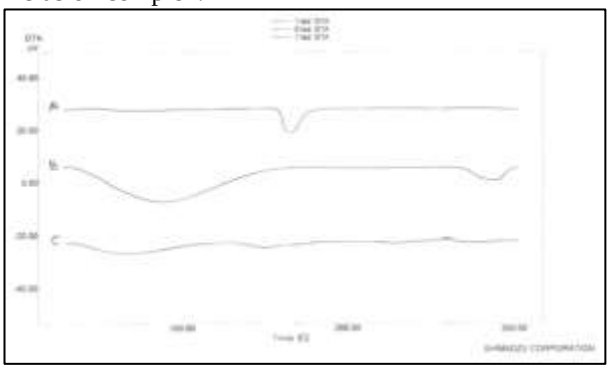

Fig. 1: DSC thermogram of A: Drug alone, B: DM-β-CD alone, C: Coevaporate.

1.2. Powder X-ray Diffraction Studies:

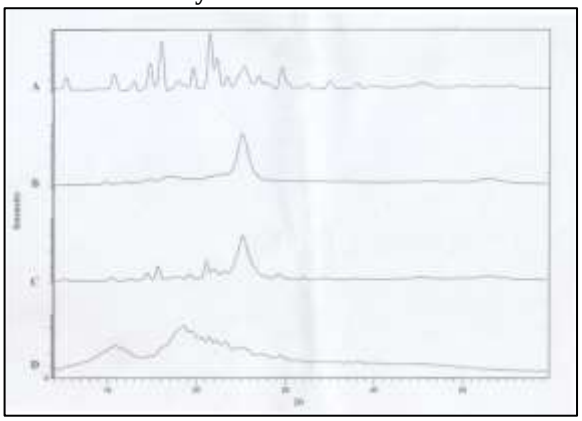

Fig. 2: Powder X-ray diffractograms of celecoxib with DM-β-CD at 1:1 molar ratio: A: Drug alone, B: DM-β-CD, C: Physical mixture, D: Coevaporate.

The powder X-ray diffraction pattern of celecoxib with DM-β-CD was shown in figure (2). The diffraction pattern of pure celecoxib showed sharp and intense diffraction peaks at scattering angles of 2θ = 6.09°, 11.43°, 15.53°, 16.82°, 22.25°, 22.92°, 27.72°, 30.31° and 33.27° (Fig. 2, trace A). The diffraction pattern of DM-β-CD (Fig. 2, trace B), showed a single peak at 2θ = 26°. While diffraction pattern of the physical mixture of celecoxib with DM-β-CD was simply a superposition of the two components of the mixture (Fig. 2, trace C). The diffraction pattern of coevaporate system of celecoxib with DM-β-CD (Fig. 2, trace D) showed

disappearance of the most characteristic diffraction peaks of pure celecoxib which may suggest its conversion to an amorphous state. These results were confirmed with that obtained from the thermal data of the drug in the coevaporate system with DM-β-CD, suggesting the formation of partial inclusion complex between celecoxib and DM-β-CD coevaporate system insolid state (Venetura et al., 2005).

1.3. Fourier Transform Infrared Spectroscopy (FT-IR):

The IR spectrum of celecoxib alone (Figs. 3, trace A) showed the following major characteristic bands at 3300-3340 for $–NH_2$ stretching, 1550-1600 for –NH stretching and 1150-1350 for S=O (sulfonamide group) stretching. The IR spectrum of pure DM-β-CD showed absorption bands between 3300 and 3700 cm^{-1} for free hydroxyl group vibrations, absorption band at 2970 cm^{-1} for bounded hydroxyl groups and a broad band at 1634 cm^{-1} due to absorbed water (Figs. 3, trace B). IR spectrum of coevaporate of celecoxib with DM-β-CD (Fig. 3, trace C) showed a higher frequency shift of NH_2 stretching band from 3340 to 3420 cm^{-1} (Hassan, 2005).

In addition, a considerable broading of the NH_2 stretching band also has been detected. These observed changes of IR spectrum of drug may be attributed to the formation of hydrogen bonding between the primary amine group ($-NH_2$) of celecoxib and the hydroxyl groups (OH) of DM-β-CD which may also suggest formation of inclusion complex between celecoxib and DM-β-CD in coevaporate system (Venetura et al., 2005). These results were confirmed by the previous DSC and X-ray analysis data.

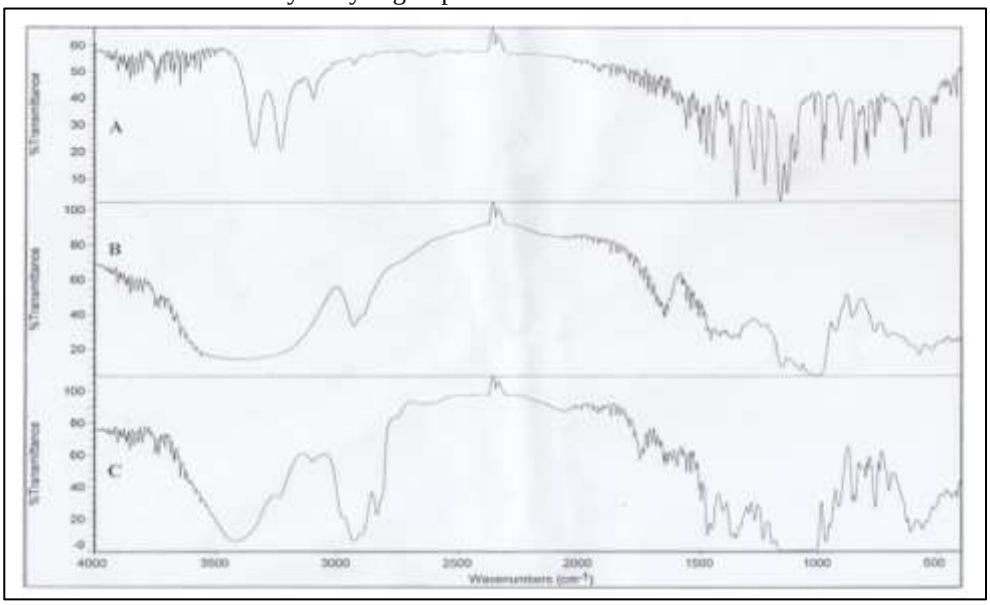

Fig. 3: IR spectra of A: Drug alone, B: DM-β-CD alone, C: Coevaporate.

2) Dissolution Studies:

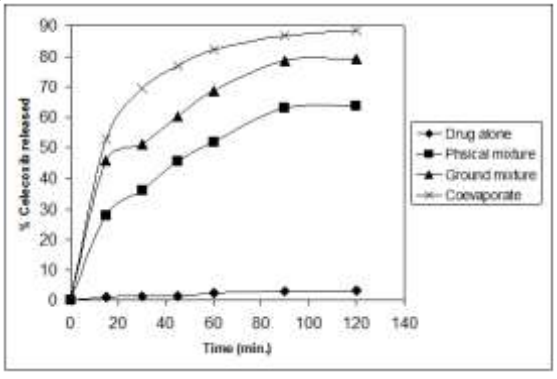

Fig. 4: Dissolution profiles of celecoxib with DM-β-cyclodextrin (1:1 M) in phosphate buffer of pH 6.8 at 37°C.

The dissolution profiles of untreated celecoxib, its physical mixtures, coground mixtures and coevaporates with DM-β-CD were presented in (Fig:4). The dissolution rate of celecoxib was improved from its ground and coevaporates mixtures with DM-β-CD than that from its physical mixtureof the same composition and both were higher than the dissolution rate of the untreated celecoxib.

3) Formulation of CelecoxibBuccoadhesive Tablets:

The composition of the formulated buccoadhesive tablets containing celecoxib / DM-β-CD coevaporate at (1:1) molar ratio using single polymer and mixture of two polymers illustrated in table 1 and 2 respectively.

Table 1: Composition of various buccoadhesive tablets containing celecoxib / DM-β-CD coevaporate at (1:1) molar ratio using single polymer.

Formula no.	Drug Formula (mg)	Cp974P (mg)	HPMC 15000 (mg)	NaAlg (mg)	SCMC (mg)	Lactose (mg)	MgSt (mg)	Polymer% of tablet wt.
F1	110	10	--	--	--	128	2	4%
F2	110	20	--	--	--	118	2	8%
F3	110	--	75	--	--	63	2	30%
F4	110	--	100	--	--	38	2	40%
F5	110	--	--	75	--	63	2	30%
F6	110	--	--	100	--	38	2	40%
F7	110	--	--	--	75	63	2	30%
F8	110	--	--	--	100	38	2	40%

Table 2: Composition of various buccoadhesive tablets containing celecoxib / DM-β-CD coevaporate at (1:1) molar ratio using mixtures of two polymers.

Formula no.	Drug formula (mg)	Cp974P (mg)	HPMC 15000 (mg)	NaAlg (mg)	SCMC (mg)	Lactose (mg)	MgSt (mg)	Polymer ratio
F9	110	20	80	--	--	38	2	1:4
F10	110	20	--	80	--	38	2	1:4
F11	110	20	--	--	80	38	2	1:4
F12	110	--	25	75	--	38	2	1:3
F13	110	--	75	25	--	38	2	3:1
F14	110	--	25	--	75	38	2	1:3
F15	110	--	75	--	25	38	2	3:1
F16	110	--	--	25	75	38	2	1:3
F17	110	--	--	75	25	38	2	3:1

*Total tablet weight= 250 mg

$). Physical Evaluation of the Formulated Celecoxib Buccoadhesive Tablets:

4.1. Weight Variation, Drug Content, Thickness, Hardness and Friability of the Prepared Buccoadhesive Tablets:

Tables (3) illustrated the physical properties of the prepared celecoxibbuccoadhesive tablets.The percent of the total drug content of the prepared tablets was found to be within the range from 98.36% ± 2.4 to 101.01% ± 3.12. These values indicated that all the prepared tablets were uniform in drug content according to B.P (2009) requirements. The thickness of all the prepared celecoxib tablets was also uniform and showed acceptable hardness values ranged from 4.85 kg ± 0.16 to 8.64 kg ± 0.56. The differences in the tablet hardness did not affect the release of the drug from hydrophilic matrices which was released by diffusion through the gel layer and/or erosion of this layer and was therefore independent of the dry state of the tablet (Dortung et al., 1998).

It's important to know that tablet friability test was performed to evaluate tablet compaction and resistance (Perioli et al., 2009). From friability data, the percent loss of the prepared tablets was also in the acceptable range of B.P. 2009 (0.166% - 0.712%). The results were found to increase by increasing the concentration of the polymer in the prepared buccoadhesive tablets.

4.2. Swelling Studies of Buccoadhesive Tablets:

Figures (5-8) showed that swelling ofth preparedbuccoadhesive tablets increased with time because the polymer gradually absorbed water due to its hydrophilicity. The outermost hydrophilic polymer hydrated and swollen and a gel barrier were formed at the outer surface. As the gelatinous layer progressively dissolved and/or dispersed, the hydration swelling release process was continued towards new exposed surfaces, thus maintaining the integrity of the dosage form (Perioli et al., 2009). A slow decrease of the hydrophilic polymer thickness then occurred until finally the whole matrix was completely dissolved. Swelling index was performed for all the formulated tablets up to 8 hrs. In general, it was obvious that, the swelling index values increased by increasing polymer concentration which was in agreement with many studies (Ismail, 2004 and Genç et al., 2000).

Table 3: Physical properties of the formulated buccoadhesive tablets containing celecoxib / DM-β-CD coevapourates (1:1) molar ratio and different bioadhesvie polymers.

Formula no.	Weight (mg ±SD), n= 20	Drug content (%±SD), n=10	Thickness (mm±SD), n= 20	Hardness (kg±SD), n= 10	Friability (% loss), n= 20
F1	251.2 ± 2.39	100.01 ± 1.41	3.81 ± 0.13	5.50 ± 0.75	0.198
F2	249.8 ± 3.01	100.10 ± 2.37	3.93 ± 0.18	7.25 ± 0.15	0.366
F3	250.4 ± 2.61	100.10 ± 1.58	4.01 ± 0.06	8.25 ± 0.28	0.434
F4	250.6 ± 3.02	99.13 ± 2.81	4.02 ± 0.11	7.15 ± 0.16	0.427
F5	251.8 ± 2.43	99.16 ± 2.80	3.98 ± 0.10	7.19 ± 0.35	0.312
F6	251.8 ± 3.42	98.36 ± 2.10	3.64 ± 0.18	8.50 ± 0.16	0.613
F7	248.4 ± 2.81	99.13 ± 2.68	3.84 ± 0.15	7.60 ± 0.35	0.418
F8	249.6 ± 3.16	100.05 ± 3.15	3.75 ± 0.16	7.25 ± 0.71	0.525
F9	251.6 ± 2.13	101.01 ± 3.12	3.81 ± 0.14	8.64 ± 0.56	0.524
F10	252.2 ± 2.19	98.68 ± 2.42	3.91 ± 0.18	7.80 ± 0.18	0.168
F11	249.2 ± 3.08	99.48 ± 2.35	3.78 ± 0.04	6.86 ± 0.40	0.318
F12	249.4 ± 2.29	100.01 ± 2.91	3.93 ± 0.14	7.86 ± 0.14	0.412
F13	250.5 ± 2.16	98.83 ± 3.31	3.88 ± 0.19	6.75 ± 0.14	0.671
F14	250.4 ± 3.13	100.04 ± 2.35	3.66 ± 0.11	7.01 ± 0.38	0.634
T15	249.4 ± 3.37	100.43 ± 2.46	3.78 ± 0.15	4.85 ± 0.16	0.464
F16	250.7 ± 3.18	99.16 ± 3.18	3.68 ± 0.35	7.05 ± 0.78	0.458
F17	252.3 ± 2.11	99.89 ± 2.05	3.92 ± 0.12	5.52 ± 0.34	0.624

4.3. Surface pH of the Tablets:

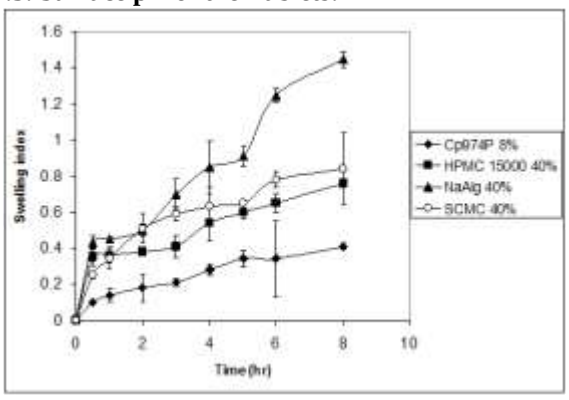

Figure 5: Swelling index of buccoadhesive tablets containing celecoxib / DM-β-CD coevaporate at (1:1) molar ratio and different bioadhesive single polymers in phosphate buffer of pH 6.8.

The values of the surface pH of the prepared buccoadhesive tablets were presented in Tables (4). The prepared buccoadhesive tablets exhibited surface pHs within the satisfactory limits around the neutral pH (5.42±0.2 - 6.81±0.11). However, the prepared buccoadhesive tablets (F2 and F19) that were containing little higher concentration of Cp974P (8%) showed slightly acidic pH (4.95±0.06 - 5.02±0.16). Therefore, it may be expected that these formulations may cause some irritation to the buccal mucosa (Ismail, 2004 and Taylan et al., 1996).

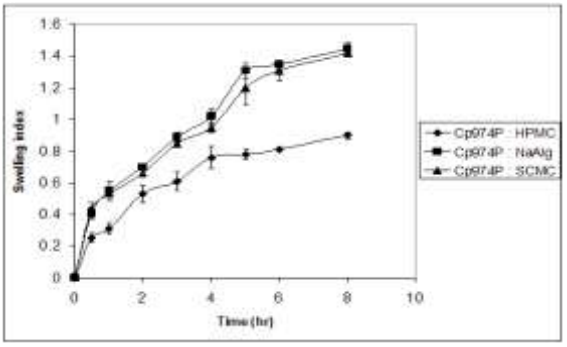

Fig. 6: Swelling index of buccoadhesive tablets containing celecoxib/DM-β-CD coevaporateat (1:1) molar ratio and 1:4 weight of Cp974P with other different polymers in phosphate buffer of pH 6.8.

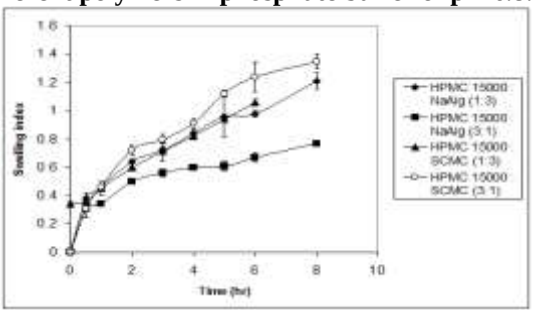

Fig. 7: Swelling index of buccoadhesive tablets containing celecoxib / DM-β-CD coevaporate at (1:1) molar ratio and different ratios of HPMC 15000 and other different polymers in phosphate buffer of pH 6.8.

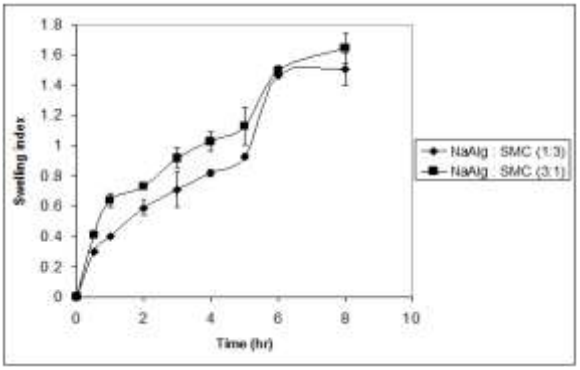

Fig. 8: Swelling index of buccoadhesive tablets containing celecoxib / DM-β-CD coevaporate at (1:1) molar ratio and different ratios of NaAlg: SCMC in phosphate buffer of pH 6.8.

Table 4: *In-vitro*buccoadhesive strength and surface pH of the formulated buccoadhesive tablets containing celecoxib / DM-β-CD coevaporate (1:1) molar ratio and different bioadhesvie polymers.

Formula no.	Bioadhesive strength (g ± SD)	Surface pH
F1	28.57 ± 3.14	5.42 ± 0.02
F2	31.29 ± 1.35	4.95 ± 0.06
F3	15.85 ± 3.46	6.05 ± 0.14
F4	19.69 ± 2.54	6.24 ± 0.03
F5	26.47 ± 3.24	6.14 ± 0.08
F6	30.18 ± 2.41	6.43 ± 0.01
F7	20.83 ± 1.56	6.25 ± 0.18
F8	27.18 ± 2.27	6.34 ± 0.06
F9	51.52 ± 3.12	6.20 ± 0.15
F10	52.13 ± 2.03	6.19 ± 0.18
F11	54.34 ± 1.56	6.23 ± 0.06
F12	48.34 ± 0.85	6.64 ± 0.10
F13	25.52 ± 2.43	6.22 ± 0.08
F14	49.43 ± 1.85	6.16 ± 0.13
T15	41.16 ± 6.20	6.56 ± 0.08
F16	44.17 ± 2.33	6.41 ± 0.06
F17	56.72 ±1.08	6.35 ± 0.002

4.4. In-vitro Bioadhesion Test:

Tables (4) showed the *in-vitro*bioadhesive strength of buccoadhesive tablets containing celecoxib / DM-β-CD coevaporate with different concentrations of the investigated polymers. The effect of the use of different concentrations for each investigated polymer on the bioadhesive strength of both types of the formulated celecoxibbuccoadhesive tablets.

It was clear that the bioadhesive strength varied considerably with different polymers. An increase in bioadhesion strength upon increasing polymer concentration was expected and may be attributed to the increased sites of bond formation (Gu et al., 1988). The maximum bioadhesive strength was obtained from tablets containing Cp974P compared to other polymers. This result could be attributed to the fact that Cp974P has great number of carboxylic acid groups (-COOH) which had the ability to form hydrogen bonding and bind strongly with oligosaccharide chains present in the buccal mucosa (Sharma et al., 2006 and Patel, et al., 2007).

5) In-Vitro Drug Release Studies:

The present of celecoxib released over a period of 8 hrs from tablets containing 110 mg of celecoxib / DM-β-CD coevaporate system (each tablet formula was equivalent to 50 mg of celecoxib) were shown in Figures (9-12). From the previous drug release data, the buccoadhesive tablet (F14) containing celecoxib / DM-β-CD coevaporate with polymer mixture; HPMC: SCMC (1:3 weight ratio) showed the most suitable release rate and properties for adhesion to the buccal mucosal membrane. Therefore, they were chosen for further stability and *in vivo* studies.

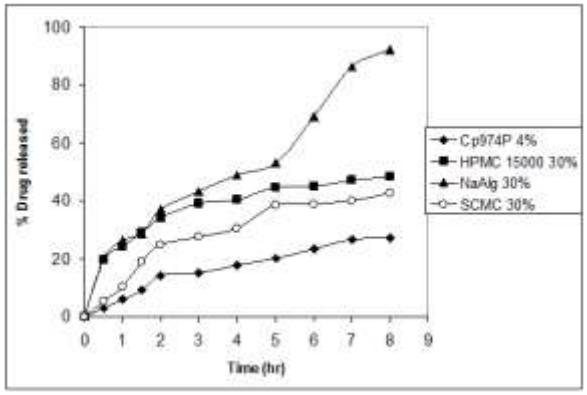

Fig. 9: Release profiles of celecoxib from buccoadhesive tablets containing celecoxib / DM-β-CD coevaporate at (1:1) molar ratio and different bioadhesive single polymers in phosphate buffer of pH 6.8.

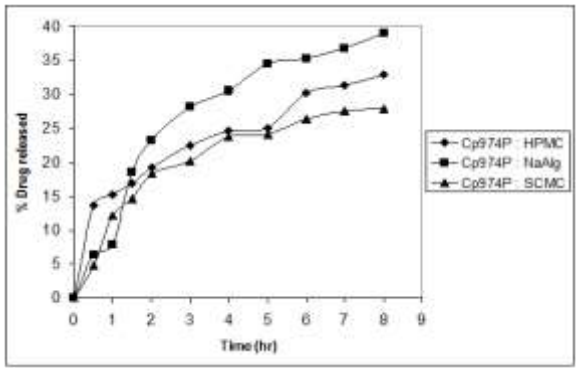

Fig. 10: Release profiles of celecoxib from buccoadhesive tablets containing celecoxib / DM-β-CD coevaporate at (1:1) molar ratio and 1:4 weight of Cp974P with other different polymers in phosphate buffer of pH 6.8.

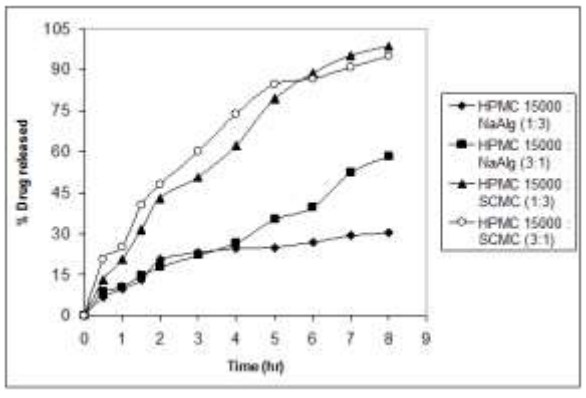

Fig. 11: Release profiles of celecoxib from buccoadhesive tablets containing celecoxib / DM-β-CD coevaporate at (1:1) molar ratio and different ratios of HPMC 15000 and other different polymers in phosphate buffer of pH 6.8.

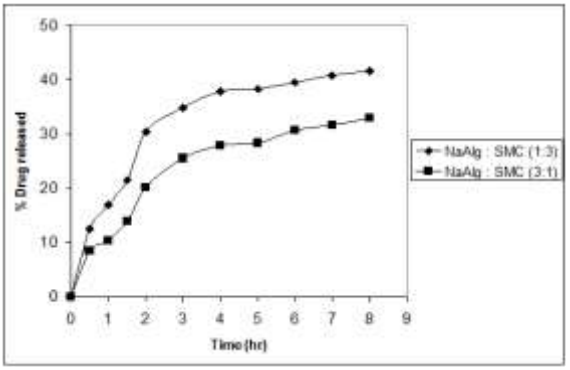

Fig. 12: Release profiles of celecoxib from buccoadhesive tablets containing celecoxib / DM-β-CD coevaporateat (1:1) molar ratio and different ratios of NaAlg: SCMC in phosphate buffer of pH 6.8.

Conclusion:

The dissolution rate of celecoxib from the coevaporate system with DM-β-CD was higher than that from corresponding ground and physical mixtures. The prepared celecoxibbuccoadhesive tablets had acceptable physical parameters, such as hardness, swelling behavior, bioadhesive strength and surface pH. The buccoadhesive tablet (F14) containing celecoxib / DM-β-CD coevaporate with polymer mixture; HPMC: SCMC (1:3 weight ratio) showed the most suitable release rate and properties for adhesion to the buccal mucosal membrane.

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