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Original article

BIOADHESIVE AND MECHANICAL PROPERTIES OF TRIAMCINOLONE ACETONIDE BUCCAL GELS

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Abstract

Bioadhesive drug delivery systems are the most widely used approach which aims to provide high drug concentrations in the oral cavity for a long period of time. A formulation which has been designed for buccal application must exhibit acceptable mechanical characteristics. Texture profile analysis is a method which determines the mechanical properties of polymeric systems. The aim of this study was to develop different buccal gel formulations with several bioadhesive polymers for oral mucosal ulcerations as an alternative to commercial product and to compare the effect of bioadhesive polymers on the mechanical and textural properties of the gel formulations. For these purposes, the gel formulations containing Triamcinolone acetonide were prepared by using Polaxamer 407, Carbopol 934, chitosan and HPMC. All the developed formulations were compared with commercial product which is containing 0.1% triamcinolone acetonide (Kenacort-A Orabese®). According to the results, it was observed that the bioadhesive properties of the formulations depends on the bioadhesive polymer concentration and molecular weight of chitosan. It was also noted that, the bioadhesive performance of the chitosan based formulations was improved with HPMC. Texture profile analysis (TPA) results indicated that mechanical properties of the developed gels are more suitable than the commercial product.

Key words: *Triamcinolone acetonide, Bioadhesion, Buccal gel, Mechanical properties, Texture profile analysis (TPA).*

Triamsinolon Asetonit Bukkal Jellerin Biyoadezif ve Mekanik Özellikleri

Biyoadezif sistemler oral kavitede uzun süre yüksek etkin madde konsantrasyonu sağlaması bakımından en yaygın kullanılan ilaç taşıyıcı sistemlerdir. Ancak bukkal mukozaya uygulanacak formülasyonların kabul edilebilir mekanik özellikler taşıması gerekir. Doku profil analizi (Texture profile analysis-TPA) polimerik sistemlerin mekanik özelliklerinin tespitinde kullanılan bir yöntemdir. Bu çalışmanın amacı farklı biyoadezif polimerler kullanarak piyasa preparatına alternatif olacak yeni jel formülasyonları geliştirmek ve kullanılan polimerlerin, formülasyonların mekanik özelliklerine etkilerini incelemektir. Bu amaçla poloksamer 407, karbopol 934, kitozan ve HPMC kullanılarak triamsinolon asetonit içeren jel formülasyonları hazırlanmıştır. Hazırlanan tüm formülasyonlar %0.1 triamsinolon asetonit içeren piyasa preparatı (Kenacort-A Orabese®) ile karşılaştırılmıştır. Elde edilen sonuçlara göre formülasyonların biyoadezif özelliğinin polimer konsantrasyonuna ve kitozanın molekül ağırlığına bağlı olduğu bulunmuştur. Ayrıca kitozan içeren formülasyonlara ilave edilen HPMC ile daha iyi biyoadezif özellik elde edilmiştir. TPA sonuçlarına göre ise geliştirilen jel formülasyonlarının mekanik özelliklerinin piyasa preparatına göre daha uygun olduğunu gösterilmiştir.

Anahtar kelimeler: *Triamsinolon asetonit, Biyoadezyon, Bukkal jel, Mekanik özellikler, Doku profil analizi.*

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INTRODUCTION

Many inflammatory and ulcerative diseases may occur at the mucous membrane lining in the oral cavity due to various environmental and genetic factors. Recurrent aphthous stomatitis (RAS) is one of the oral mucosal diseases which is seen 1-2% of the general population (1). Topical application of drugs is mainly prefered for treatment of ulcerative and inflammatory mucosal diseases such as RAS (2).

Conventional ointments, creams, mouthwashes, tablets and lozenges are the most widely available preparations for local treatment of the RAS. Although dosage forms provide high drug levels in the oral cavity, they can be washed out easily from the applied region due to the physiological removing mechanisms like washing effect of saliva, swallowing, and tongue movement. Therefore, the therapeutic drug level decreases on the mucosa (3-5). There is also a requirement for a comfortable vehicle that will coat the oral lesions, so semisolid dosage forms especially gels may be the most suitable dosage forms for treatment of the oral mucosal lesions. Because they can be easily spread on the lesions as a thin film layer and help to protect the lesions. Compared with the tablets, the anotomical shape of the mouth will not be affected by applying the gel formulations because of their flexibilty features (3, 6, 7). By the way of addition RAS is characterised by several painful, small round, especially take place in the buccal mucosa. So uniform treatment can not be attained by applying single tablet (8).

All these type of problems have made the researchers to find out bioadhesive drug delivery systems. Bioadhesive gel formultions appear to be particularly attractive for the development of drug delivery systems to improve intraoral administration and reduce the frequency of application and the amount of drug administered. The most important feature of these systems is providing the prolonged and improved contact between the active substance and the mucosa (4, 9). "Bioadhesion" term was defined in 1986, as attachment of a synthetic or natural macromolecule to mucous or an epithelial surface (3, 10). Many bioadhesives are made by synthetic or natural polymers. Different types of chemical bonds such as covalent bonds, hydrogen bonds, ionic bonds and Van Der Waals bonds, consist to develop bioadhesion between polymer and biological surface/mucus (10, 11).

Recent studies suggest that bioadhesive formulations desinged for buccal applications should exhibit suitable and acceptable mechanical properties including acceptable viscosity, easy of expression from the container, easy of application, good spreadability, appropriate hardness and prolonged residance time in the oral cavity. These mechanical properties may affect the performance of the formulations and their acceptance by patients (12, 13). Additionally, some diffuculties were reported when the conventional orabase formulations contained 0.1% Triamcinolone acetonide (Kenalog) were applied (14).

Triamcinolone acetonide which is one of the long acting synthetic glucocorticoids was selected as model active substance for treatment oral mucosal ulcerations. A polyacrilic acid (PAA) polymer (Carbopol 934), a cationic bioadhesive polymer (chitosan) and a cellulose ester derivative (HPMC) were used as examples of polymers that have been reported to possess adhesive polymers (15-17). Different polymeric gel formulations were developed based on carbopol 934 - poloxamer 407 combinations, two different molecular weight chitosan and chitosan – HPMC combinations. Poloxamer 407 which is a nonionic surfactant composed of polyoxyethylene-polyoxypropylene copolymers used for good gelling properties (18). The gel formulations were evaluated in terms of pH, viscosity, mechanical/textural properties and work of bioadhesion. Texture profie analysis (TPA) was used to determine mechanical/textural properties of each formulation.

The aim of this study is to characterize the mechanical and adhesive properties of buccal gel formulations prepared with different bioadhesive polymers. All the developed formulations were compared with commercial product contained 0.1% triamcinolone acetonide (Kenacort-A Orabese®) and the suitability of different gel formulations as drug delivery system for buccal delivery was investigated.

EXPERIMENTAL

Materials

Triamcinolone acetonide (TA) was kindly provided by I.E. Ulagay Drug Company (Turkey). Carbopol 934® (C934) (Noveon-USA), high molecular weight chitosan (HMW - viscosity ≥ 400mPa), medium molecular weight chitosan (MMW- viscosity 200mPa – 400mPa) (Fluka Biochemika -Japan), HPMC-Methocel E 4M (Colorcon LTD-USA) were used as bioadhesive polymers. Poloxamer 407® (P407) (BASF-Germany) were used for its good gelling property. Transcutol (TC) (Fluka Biochemika, Japan) and propylene glycol (PG) (Sigma-Aldrich, USA) were selected as penetration enhancer. As the commercial orabase product contained 0.1% TA (Kenacort–A orabase®) was used. All other reagents were analytical grade.

Preparation of the mucoadhesive delivery systems

P407 and C934 gel systems, containing TA were prepared by cold method (19). While P407 was used because of its thermo-gelling property, C934 was chosen due to its bioadhesive characteristic (18, 20). P407 was added into cold water (5^0C) and left overnight in the refrigerator to complete polymer desolvation. C934 was added into appropriate amount of water and were kept for 24 hours for desolvation. After then it was neutralized to pH 6 using NaOH solution and then mixed with P407 solution.

-For F3 and F4 coded formulations, TA was dispersed in PG and then added final gel formulation.

-For F3-A and F4-A coded formulations TA was dispersed in PG and added gel formulation, TC was added as penetration enhancer finally.

-For F3-C and F4-C, TA was dissolved into TC and added gel formulation. PG was added finally.

CM-3, CH-3 coded formulations were prepared by dissolving chitosan (MMW or HMW) in dilute lactic acid solution (1.5% v/v). For X1 and X2; HPMC was dissolved into dilute lactic acid solution (1.5% v/v) with gently stirring. After polymer desolvation chitosan was added into the solution and dissolved with sonication (Sonics Vibro Cell). For all chitosan based formulations TA was dissolved into TC and added gel formulation PG was added as penetration enhancer finally. Compositions of the gels are seen in Table 1.

Table 1. Composition of the gel formulations.

	P407 (w/w)	**C934 (w/w)**	**TC (w/w)**	**PG (w/w)**	**TA (w/w)**
F3	15	2	-	12	0.1
F3-A	15	2	10 *2	12 *1	0.1
F3-C	15	2	10 *1	12 *2	0.1
F4	20	1.5	-	12	0.1
F4-A	20	1.5	10 *2	12 *1	0.1
F4-C	20	1.5	10 *1	12*2	0.1
	HPMC (w/w)	**chitosan (w/w)**	**TC (w/w)**	**PG (w/w)**	**TA (w/w)**
X1	1	3(MMV)	10*1	12*2	0.1
X2	2	3(MMV)	10*1	12*2	0.1
CM-3	-	3(MMV)	10*1	12*2	0.1
CH-3	-	3(HMV)	10*1	12*2	0.1

*1 added first *2 added second

pH measurements

The pH measurements were performed by a pH meter (Inolab) at room temperature. 10% disperse solution of the commercial product was prepared for measuring the pH. All measurement was carried out three parallels.

Viscosity measurements

The viscosity measurements were carried on 25 ± 1°C using digital viscometer (Brookfield DV II) with a spindle no: T96 at 20 rpm. All analyses were performed at least three times.

Texture profile analysis of TA gels

The mechanical properties of the gels were determined using software-controlled penetrometer, TA-XT Plus texture analyzer (Stable Micro System, UK) equipped with a 5 kg load cell. In briefly, a defined mass of each formulation (50 g) was transferred into a beaker and was kept in the ultrasonic water bath to remove air bubbles for 45 min. After this, temperature of each sample was allowed to equilibrate to 20±1°C. In Texture profile analysis, the perspex probe of 10 mm diameter was compressed twice into each gel sample at a defined rate of 2 $mm.s^{-1}$ to a depth of 15 mm. A delay period was 15 s between the two compressions. At least five replicate analyses were performed for each formulation at room temperature using a fresh sample in each case. Data collection and calculation were performed using the Texture Exponent 3.0.5.0 software package of the instrument. Mechanical parameters such as hardness, compressibility, cohesiveness and elasticity were defined from the resultant force-time plot. (13). Hardness is defined as the force required to attain a given deformation or as the maximum peak force during the first compression cycle. Compressibility defines the work required to deform the product during the first compression of probe. Cohesiveness describes the ratio of the area under the force-time curve produced on the second compression cycle to that produced on the first compression cycle, where successive compressions are separated by a defined recovery period. Elasticity defines the ratio of the time required to achieve maximum structural deformation on the second compression cycle to that on the first compression cycle, where successive compressions are separated by a defined recovery period (21). Each experiment was carried out five times.

Mucoadhesion testing

The mucoadhesive properties of the formulations were evaluated with a 5 kg load cell using TA-XT Plus texture Analyser equipped (21-24). Freshly excised bovine buccal tissue was frozen at -30°C. A section that possessed 2 mm thickness was taken from inner part of the surface of the frozen buccal mucosa and was attached to the lower end of the TPA probe (P 10 mm Perspex). Sample of the gels were packed into shallow cylindrical vessels. Temperature of each sample was allowed to equilibrate to 37 ± 0.1°C by storage in an oven. The probe holding the buccal mucosa was lowered onto surface of the gel with a constant speed of 0.5 $mm.s^{-1}$ and contact force of 0.0001 N applied. After keeping in contact for 180 s, the probe was then moved vertically upward at a constant speed of 0.07 $mm.s^{-1}$. The area under the curve (AUC) was calculated from force-distance plot as the work of mucadhesion. The equation given below was used to calculate the work of mucoadhesion (mJ/cm^2). Each experiment was carried out five times.

$$\text{Work of mucoadhesion } \left(mJ/cm^2\right) = \frac{AUC}{\pi r^2} \qquad \text{(Equation 1)}$$

Where, πr^2 = the mucosal surface being in contact with gel.

Statistical analysis

The effect of the polymer concentration and polymer type on the hardness, cohesiveness, compressibility and elasticity at the formulations were statistically evaluated using a one way analysis of variance ANOVA and paired-T Test method.

RESULTS AND DISCUSSION

pH and viscosity results are shown in Table 2 and 3. For chitosan based formulations, the pH values are lower than physiological pH of the oral cavity and the pH of the commercial product because of using lactic acid. The pH values of P407 - C934 combinations were found between 6.17 ± 0.01 and 6.78 ± 0.02. According to these results P407 - C934 gel systems were more applicable to the buccal mucosa than chitosan based formulations and the commercial product.

Table 2. pH values of the formulations.

Formulation code	25 ± 1°C		Formulation code	25 ± 1°C	
	pH (n=3)	SD*		pH (n=3)	SD*
F3	6.17	0.01	**F4**	6.43	0.02
F3-A	6.54	0.03	**F4-A**	6.38	0.01
F3-C	6.30	0.02	**F4-C**	6.78	0.02
CH-3	4.44	0.01	**X1**	4.72	0.01
CM-3	4.53	0.00	**X2**	4.17	0.01
Kenacort-A Orabase®	5.13	0.01			

* Standard deviation

The viscosity of the semisolids should be allowed to express from the container and spread on the lesion easily. At the same time, formulations should have appropriate retention characteristics to prevent flowing and remove. Although enhanced viscosity can more suitable for easily spread on the lesions as a thin film layer, conventional dossage form e.g mouthwashes, suspensions easily remove from the mucosa. Otherwise, ointments or creams can stay at the application site with poor mouth feeling, because of the high viscosity values (25). In a similar way, viscosity values of the commercial product are not convenient for the applying to the oral lesions.

It was found that the viscosity values of the F3 – F4 coded formulations depended on P407 concentrations. Transcutol which was added as a penetration enhancer (A and C coded formulations) reduced the viscosity values of the formulations. P407 - C934 combinations with TC are more favorable for topical application than commercial product. On the other hand, viscosity values of the chitosan based formulations increased significantly with the increasing molecular weight of chitosan. It was found that, CM-3 coded formulation was not appropriate for the applying buccal mucosa because of its low viscosity. HPMC was added to CM coded formulations to increase viscosity. Eventually, the viscosities of X1 and X2 coded formulations were the best.

Table 3. Viscosity values of the formulations.

Formulation code	25 ± 1°C		Formulation code	25 ± 1°C	
	Viscosity (Pa.s)	SD*		Viscosity (Pa.s)	SD*
F3	175.56	3.88	**F4**	231.78	2.05
F3-A	111.56	2.51	**F4-A**	155.44	1.33
F3-C	111.78	1.30	**F4-C**	163.11	1.36
CH-3	29.00	0.83	**X1**	10.06	0.68
CM-3	6.28	0.36	**X2**	26.89	1.24
Kenacort-A Orabase®	200.00	1.63			

* Standard deviation

Mechanical properties

The basic parameters for designing of mucoadhesive gels are ease of removal of the gel from the primary package, ease of application of the product to the desired region and retention at the application site without disintegration (26). The buccal semisolid formulations should have appropriate mechanical properties for the maximum benefit of the patient from the formulation. Texture profile analysis was used to investigate effects of content of the formulation on the hardness, compressibility, elasticity and the cohesiveness of the gels and to determine the mechanical properties of the prepared mucoadhesive buccal gels (Table 4) (13, 27, 28).

Table 4. Mechanical and mucoadhesive properties of gel formulation (n=5).

Codes	Hardness (N) ± SD	Cohesiveness ± SD	Compressibility (N.mm) ± SD	Elasticity ± SD	Work of mucoadhesion (mJ/cm^2) ± SD
F3	0.26 ± 0.03	0.86 ± 0.03	0.90 ± 0.11	0.91 ± 0.01	0.10±0.02
F3-A	0.23 ± 0.02	0.84 ± 0.03	0.79 ± 0.07	0.90 ± 0.01	0.11±0.01
F3-C	0.25 ± 0.02	0.86 ± 0.05	0.86 ± 0.02	0.91 ± 0.01	0.11±0.01
F4	0.59 ± 0.06	0.93 ± 0.03	1.84 ± 0.14	0.96 ± 0.01	0.08±0.00
F4-A	0.44 ± 0.05	0.92 ± 0.02	1.52 ± 0.19	0.96 ± 0.01	0.09±0.00
F4-C	0.39 ± 0.05	0.94 ± 0.04	1.22 ± 0.09	0.96 ± 0.00	0.09±0.02
CM-3	0.02 ± 0.00	0.94 ± 0.02	0.09 ± 0.00	1.05 ± 0.10	0.01±0.03
CH-3	0.04 ± 0.00	0.95 ± 0.01	0.12 ± 0.01	0.98 ± 0.01	0.03±0.06
X1	0.02 ± 0.00	0.93 ± 0.03	0.09 ± 0.01	1.02 ± 0.02	0.11±0.00
X2	0.03 ± 0.00	0.96 ± 0.01	0.10 ± 0.00	1.00 ± 0.02	0.12±0.01
Kenacort-A Orabase®	0.87 ± 0.03	0.63 ± 0.12	1.92 ± 0.13	0.96 ± 0.06	0.01±0.01

The hardness expresses the applicability of the gel to the desired site. The gels should have low hardness value to be administered to the buccal mucosa easily (27). The hardness values of the gel formulations including P407-C934 (F3 series and F4 series) improved significantly due to the increment in the P407 polymer concentration ($P < 0.05$). The formulations including 20% P407 and 1.5% C934 without TC (F4 0.59 ± 0.06 N) showed the highest hardness values because of the increased viscosity, and acceptable hardness results were gained from all P407-C934 formulations. As may be observed, viscosity of formulations significantly increased the magnitude of hardness.

A coded formulations including dispertion of the TA and C coded formulations including solution of the TA were compared to investigate the effect of physical condition of TA on mechanical properties. No significant differences were found by statistically ($P > 0.05$) for F3 and F4 coded formulations. Thereby, hardness is not affected by physical condition of the drug.

The mechanical properties of gels composed of MMW chitosan, HMW chitosan and HMW chitosan-HPMC combinations are presented in Table 4. Raising molecular weight of chitosan, significantly increased formulation hardness. While hardness of CM-3 coded formulation was 0.02 ± 0.00 N, CH-3 was 0.04 ± 0.00 N. ($P< 0.05$). Hardness values of chitosan based gels were affected by polymer molecular weight and also viscosity of formulation. Different amount of HPMC (1% and 2% respectively) was added to MMW chitosan formulations for X1 and X2 formulations. Although hardness of formulation was significantly affected by polymer concentration and viscosity of formulation (29), increasing the concentration of HPMC from 1% to 2% did not change the hardness values interestingly. When hardness values of the CM-3, X1 and X2 were compered, no significant difference were found statistically ($P > 0.05$).

Table 4 presents the mechanical properties of the commercial product. When all hardness test results were compared, commercial product shows the highest hardness value (0.87 ± 0.03 N). It shows that, applying this product to the desired side isn't as easy as developed formulations. MMW chitosan-HPMC gel systems were observed to have lower hardness values than the other gel formulations and commercial product.

The buccal administration of drugs has gained interest because the oral cavity forms a convenient and easily accessible site for local and systemic drug delivery (30). However, the low flux associated with buccal mucosal delivery, a major limitation of the buccal route of administration, is the lack of dosage form retention at the site of absorption (31). Product cohesiveness has been reported to describe spatial aspects of structural reformation following product compression (28. 32, 33, 34). The cohesiveness of the polymer is high if its attractive force of its own molecules is high in the gel. This parameter increases the performance of the product at the application site. The high value of cohesiveness provides full structural recovery following gel application (28).

In this study, the increment of the cohesiveness of P407-C934 gels was significantly affected by P407 amount used. When the P407 concentration increased from 15% (F3) to 20% (F4), the cohesiveness also increased significantly ($P < 0.05$). For example, cohesiveness of the F3 coded formulation was 0.86 ± 0.03 while that of F4 was 0.93 ± 0.03 due to higher viscosity value of the F4. No significant differences were found statistically ($P > 0.05$) between F3, F3-A and F3-C, besides F4 series. Thereby, cohesiveness is not affected by physical condition of the drug.

When the chitosan based formulations were compared, similar results were found statistically ($P > 0.05$). According to these results, cohesiveness is not affected by adding different amount of HPMC (1% and 2%) to the MMV chitosan gels.

When the polymers used for the preparation of gels were compared, the cohesiveness results of different gel formulations were closer to each other, and commercial product showed the lowest cohesiveness value (0.63 ± 0.12). This data shows that, developed formulations are more convenient than commercial product in terms of application.

The compressibility expresses taking the prepared gel from the container and the simplicity of the spreadibility on the application site. The compressibility value should be low to take the prepared gel from the container and to be easily spread on the mucosal epithelia (27, 28).

Compressibility properties of the P407-C934 gel systems increased significantly with the increment in the P407 concentrations ($P < 0.05$). F3 series formulations have lower compressibility values than F4 series formulations due to P407 concentration, also lower viscosity values. No significant differences were found by statistically ($P > 0.05$) between F3, F3-A and F3-C, besides F4 series. Thereby, compressibility is not affected physical condition of the drug.

While compressibility values of CM-3 was 0.09 ± 0.00 N.mm, CH-3 was 0.12 ± 0.01 N.mm. Rising of the molecular weight of chitosan, decreased the compressibilty properties statistically ($P < 0.05$).

However, adding HPMC to CM-3 coded formulations increased the viscosity without any effect on the compressibility. When compressibility values of the CM-3 (0.09 ± 0.00N.mm), X1 (0.09 ± 0.01N.mm), and X2 (0.10 ± 0.00 N.mm) were compared, no significant difference was found statistically ($P > 0.05$).

Commercial product shows the highest compressibility value (1.92 ± 0.13 N.mm). Similarly F4 coded formulation (20% P407 – 1.5% C934) have higher compressibility values than other formulations. Acceptable compressibility values were obtained from all developed formulations except F4. When obtained results were evaluated and compared with the commercial product, developed different polymer based formulations except F4 have aproppriate compressibility for applicability to the buccal mucosa.

In TPA, lower numerical values in the elasticity mode indicate greater product elasticity, and therefore, increasing the concentration of polymers resulted in decrease product elasticity (32). The elasticity value of F3 (0.91 ± 0.01) is lower than the elasticity value of F4 (0.96 ± 0.01). It means that F3 formulation has more elastic property than F4 formulation.

The results obtained for chitosan based formulations were compared and no significant differences were found statistically ($P > 0.05$). However P407-C934 formulations are more elastic than chitosan based formulations ($P < 0.05$). Lower numerical values as determined by TPA in the elasticity mode increase greater product elasticity (29). Different amount of HPMC (1% - 2%) which is added to CM-3 coded formulations does not affect the elasticity of formulation statistically ($P > 0.05$). MMW chitosan-HPMC combinations (X1 and X2) were observed to be less elastic than the P407-C934 gel formulations. Similar elasticity values were achived with commercial product and developed formulations.

Mucoadhesion studies

In this investigation, the mucoadhesive properties of prepared gel formulations were examined using texture profile analysis by evaluation of the detachment force required to overcome the adhesive bond between each formulation and the buccal mucosa. The polymers employed in these formulations have been described as bioadhesive and, therefore, it would be anticipated that the formulation would display good mucoadhesive properties (35, 36). It also was noted that factors such as the molecular weight of polymer, the type and degree of cross-linking agent, molecular architecture and the polymer amount in the gel influenced the mucoadhesive performance (35,37,38).

The results related to the work of mucoadhesion are given in Table 4. According the results obtained for P407-C934 gel systems, the adhesive properties of the formulations increased as a function of polymer concentration and viscosity. Decreasing concentration of C934 from 2 % to 1.5 % (w/w), significantly decreased formulation adhesiveness ($P < 0.05$). Adhesiveness of chitosan based gels was affected by polymer molecular weight and also viscosity of formulation. While the bioadhesion work of CM-3 coded formulation was 0.01 ± 0.03 mJ/cm^2), CH-3 was 0.03 ± 0.06 mJ/cm^2) ($P < 0.05$). Interestingly, adding HPMC (1% and 2% respectively) to MMW chitosan formulations improved adhesiveness significantly without any change or the other mechanical properties. The highest work of mucoadhesion was determined for the formulation coded X2; 0.012 ± 0.01 mJ/cm^2, whereas the lowest work of mucoadhesion was determined for the formulation coded as CM-3 0.01 ± 0.03 mJ/cm^2. Work of bioadhesion value of the commercial product was computed at the same conditions. Because of it's high viscosity value bioadhesion work of commercial product was found 0.01 ± 0.01 alike CM-3 coded formulation.

CONCLUSIONS

Triamcinolone acetonide is one of the therapeutic agents for the treatment of oral mucosal ulceration. Conventional commercial products including TA are available in the market (Kenacort –A orabase® / Kenalog). Furthermore, a difficulty of applying orabase and low patient tolerance were reported. In the study, an alternative mucoadhesive buccal drug delivery system containing TA was developed for the treatment of oral mucosal ulcers. Buccal gel formulations were prepared using with three different types of bioadhesive polymers Carbopol 934, chitosan and HPMC and disadvantages like difficulties of applying orabase and low patient tolerance was intended to eliminate.

According the TPA results, among the formulations, lowest hardness and compressibility, highest cohesiveness and elasticity values of chitosan – HPMC combinations allow the most convenient textural properties. Also we have concluded that, the limited mucoadhesiveness was attained with MMW chitosan. However mixing chitosan with HPMC can be improved the adhesive performance of the formulations without affecting the mechanical properties. When we compared the mucoadhesion studies of the commercial product and developed formulations values of our formulations guarantee the achievement of therapeutic concentration in the action side and improvement of patient's compliance. In conclusion, chitosan, and HPMC combinations can be used as vehicle for active substance to the oral cavity because of their good textural and mucoadhesive properties.

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