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მედიცინის ფაკულტეტი
AKAKI TSERETELI STATE UNIVERSITY
FACULTY OF MEDICINE

II საერთაშორისო სამეცნიერო–პრაქტიკული ინტერნეტ-კონფერენცია

თანამედროვე ფარმაცია – მეცნიერება და პრაქტიკა

შრომათა კრებული

THE II INTERNATIONAL SCIENTIFIC-PRACTICAL INTERNET-CONFERENCE

MODERN PHARMACY – SCIENCE AND PRACTICE

PROCEEDINGS

ქუთაისი
KUTAISI. GEORGIA
01.12.2020-21.12.2020

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THE INFLUENCE OF COMPRESSION FORCE ON MECHANICAL AND TEXTURAL PROPERTIES OF COMPRESSIBLE MEDICATED CHEWING GUMS

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The aim of the present study was to find out the influence of compression force on the mechanical and textural characteristics of compressible medicated chewing gums with lysozyme hydrochloride and ascorbic acid. Four batches of MCGs were obtained on a laboratory single-punch tablet machine with applying different forces, i.e., 5, 7, 10 and 15 kN. According to mechanical evaluation, resistance to crushing and friability of MCGs changed slightly with increasing compression force, and all batches met the requirements of Ph.Eur. on these attributes. According to the texture analysis, increasing compression force leads to harder and more adhesive gums, which can cause difficulties in chewing MCGs and, consequently, impairment of their consumer properties.

According to the results obtained, applying high compression force during the manufacturing process of medicated chewing gums is not only disadvantageous from the technological point of view, but also is undesirable based on biopharmaceutical considerations, since it may negatively affect perceptive sensations under the using of this dosage form.

Introduction and aim: In recent years the pharmaceutical research field has shown a growing interest towards patient friendly drug delivery systems. One of those is medicated chewing gum (MCG). Considering MCG as a platform for drug delivery it is clearly evident that the main feature of its administration is relatively long mastication, that gives valuable benefits: such therapy is stressless (because the act of chewing itself has been found to relieve stress), a medication does not need to be injected or swallowed with water (which can be difficult for some patients) [1,2]. The feature of continuous chewing also makes a prime opportunity for using MCGs in dental prophylaxis and treatment. Chewing process is considered to have a positive effect on the oral healthcare through facilitating the removal of sugars and bacterial fermentation end products, increasing the buffering action of saliva, enhancing the degree of remineralization of teeth, stimulation of saliva production, etc. [3,4]. In our previous works we have substantiated the composition and method for preparation of compressible MCGs with lysozyme hydrochloride and ascorbic acid, which are intended for the prevention and treatment of dental diseases, in particular inflammatory diseases of the periodontium (gingivitis, periodontitis), mucous membranes (stomatitis), caries and manifestations of xerostomia [5-8]. A directly compressible gum base Health-in-Gum® was used (Cafosa, Spain) to obtain MCGs by a simple compression method on a common tableting machine [9-11]. The aim of our work is to study mechanical and textural characteristics of MCGs depending on the compression force applied, as one of the most important parameters affecting the quality of compressed dosage forms.

Research methodology: Round flat-faced gums with a mass of 1000 mg and a diameter of 13 mm were produced on a laboratory single-punch tablet machine (model HTM-01E, Mariupol Plant of Technological Equipment, Ukraine) equipped with a force-measuring tool. Four batches of MCGs compressed at different force values, i.e. 5, 7, 10 and 15 kN, were obtained. Mechanical resistance of MCGs was assessed by two pharmacopoeial tests, which are “Resistance to crushing of tablets” (Ph.Eur. 9.0, chapter 2.9.8) and “Friability of uncoated tablets” (Ph.Eur. 9.0, chapter 2.9.7) using Monsanto hardness tester (Campbell Elec., India) and PTF 20E friability apparatus (Pharma Test, Germany), respectively [12]. The texture properties of MCGs were investigated by penetration test using a texture analyzer TA.XT.plus (Stable Micro Systems Ltd, Godalming, Surrey, UK) using as a reference sample a commercially available compressed functional chewing gum “XD Extra Drive AntiStress Relax”. The

penetration test evaluates the deformation response of the product to a stainless steel needle probe P/2N (2 mm thickness). To carry out the test, the gum was placed by its center under a needle probe, which then was set to penetrate into the sample at a constant load of 5 kg and a speed of 2 mm/s to a depth of 3 mm. Two main parameters were registered: hardness – the maximum force value required for a probe to overcome mechanical resistance of the product while reaching penetration target; and adhesiveness – the force value required for a probe to overcome attractive forces (sticking) between its surface and the surface of the product being investigated [10]. The analysis was performed at room temperature (25 ± 2)ºC. Statistical analysis was performed using Microsoft Office Excel 2016. All experimental determinations were done in triplicate and results are presented as mean value ± standard deviation (SD). Significant levels were defined at $p < 0.05$.

Results and implications: According to results of mechanical resistance characteristics of MCGs, increasing pressure during the manufacturing process resulted in the enhanced resistance of gums to mechanical stress. Nevertheless, even MCG batch obtained at the lowest compression force completely met the requirements of Ph.Eur. It should be noted that resistance to crushing test did not lead to any break of gums but only deformation which is obviously related to the plastic and elastic nature of the chewing gum base. The unbreakable behavior of MCGs during resistance to crushing test actually reflects the main feature of this dosage form, as it is intended for chewing and thus must undergo plastic and elastic deformation, providing a relatively long mastication process. And contrary to common tablets, hardness of MCGs is not so much important for mechanical stability (e.g., during transportation) but rather for chewiness – the extent of deformation caused by a certain load applying to the gum. For objective evaluation of product chewiness a texture profile analysis is often used. According to the hardness as well as adhesion values MCG batches are ranged as follows: 15 kN > 10 kN > 7 kN > 5 kN. That is, the more compression force was applied, the harder and more adhesive gums were obtained. That's why unreasonably high compression force eventually may lead to the difficulty in chewing MCGs. Consequently, this will contribute to the impairment of the product consumer properties. At the same time the comparison with commercially available compressed chewing gum "XD Extra Drive AntiStress Relax" revealed the most textural similarity of the reference sample to MCGs obtained at 5 and 7 kN.

Conclusion: All batches of MCGs compressed at 5, 7, 10 and 15 kN compression force values completely met the requirements of Ph.Eur. on resistance to crushing and friability tests; however, change in compression force resulted in the differences of textural properties of the samples. The higher compression force led to harder and more adhesive gums, which may be not acceptable for patients suffering from painful chewing caused by periodontal tissues inflammation. Thus, based on the results obtained, it can be concluded that it is optimal to use low values of the compression force (5 or 7 kN) to obtain compressible MCGs. The aim of our further work is to establish the final compression force and to study its effect on the organoleptic, biopharmaceutical and consumer characteristics of medicated chewing gum.

Keywords: Compressible medicated chewing gums, compression force, mechanical resistance, textural analysis, lysozyme hydrochloride, ascorbic acid.

References

1. Kubo KY, Iinuma M, Chen H. Mastication as a Stress-Coping Behavior // Biomed Res Int. 2015. – Vol. 2015. – P. 876409.
2. Smith AP. Chewing gum and stress reduction // J Clin Transl Res. 2016. – Vol. 2. – P. 52–54.
3. Akbal O, Cevher E, Araman AO. The development and in vitro evaluation of benzydamine hydrochloride medicated chewing gum formulations // Istanbul J Pharm. 2017. – Vol. 47. – P. 45–51.
4. Wessel SW, van der Mei HC, Maitra A, Dodds MW, Busscher HJ. Potential benefits of chewing gum for the

delivery of oral therapeutics and its possible role in oral healthcare // Expert Opin Drug Deliv. 2016. – Vol. 13. – P. 1421–1431.
5. Maslii Yu, Ruban O, Yevtifieieva O, Hrudko V, Gureyeva S, Goy A, Kolisnyk T. Development and uniformity evaluation of low-dose medicated chewing gums prepared by compression method // Ceska Slov Farm. 2020. – Vol. 69. – P. 33–42.
6. Maslii Yu, Ruban O, Kolisnyk T. Investigations with the aim of obtaining a mass for pressing medicated chewing gums "Lysodent C" // ScienceRise: Pharm Sci. 2019. – Vol. 3. – P. 11–16.
7. Maslii Yu, Ruban O, Kutsenko S. Selection of flavour additives and method of their introduction in the composition of compressed medicated chewing gums // EUREKA: Health Sciences. 2020. – Vol. 2. – P. 59–66.
8. Maslii YuS, Ruban OA, Kolisnyk TE, Liapunova OA. The substantiation of the method for introduction of lysozyme hydrochloride and ascorbic acid in the composition of the medicated chewing gum “Lysodent C” // Ukr Biopharm J. 2019. – Vol. 3. – P. 14–22.
9. Kaushik P, Kaushik D: Medicated Chewing Gums: Recent Patents and Patented Technology Platforms // Recent Pat Drug Deliv Formul. 2019. – Vol. 13. – P. 184–191.
10. Al Hagbani T, Nazzal S. Development of postcompressional textural tests to evaluate the mechanical properties of medicated chewing gum tablets with high drug loadings // J Texture Stud. 2018. – Vol. 49. – P. 30–37.
11. Al Hagbani T, Nazzal S: Medicated Chewing Gums (MCGs): Composition, Production, and Mechanical Testing // AAPS PharmSciTech. 2018. – Vol. 19. – P. 2908–2920.
12. Council of Europe. European Pharmacopoeia, 9th ed. Strasbourg: Council of Europe, 2016.

შეკუმშვის ძალის გავლენა დაწნეხილი სამკურნალო საღეჭი რეზინების მექანიკურ და სტრუქტურულ თვისებებზე

იულია მასლიი, ტეტიანა კოლისნიკი, ოლენა რუბანი
ფარმაციის ეროვნული უნივერსიტეტი, ხარკოვი, უკრაინა

რეზიუმე

წინამდებარე კვლევის მიზანს წარმოადგენდა შეკუმშვის ძალის გავლენის გარკვევა დაწნეხილი სამკურნალო საღეჭი რეზინის მექანიკურ და ტექსტურულ მახასიათებლებზე, რომლებიც შეიცავს ლიზოციმ ჰიდროქლორიდს და ასკორბინის მჟავას. მიღებული იქნა დაწნეხილი სამკურნალო საღეჭი რეზინის ოთხი პარტია ლაბორატორიული ერთსაფეხურიან სატაბლეტო წნეხზე სხვადასხვა ძალების გამოყენებით, ე.ი. 5, 7, 1 ძალის გამოყენებით. 0 და 15 კნ. მექანიკური შეფასების მიხედვით, შეკუმშული სამკურნალო საღეჭი რეზინების დარტყმითი წინაღობა და ფორიანობა ოდნავ შეიცვალა დაწნევის ძალის გაზრდით, და ყველა პარტია აკმაყოფილებდა Ph.Eur–ოს მოთხოვნებს. სტრუქტურის ანალიზის მიხედვით, შეკუმშვის ძალის უფრო და უფრო მომატება იწვევდა წებოვანი და ადჰეზიური საღეჭი რეზინების წარმოქმნას, რამაც შეიძლება გამოიწვიოს სირთულეები შეკუმშვადი სამკურნალო საღეჭი რეზინების ღეჭვისას და შესაბამისად, გამოიწვიოს მათი სამომხმარებლო თვისებების გაუარესება.

მიღებული შედეგების მიხედვით, მაღალი დაწნეხვის ძალის გამოყენება სამკურნალო საღეჭი რეზინების წარმოების პროცესში არამარტო არახელსაყრელია ტექნოლოგიური თვალსაზრისით, არამედ არასასურველია ბიოფარმაცევტული მოსაზრებებითაც, რადგან ამან შეიძლება უარყოფითად იმოქმედოს აღქმით შეგრძნებებზე ამ სამკურნალწამლო ფორმის გამოყენებისას.

DIRECTION 2. ELABORATION OF FORMULATION AND TECHNOLOGY OF MODERN COSMECEUTICALS, CHEMICAL-PHARMACEUTICAL AND BIOTECHNOLOGICAL PREPARATIONS. THEIR BIOPHARMACEUTICAL AND PHARMACOLOGICAL STUDY
მიმართულება 2. თანამედროვე ქიმიურ-ფარმაცევტული, კოსმეტიკური და ბიოტექნოლოგიური პრეპარატების რეცეპტურისა და ტექნოლოგიის შემუშავება, ბიოფარმაცევტული შესწავლა