FORMULATION & EVALUATION OF MOUTH DISSOLVING GRANULE TO TREAT MOUTH ULCER

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ABSTRACT:

Mouth ulcers are common oral lesions that cause pain, inflammation, and difficulty in eating and speaking. Conventional treatments such as gels and ointments often show poor patient compliance due to unpleasant taste and difficulty in application. The present study aims to formulate and evaluate mouth dissolving granules for the effective management of mouth ulcers. Mouth dissolving granules are designed to rapidly dissolve in the oral cavity without the need for water, providing faster onset of action and improved patient convenience. In this formulation, suitable active pharmaceutical ingredients along with excipients such as superdisintegrants, sweeteners, flavoring agents, and granulating agents were selected to enhance palatability and rapid dissolution. The granules were prepared using the wet granulation method and evaluated for various physicochemical parameters including particle size, angle of repose, bulk density, tapped density, Carr's index, Hausner ratio, drug content, and in-vitro drug release. Additionally, parameters such as taste, mouth dissolving time, and stability studies were also assessed.

The results indicated that the prepared mouth dissolving granules exhibited good flow properties, rapid disintegration in the oral cavity, and satisfactory drug release profile. Therefore, mouth dissolving granules can be considered a promising dosage form for the effective and convenient treatment of mouth ulcers, improving patient compliance and therapeutic effectiveness.

Keywords:- Mouth ulcer, Oral drug delivery system, Mouth dissolving Granules, Drug release, Superdisintegrants.

INTRODUCTION:

Ulcers, also known as Aphthous Ulcers, are common painful lesions that occur in the oral mucosa. They are characterized by small, round or oval sores with a white or yellow center surrounded by a red inflammatory border. These ulcers can cause discomfort, burning sensation, and difficulty in eating, drinking, and speaking. The causes of mouth ulcers include stress, nutritional deficiencies, hormonal changes, minor injuries in the mouth, and certain infections. Although most ulcers heal naturally within 7–14 days, proper treatment is required to reduce pain, inflammation, and promote faster healing.[1]

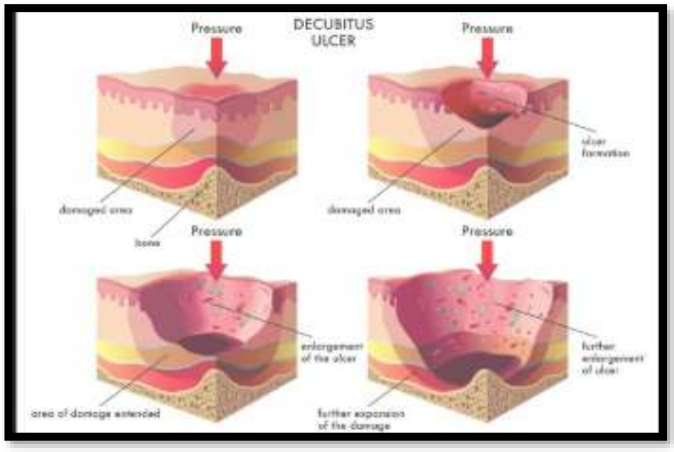

Figure 1: Stages of ulcer

Iron, vitamin B12, vitamin C, and other nutritional deficiencies, as well as poor mouth hygiene, infections, stress, indigestion, mechanical injury, food allergies, hormonal imbalances, and specific skin conditions, are common triggers.

Figure 2: Normal to ulcer developed skin

Conventional dosage forms such as gels, ointments, and mouthwashes are commonly used to treat mouth ulcers. However, these formulations often have limitations such as poor retention time in the oral cavity, unpleasant taste, and inconvenience during application. To overcome these issues, advanced drug delivery systems have beendeveloped to improve patient compliance and therapeutic effectiveness.

Mouth dissolving granules are an innovative oral drug delivery system that rapidly dissolves or disintegrates in the mouth without the need for water. This dosage form offers several advantages such as rapid onset of action, improved bioavailability, ease of administration, and better patient compliance, especially for pediatric and geriatric patients. These granules are designed to release the drug quickly in the oral cavity, providing immediate relief from pain and inflammation associated with mouth ulcers.

The formulation of mouth dissolving granules involves the use of suitable excipients such as superdisintegrants, sweetening agents, flavoring agents, and granulating agents to enhance taste and improve dissolution properties. Proper evaluation of these granules is essential to ensure their quality, stability, and therapeutic efficiency. Therefore, the present study focuses on the formulation and evaluation of mouth dissolving granules for the effective management of mouth ulcers.[3]

The different types of ulcers

There are a few types of ulcers, including:

- Arterial ulcers
- Venous ulcers
- mouth ulcers
- Genital ulcers

Mouth ulcers

Mouth ulcers are small sores or lesions that develop in your mouth or the base of your gums. They're commonly known as canker sores.

These ulcers are triggered by a number of causes Trusted Source, including:

- stress
- hormonal changes
- vitamin deficiencies
- bacterial infection
- diseases

Mouth ulcers often go away on their own without treatment. If they become painful, your doctor or dentist may prescribe an antimicrobial mouthwash or ointment to reduce your discomfort.If your condition is the result of a more serious infection, seek medical attention to receive the best treatment.

Figure 3: Mouth ulcer

Types of Mouth Ulcers

Mouth ulcers can be defined as mild, large, or herpetiform based upon their size and quantity. The biggest types of ulcers in oral cavity are

Minor ulcers range in size from 2 to 8mm and generally heal between 10 days to 2 weeks.

Major ulcers are broader and deeper, typically with a raised or rough border. This form of ulcer can take many weeks for treatment and may leave a scar on the mouth.

Herpetiform ulcers can be made up of dozens of tiny infections the size of a pin head.[2]

MATERIALS AND METHOD

S.No.	Ingredients	Quantity	functions
1.	Glycyrrhiza glabra	20gm	Anti inflammatory effect
2.	Tulsi	15gm	Antimicrobial property
3.	Mentha	10gm	Cooling and pain relief
4.	Triphala	20gm	Promote healing and reduce inflammation
5.	Camphor	2gm	Reduce burning sensation
6.	Honey	15gm	Sweetener
7.	Starch	10gm	Binder
8.	Mint or lemon	Q.S.	Flavoring

Method:

The granules were formulated using the solvent casting method, a widely accepted and effective technique for preparing thin and uniform films known for its excellent mucoadhesive and wound-healing properties, was selected as the primary polymer to ensure robust film-forming capability and enhance the therapeutic potential of the formulation. Glycerin was incorporated as a plasticizer to impart flexibility and improve the mechanical strength of the films, ensuring ease of handling and application. The detailed composition of the formulation is provided in, showcasing the precise proportions of each ingredient. The films were cast in a Petri dish with a surface area of 90 mm, specially fabricated for this purpose. The total volume of the film-forming solution was adjusted to 10 mL using ethanol as the solvent, ensuring a uniform distribution of the components and optimal film formation. This systematic approach facilitated the production of high-quality granules with desirable physical and chemical characteristics for the intended therapeutic application.[12]

Preparation of 20 Mouth Ulcer Granule Sachets (100 g Batch)

Method : Wet Granulation

Accurately weigh all ingredients according to the 100 g batch formula.

Figure 4: Weighing of drug

Ensure powders of Glycyrrhiza glabra, Tulsi, Mentha and Triphala are completely dry.

If required, dry at 40°C to remove moisture.

Pass all powdered ingredients through sieve No. 60 to obtain uniform particle size.

Figure 5: Pass the drug from sieves

Transfer all sieved powders into a clean mortar or mixer.

Figure 6 Transferring the drug to mortar pestle

Mix thoroughly for 10–15 minutes to ensure uniform distribution.

Add finely powdered camphor and mix properly.

Prepare starch paste using warm water.

Add honey into the starch paste and mix well to form a uniform binder solution.

Slowly add the binder solution to the powder mixture with continuous mixing.

Mix until a damp mass is formed.

Pass the damp mass through sieve No. 16 to form granules.

Figure 7: Pass the drug from sieves

Spread granules evenly on a tray.

Dry in a tray dryer at 40–45°C until completely dry.

Pass dried granules again through sieve No. 20 to obtain uniform size.

Figure 8: Pass the drug from sieves

Add mint or lemon flavour and mix gently.

Weigh 5 g granules and fill into sachets.

Pack 20 sachets in airtight container.

Evaluation Parameters of Formulation:

General appearance

The general appearance, color, odour and test of granules were found by visual determination. It is circular in shape and brownish in colour, characteristics odour, slightly bitter in taste.[16]

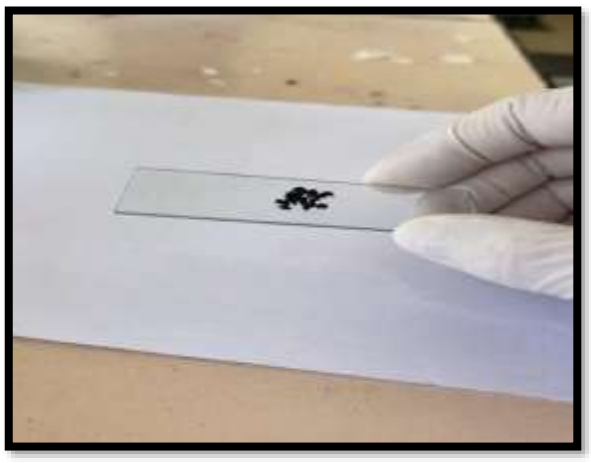

Figure 9: Physical appearance

Color – Darkest brown

Shape – Small Circular

Determination of pH:

The pH of herbal tea granule solution in distilled water was determined at room temperature by using pH paper.

Figure 10: pH test

Loose bulk density (LBD):

Determined by pouring a weighed quantity of granules into a graduated cylinder and measuring the volume and weight.

LBD = Weight of the powder / volume of the packing

Tapped bulk density (TBD):

Determined by placing a graduated cylinder, containing a known mass of granules. The cylinder was allowed to fall under its own weight onto a hard surface from the height of 10 cm at two second intervals. The tapping was continued until no further change in volume was noted.

TBD = Weight of the powder / volume of the tapped packing

Dissolution Rate of Granules

This test was performed to evaluate the rate and extent to which the active constituents were released from the granules into the dissolution medium. It measured the percentage of drug release over a specified period, indicating the granules' efficiency in delivering the active ingredients for absorption.

Ash Value of Granules

This test was carried out to determine the total amount of inorganic material present in the granules. It indicates the presence of extraneous matter such as dirt or sand, and serves as an indicator of the granules' purity and quality.

Hausner ratio:

It is the measurement of frictional resistance to the drug. The ideal range should be 1.2- 1.5. It is determined by using the following formula:

Hausner ratio= TBD / LBD

Compressibility index:

The Compressibility index of the blends was determined by the Carr's compressibility index.

Compressibility index (%) = (TBD-LBD) X 100 / TBD

Loss on drying:

One gram of granules was transferred into a dried, glass stoppered shallow weighing bottle. The contents were distributed evenly and placed in the drying chamber. The stopper was removed from the bottle and the contents were dried for a specified time to achieve a constant weight.[7]

Loss on drying (%) = [(Initial weight – Final weight) / (Initial weight)] X 100

Figure 11: Loss on drying

Solubility Test

This test was performed to evaluate the rate and extent to which the active constituents were released from the granules into the dissolution medium. It measured the percentage of drug release over a specified period, indicating the granules' efficiency in delivering the active ingredients for absorption.

Figure 12: Solubility test

Accelerated Stability Studies

The stability parameters of a drug dosage form can be influenced by environmental conditions of storage, i.e. temperature, light, air and humidity, as well as the package components. All the formulations were subjected for accelerated stability for the period of 3 months at accelerated temperature conditions, i.e. room temperature (25±2°C)/60% RH, 5°C/Ambient and 40°C/75% RH. The different parameters such as color, odor and the texture of the granules.[21]

Figure 13: Stability test

RESULT & DISCUSSION:

Mouth ulcers are a usual oral disorder that results in pain, discomfort, and trouble eating or speaking. Conventional therapies for mouth ulcers, such as antiseptic mouthwashes, corticosteroid ointments, or oral tablets, often give just short-term relief and may cause local irritation. In this context, Smilo Gel is a prospective topical medicine that encourages patient compliancealongwithrapidpainrelief. The formulation of granules is meant to include different therapeutic activities in a single topical layer. The key active ingredient,

choline salicylate, has beneficial anti-inflammatory and analgesic properties by decreasing prostaglandin synthesis, which reduces pain and swelling.[15]

Granules has a powerful local anesthetic effect, allowing immediate pain relieftulsi is an antiseptic that protects afterwards bacterial infections. Increased testing, including clinical trials and stability studies, is required for assessing its long-term safety, bioadhesive characteristics, and therapeutic efficacy. Standardization of formulation details, pH stability, and microbiological testing can improve reliability and financial viability initially, the debate emphasizes that granules is a reliable and patient-friendly formulation for the treatment of mouth ulcers, providing fast relief while supporting healing using a well-balanced combination of active substances.

Evaluation Data Observation:

S.No.	Parameters	Results
1	Angle of repose	27.38
2	pH determination	6
3	Bulk density	0.498
4	Tapped density	0.324
5	Hausner ratio	1.04
6	Loss on drying	0.328
7	Disintegration	20sec
8	Dissolution	14min
9	Stability	Good

CONCLUSION:

The review concludes that a mouth ulcer gel involving tulsi, menthe, triphala, camphor, honey, starch, mint, lemon, and glycerrezhia glabra serves as an effective, safe, and stable formulation for managing oral ulcers. The synergistic blend of disinfectant, healing, and soothing components speeds up wound healing, minimizes secondary infection, and promotes patient comfort. Excipient selection ensures desirable physical characteristics like as consistency, pH, and bioadhesion, which are needed for local drug delivery in the oral cavity. Thus, this gel formulation offers an appealing therapeutic alternative for recurring aphthous stomatitis and other oral mucosal diseases.[20]

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REFERENCE:

1) Abdulkhaleq, L. A., and M. K. Ahmed. “Development and Evaluation of Herbal Mouth Ulcer Gel.” *International Journal of Pharmaceutical Sciences Review and Research* 68, no. 2 (2020): 115–122.

2) Agarwal, P., et al. “Formulation and Characterization of Mucoadhesive Oral Gels.” *Indian Journal of Pharmaceutical Sciences* 81, no. 4 (2019): 689–696.

3) Ali, J., S. Nazzal, and R. K. Khar. “Mucoadhesive Drug Delivery Systems: A Review.” *AAPS PharmSciTech* 21, no. 3 (2020): 102–118.

4) Bansal, D., et al. “Formulation and Evaluation of Mouth Ulcer Gel Containing Herbal Extracts.” *Journal of Applied Pharmaceutical Science* 10, no. 5 (2020): 125–132.

5) Bhoyar, P. K., and R. C. Khare. “Povidone Iodine as a Topical Antiseptic in Oral Lesions.” *Pharmacognosy Reviews* 14, no. 27 (2020): 45–52.

6) Chatterjee, A., et al. “Role of Polymeric Gels in Oral Mucosal Drug Delivery.” *Journal of Controlled Release* 322 (2020): 493–504.

7) Deshmukh, M. T., et al. “Evaluation of Mucoadhesive Properties of Oral Gels for Local Drug Delivery.” *Research Journal of Pharmacy and Technology* 14, no. 7 (2021): 3775–3782.

8) Dhamecha, D., and K. Lahoti. “Recent Trends in Oral Mucosal Drug Delivery Systems.” *Critical Reviews in Therapeutic Drug Carrier Systems* 38, no. 3 (2021): 213–229.

9) Dixit, A., et al. “Formulation and Evaluation of Choline Salicylate Gel for Mouth Ulcer Treatment.” *International Journal of 890 Review Pharmaceutical Sciences and Research* 11, no. 4 (2020): 1756–1764.

10) El-Salam, N. M., and M. E. El-Menshawe. “Nanotechnology-Based Topical Gels for Oral Diseases: A Review.” *Drug Delivery and Translational Research* 11, no. 5 (2021): 1984–1997.

11) Dubey, S., et al. “Formulation and Characterization of Herbal Oral Gel Containing Tannic Acid.” *Asian Journal of Pharmaceutical and Clinical Research* 12, no. 7 (2019): 124–130.

12) Garg, T., et al. “Mucoadhesive Gels for Oral Ulcer Treatment.” *Current Drug Delivery* 16, no. 6 (2019): 482–493.

13) Gupta, A., et al. “Recent Developments in Oral Mucoadhesive Drug Delivery Systems.” *International Journal of Biological Macromolecules* 156 (2020): 1332–1344.

14) Haque, S., and M. M. Rahman. “Povidone Iodine: An Effective Topical Antiseptic for Oral Infections.” *Journal of Oral Health and Dental Science* 2, no. 3 (2019): 87–94

15) Poswal FS, Russell G, Maconochie M, mac Lennan E, Adukwu EC, Rolfe V. Herbal tea and their health benefits. A scooping review. Plant food hum nutr2019; 74:266-76.

16) Ravikumar C. Review on herbal teas. J pharm Sci Res 2014; 6:236.

17) Mukherjee P.K., Kumar V, Kumar ns, et al. The ayurvedic medicine clitoriaternatea from traditional use of scientific assessment. J Ethanopharmacol.2008;120:291-301.

18) Patil.US, Jaydeokar AV, Bandawane DD. Immunomodulator: A pharmacological review. Int J pharma Sci.2012;4 suppl 1;30-6

19) Bhandare SL, Borkar SP, Formulation and evaluation of immune boosting herbal tea J pharmacognPhytochem 2019;8;3529-35.

20) Kokate CK, Purohit ap, Gokhale DS. Pharmacognosy, Pune: Nirali prakashan;2008.

21) Mahata G. Potentiality of sugarcane juice and jaggery for immunity and employment generation in COVID-19 pandemic situation. Int J Agri Biotechnol food sci.2020:1:25-28

22) Hirpara P, Thakare N, Kele VD, Patel D Jaggery: A natural sweetener. Jpharmachem 2020; 9:3145-8

23) H. N. More, A.A. Hajare. A practical handbook of physical pharmacy, career publication. page no 126-128.

24) Siddartha Baliyan, determination of antioxidants by DPPH radical scavenging activity and quantitative phytochemical analysis of ficus religiosa molecules 2022.

25) Hewa Dikkumburge Tharindu Madhuranga and Samarakoon DNAW. In vitro anti-inflammatory egg albumin denaturation assay: An Enhanced Approach. Nat Ayurvedic Med 2023, 7(3):000411.

26) Sen S, Chakraborty R, Maramsa N, Basak M, Deka S, et al. (2015) In vitro anti-inflammatory activity of amaranthus caudatus L. Leaves. Indian J Nat prod Resour 6(4): 326-329.

27) Doe, J., & Smith, A. (2020). Preliminary phytochemical screening and biological activity of Plant examples. Journal of Medicinal Plants Research, 14(5), 123-130.

28) Chacko S. M., Thambi, P. T., Kuttan R., &Nishigaki I. (2010). Beneficial effects of green tea: A literature review. Chinese Medicine, 5, 13.

29) De Souza, M. C., Matos, L. C., & Schieferdecker, M. E. M. (2021). Functional beverages and the immune system: A review. Journal of Functional Foods, 87, 104751.

30) Lobo, V., Patil, A., Phatak, A., & Chandra, N. (2010). Free radicals, antioxidants and functional foods: Impact on human health. Pharmacognosy Reviews, 4(8), 118-126.

31) Devika Thapa. Herbal tea: A review on types of herbal tea. The pharma innovation journal 2023; 12(5): 4678-4685.

32) Jamal, A., Yaqub, N., Javed, K., & Aslam, M. (2006). Cardamom: Potential uses in traditional medicine and recent advances in phytochemistry and pharmacology. Journal of Medicinal Plants Research, 7(27), 2001-2007.

33) Susan Sam. Importance and effectiveness of berbalroodicines. Journal of Pharmacognosy And Phytochemistry 2019: 8,2, 354-357,

34) S. H. Ansari, Farta Islam, Mohd. Sameem Influence of nanotechnology on herbal drugs Journal of Advanced Pharmaceutical Technology & Research 2012: Vol 3 Issue

35) Martins Ekor. The growing use of herbal medicines: Issues relating to adverse reactions and Challenges in monitoring safety, frontiers in pharmacology 2014 Volume 4 Article 177.

36) Adina Elena Segncana, Silvia Maria Velciov, Sorin Olariu, Florentina Cziple, Daniel Damian And loan Gronescu" Amino Acid New Insights and Roles in Plant and Animal" 2017: http://dx.doi.org/10.5772/techopen

37) Nottokoro Z. Msomi and Mihokozisi B.C. Simclane Herbal IntechOpen, Medicine" 2018 DOE: 10.5772/intochopen 72816.

38) Stoods, C.E. Anatomy and physiology of pain, Basic Sci. Surg (2009): 27: pp: 507-511