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FORMULATION AND PREPARATIONOF DOMPERIDONE MALEATE BUCCAL TABLETS

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ABSTRACT

Throwing up, retching, heaving, hurling, puking, tossing, or getting ill are all colloquial terms for vomiting, which is the forced voluntary or involuntary evacuation of stomach contents through the mouth or, less frequently, the nose. Vomiting is sometimes referred to scientifically as "emesis." There are various forms of regurgitation. One particular dopamine receptor (D2) blocker is domperidone maleate. Prolactin is released, gastrointestinal peristalsis is accelerated, and it is an antiemetic utilized in dopaminergic mechanism research. It functions as a peristaltic stimulant and a delayed adjuvant for gastric emptying. Domperidone maleate is a member of the dopamine receptor antagonist-prokinetic agent class of medications. It is a derivative of benzimidazole. Domperidone's ability to inhibit peripheral dopamine receptors is linked to its gastroprokinetic characteristics. Domperidone maleate reduces the pressure in the esophageal sphincter, increases gastric and esophageal peristalsis, and speeds up the process of emptying the stomach. Domperidone's ability to inhibit dopamine receptors both at the stomach level and in the chemoreceptor trigger zone is linked to its antiemetic effects. The D2 and D3 dopamine receptors, which are positioned in the chemoreceptor trigger zone, which is situated just outside the blood-brain barrier and governs a number of functions including nausea and vomiting, are highly affinitated by this substance.

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INTRODUCTION

Drugs applied or stored in the buccal region can be administered topically by buccal administration, which allows the medication to permeate through the oral mucosa and reach the bloodstream immediately. In terms of biology, the product is applied to cure both the local and systemic ailment by sitting between the cheek and the upper gingiva (gums).

The goal of buccal administration is to administer medication through or within the buccal mucosa to have a systemic or localized effect. Because drugs taken through the buccal mucosa avoid the hepatic first-pass impact and gastrointestinal enzymatic degradation, this route is very appealing. Compared to the nose, rectum, and vagina, the mouth offers a comparatively big region and easy accessibility for the application of drugs.The buccal mucosa consists of a surface layer of stratified squamous epithelium linked to the underlying connective tissue (lamina propria and submucosa) by a basal lamina. In the connective tissue, a network of blood capillaries is present where drugs that have permeated through the epithelium can enter the systemic circulation.

Mechanism of buccal absorption: Through the intercellular gaps of the epithelium, nonionized species passively diffuse into the buccal cavity. This process is mainly controlled by a concentration gradient. The main mode of transport is the passive movement of non-ionic species over the buccal cavity's lipid membrane. Like many other mucosal membranes, the buccal mucosa has been described as a lipoidal barrier to drug transit; the more lipophilic the drug molecule, the easier it is to absorb. [1-5]

Factors affecting buccal absorption:

1. Membrane Factors:

This involves a degree of keratinization, the surface area available for absorption, mucus layer of the salivary pellicle, intercellular lipids of epithelium, basement membrane, and lamina propria. In addition, the absorptive membrane thickness, blood supply/ lymph drainage, cell renewal, and enzyme content will all contribute to reducing the rate and amount of drug entering the systemic circulation.[6-7]

2. Environmental Factors:

a. Saliva: The thin film of saliva coats throughout the lining of buccal mucosa and is called salivary pellicle or film. The thickness of the salivary film is 0.07 to 0.10 mm. The thickness, composition, and movement of this film affect the rate of buccal absorption.

b. Salivary glands: The minor salivary glands are located in the epithelial or deep epithelial region of the buccal mucosa. They constantly secrete mucus on the surface of the buccal mucosa. Although mucus helps to retain mucoadhesive dosage forms, it is a potential barrier to drug penetration.

c. Movement of buccal tissues: Buccal region of the oral cavity show less active movement. The mucoadhesive polymers are to be incorporated to keep dosage form at the buccal region for long periods to withstand tissue movements during talking and if possible, during eating food or swallowing.**[8]**

Advantages of buccal tablets:

1. Avoids first-pass metabolism.
2. Abundance of blood vessels.
3. Ease of administration.
4. Rapid onset of action.
5. Sustained release.[9-12]

Disadvantages of buccal tablets:

1. Drugs that are unstable at buccal pH cannot be administered.
2. Drugs that have a bitter taste or unpleasant taste or an obnoxious odor or irritate the mucosa cannot be administered by this route.
3. Drug required with small dose can only be administered.
4. Those drugs which are absorbed by passive diffusion can only be administered by this route.
5. Eating and drinking may become restricted.[13,14]

Ideal features of buccal tablet:

1. Non-toxic, non-irritant and pure.
2. Good spreadability, wetting, swelling, solubility, and biodegradable if possible.
3. Adhesion should be quick and with sufficient mechanical strength.
4. Should have peel, tensile, shear strength.
5. Should easily incorporate drug in the formulation & it should not be an obstacle in drug release.
6. It should be cost-effective.[15-18]

FORMULATION & DEVELOPMENT

Ingredients	Quantity required						Role
	F1	F2	F3	F4	F5	F6	
Domperidone maleate	5 mg						Anti-emetic
Polymer	10mg	15mg	10mg	15mg	10mg	15 mg	Mucoadhesive
Lactose	85mg	80mg	85mg	80mg	85mg	80mg	Diluent
Isopropyl Alcohol	3-5 q.s						Granulating liquid
Talc	0.5mg						Lubricant
Magnesium stearate	1mg						Glidant
Aerosil	0.5mg						Antiadherent

F1: 10% HPC; F2: 15% HPC; F3: 10% Sodium alginate; F4: 15% Sodium alginate;
F5: 10% HPMC; F6: 15% HPMC

PROCEDURE

A) Preparation of granules

1. Weigh 0.005 g of Domperidone maleate and pour it into a mortar pestle. Add sufficient quantity of Polymer and Lactose to it.
2. Mix the powders thoroughly and then add 3-5 ml IDP drop by drop to enhance dough formation.
3. After the dough is formed, pass it through 10# using a spatula and allow it to dry for 10-15 min.
4. The dried granules are then passed through 20# to obtain fine and uniform-sized granules.

B) Preparation of Tablets

1. Weigh the granules and add 0.5% Talc, 1% Mg Stearate and 0.5% Aerosil to it. This will provide lubrication to the granules.
2. Weigh 0.1 g from the granules and form different batches. Also, form batches of plain lactose to check tablet compressibility.
3. The formed batches of granules are then poured into tablet compressing equipment.
4. The hardness, thickness, and punching dies are set accordingly and the tablet is compressed.[19,20]

Category: Antiemetic agent.
Storage: Store in a cool and dry place and do not freeze. Keep away from the light.

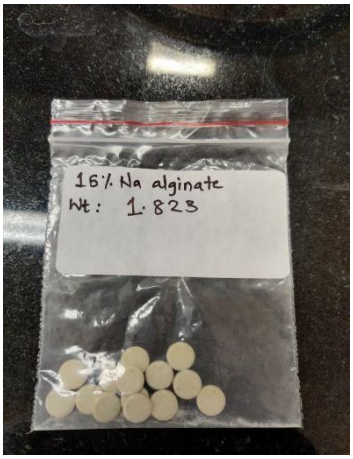

Fig. No. 1: Buccal Tablets F4.

EVALUATION:[28-30]

A) GRANULES

Appearance

1. Colour
2. Odour
3. Texture
4. **Angle of Repose:**

a. The granules are poured through a funnel to form a cone.
b. The tip of the funnel should be held close to the growing cone and slowly raised as the pile grows.
c. Pouring is stopped when the pile reaches a predetermined height or width.
d. The horizontal distance from the middle of the pile to the edge was measured by using the ruler.
e. The equation tan -1(height/width) had been used to find the angle of repose.[21,22]

Angle of Repose	Flowability
<25	Excellent
25-30	Good
30-40	Passable
>40	Very Poor

5. Bulk Density:

- It is determined by pouring perceived bulk drug into a graduate cylinder via-alarge funnel and measuring the volume and weight.

6. Tapped Density:

- It is determined by placing a graduated cylinder containing a known mass of drug or formulation on a mechanical tapper apparatus, which is operated for a fixed number of taps until the powder bed volume has reached a minimum.

7. Carr's Index:

- A volume of a powder is filled into a graduated glass cylinder and repeatedly tapped for a known duration.
- The volume of powder after tapping is measured.

Carr's index (%) = Tapped density- Bulk density X 100

Tapped density

Flow description	% Compressibility
Excellent flow	5-15
Good	16-18
Fair	19-21
Poor	22-35
Very poor	36-40
Extremely poor	>40

8. Hauser Ratio:

Hauser Ratio= Tapped density

Bulk density

Flow character	Hauser Ratio
Excellent	1.00-1.11
Good	1.12-1.18
Fair	1.19-1.25
Passable	1.26-1.34
Poor	1.35-1.45
Very poor	1.46-1.59
Very very poor	>1.60

B) BUCCAL TABLETS

1) Appearance
2) Color
3) Weight variation:
   - Weight variation test was performed on 20 tablets each batch using an electronic balance and the average value was calculated.
4) Hardness:
   - Hardness was conducted for 3 tablets from each batch using Monsanto hardness tester and average value was calculated.
5) Drug permeation:
   - A tablet was placed on a membrane.
   - This membrane was then placed onto the diffusion cell.
   - Studies were carried out at 37 ± 0.5˚C using 6.8 pH phosphate buffer solution as the medium.
   - At intervals of 10 mins, 5ml aliquot was withdrawn, and absorbance was recorded at 283nm.[23,24]

Fig. No. 3 Diffusion Cell Apparatus.

6) Bioadhesion Test:

- Take 100ml of distilled water in a beaker
- Stick the nylon membrane to the mucoadhesive apparatus
- Stick the tablet to the membrane using few drops of water
- assemble the apparatus properly and ensure that membrane gets properly dipped into the distilled water
- Note the time at which the tablet gets detached from membrane.[25-27]

RESULT AND DISCUSSION:

Results for Granules:

Sr. No	Tests performed	Formula 1	Formula 2	Formula 3	Formula 4	Formula 5	Formula6
1	Angle of repose	8.97°	10.70°	13.38°	15.8°	15.64°	17.9°
	Result	Excellent flow	Excellent flow	Excellent flow	Excellent flow	Excellent flow	Excellent flow
2	Bulk Density	0.5879 g/cm^3	0.5513 g/cm^3	0.5822 g/cm^3	0.4678 g/cm^3	0.5179 g/cm^3	0.5095 g/cm^3
3	Tapped Density	0.6467 g/cm^3	0.6738 g/cm^3	0.6128 g/cm^3	0.5068 g/cm^3	0.5885 g/cm^3	0.579 g/cm^3
4	Carr's Index	9.09	18.1	4.9	7.69	11.9	12
	Hausner Ratio	1.100	1.222	1.0525	1.083	1.136	1.137
	Result	Excellent	Fair	Excellent	Excellent	Good	Good
5	Compressibility Index	10	22.22	5.263	8.33	13.63	13.63
	Result	Excellent	Poor	Excellent	Excellent	Excellent	Excellent

- Formula 1- 10% Hydroxypropyl Cellulose (HPC)
- Formula 2- 15% Hydroxypropyl Cellulose (HPC)
- Formula 3- 10% Sodium Alginate
- Formula 4- 15% Sodium Alginate
- Formula 5- 10% Hydroxypropyl methylcellulose (HPMC)
- Formula 6- 15% Hydroxypropyl methylcellulose (HPMC)

Results for Tablets:

Sr. No	Test performed	Formula 1	Formula 2	Formula 3	Formula 4	Formula 5	Formula 6
1	Bioadhesion Test (secs)	22.5	4	No bioadhesion seen	70.5	6	8.5
2	Dissolution Test	< 50% in 20 mins			56% in 20 mins	< 50% in 20 mins	
3	Hardness (kg/sq.cm)	0.5-1					
4	Diffusion Test	4 – 5 % in 40 mins					
5	Drug content (%)	-			95.6%	-	
6	Weight Variation (g) (Avg ± STD)	0.1035 ± 0.007309	0.0995 ± 0.003728	0.1035 ± 0.005811	0.1026 ± 0.004899	0.1050 ± 0.004243	0.0976 ± 0.002658

Granules of Domeperidone maleate using various polymers and their concentrations gave satisfactory result with respect to appearance and flow properties.

Tablets of Domepridone maleate prepared using 15% sodium alginate as mucoadhesive polymer gave favourable result. The formulation showed rapid drug release and overall satisfactory desired results with 15% sodium alginate as mucoadhesive polymer.

CONCLUSION

The project study involved formulation and evaluation of buccal tablets of an antiemetic drug, Domeperidone maleate. It is involved study of various variables such as types of mucoadhesive polymers and their concentrations. It was found that 15% sodium alginate gave promising result with respect to every evaluation test performed. The important result was for bioadhesion and drug release study. It was an attempt made to understand designing and formulation aspects of buccal tablet system and use of core excipients being required for such formulations. The study gave an insight of formulation and evaluation considerations and helped to develop an analytical approach as well. Buccal tablet systems can prove a superior alternative to conventional tablets for Domeperidone maleate drug and can also improve patient compliance.

REFERENCES

1. Scheuplein, R.J.; Montagna, W.; Stoughton, R.B. & Van Scott, E.J. Ed: Pharmacology and the skin. 36-37, Univ. of Chicago Press, Chicago, Illinois (1972).
2. Tregear, R.T.: Physical functions of skin, Academic Press, London(1966).
3. Day, T.D. J.Physiol. (London), 117, 1-8 (1952).
4. Gibaldi M. &Kanig J.L. J. Oral. Ther. Pharmac., 1, 440-450 (1965).
5. Tolo, K.J.: Arch. Oral. Biol. 19, 259-263 (1974).
6. Malkinson, F.D.; Montagna, W. & Lobitz, W.C. Jr., Ed: Theepidermis, 435-442, Academic Press, New York and London (1964).
7. Winkelmann, R.K.: Br. J. Derm. 81, Suppl. No.4, 11-20 (1969).
8. Kaaber, S. Acta. Odontol. Scand., Suppl no.66. (1974).
9. Squier, C.A. "Effect of Enzyme digestion on the permeability barrier in keratinizing and non-keratinizing epithelia": Br. J. Dermatol., 111,253-264 (1984).
10. Squier, C.A.& Johnson N.W. Brit. Med. Bull., 31, 169-175 (1975).
11. Kurosaki, Y. ToshihitoTakatori, Hidekatsu Nishimura, Nakayama, T. & Kimura T. "Regional Variation in oral mucosal drug absorption; Permeability and degree of keratinization in hamster oral cavity". Pharm. Res., 8, 1297-1301 (1991).
12. Stratford, R.E. Jr. & Lee, V.H.L. :"Amino peptidase activity in homogenates of various absorptive mucosae in the albino rabbit: implications in peptide delivery". Int. J. Pharm., 30, 73-82 (1986).
13. Garren, K.W. and Repta, A.J. "Buccal drug absorption, comparitive levels of esterases and peptidase activity in rat and hamster buccal and intestinal homogenates". Int. J. Pharm. 48, 189-194 (1988).
14. Daems, W.T.; Wissie, E. ;Brederoo, P. & Dingle J.T. Ed: Lysosomes: a laboratory handbook, 150-199 (1972). North Holland, Amsterdam and London.
15. Wolff, K. & Schreiner, E. Arch. Klin. Exp. Derm. 235, 203-220 (1969).
16. Squier, C.A.: J. Ultrastruct. Res., 43, 160-177 (1973).
17. Bernidge, M.J. &Oschman, J.L. Transporting epithelia, AcademicPress, New York & London (1972).
18. Davis, W.W.; Wright, W.E.; Montagna, W., Stoughton, R.B. & Van Scott, E.J. Ed; Pharmacology and the skin. 37-49 (1972).Appleton-Century-Crofts, New York.
19. Ussing, H.H.; Erlij, D. & Lassen, U. : Annu. Rev. Physiol. 36, 17-49 (1974).

20. Seigel, I.A.; Hall, S.H. & Stambaugh, R: Current concept of the Histology of oral mucosa, 274-286, Thomas Springfeild, Illinois(1971).
21. Barnet, M.L. & Szabo, G. J. Periodontal Res. 8, 117-126 (1973).
22. Tolo, K.J.: Arch. Oral. Biol. 16, 881-888 (1971).
23. Wills, J.H.; Montagna, W.; Stoughton, R.B. & Van Scott, E.J., Ed: Pharmacology and the skin, 169-176, Appleton-Century-Crofts.. New York (1972).
24. Tolo, K.J. & Jonson, B.J.: Arch. Oral. Biol. 20, (1975).
25. Walton, R.P.: J. Am. Med. Assoc., 124, 138-143 (1944).
26. Bickel, M.H. & Weder, H.J. J. Pharm. PHarmacol. 21, 160-168 (1969).
27. Beckett, A.H. & Moffat A.C. Ibid., 22, 15-19 (1970).
28. Reza-Tavakoli, M. Saberi & Kenneth L. Audus. "Physio-chemical factors affecting Beta-adrenargic antagonist permeation across cultured hamster pouch buccal epithelium", Int. J. Pharm. 56, 135-142 (1989).
29. Stoughton, R.B.; Montagna, W. &Vanscott, E.J. Ed: Pharmacology and the skin, 535-546, Appleton-century-crofts, New York (1972).
30. Minako Tanaka; Norio Yangibashi, Fukuda, H. & Nagai, T. "Absorption of salicylic acid through the oral mucous membrane of Hamster cheek pouch". Chem. Pharm. Bull., 28 (4) 1056-1061 (1980).