Available online on 30.08.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Research Article

Preformulation Studies of Rapid Dissolving Films Containing Granisetron Hydrochloride

Alok Khunteta[1], Manish Kumar Gupta[2]*, Surendra Kumar Swarnkar[3]

[1] Professor, LBS College of Pharmacy, Jaipur, India

[2] Associate Professor, School of Pharmaceutical Sciences, Jaipur National University, Jaipur, India

[3] Assistant Professor, LBS College of Pharmacy, Jaipur, India

ABSTRACT

Rapid-dissolving solid drug dosage forms for application onto the oral cavity for the pediatric population seem to be very appropriate, especially in preterm and term infants. The delivery of drugs via the oral mucosa offers easy application, prevents drug degradation by gastrointestinal fluids, avoids first-pass metabolism and potentially improves bioavailability. Granisetron hydrochloride (GSH) drug is used as antiemetic agent. Proposed work comprise of preformulation studies of Granisetron hydrochloride. For that, physicochemical parameters were determined; like melting point of GSH was determined using melting point apparatus, Granisetron hydrochloride was scanned in the distilled water, Acid buffer, pH 1.2 and Phosphate buffer, pH 6.8. The IR spectrum of pure drug (GSH), Pullulan, METHO K3P, METHO E3P, METHO E15P and POLYOX WSR N10 were recorded in potassium bromide using Shimadzu FTIR – 8400S(CE). Solubility of Granisetron hydrochloride was determined using shake flask method. Standard Plot of Granisetron hydrochloride in distilled water, Acid buffer, pH 1.2 and Phosphate buffer, pH 6.8 were taken, all the parameter obtained were satisfactory, which will be used further for formulation of rapid dissolving film.

Keywords: Rapid dissolving film, Granisetron hydrochloride (GSH), Preformulation.

Article Info: Received 08 July 2019; Review Completed 11 Aug 2019; Accepted 20 Aug 2019; Available online 30 Aug 2019

Cite this article as:

Khunteta A, Gupta MK, Swarnkar SK, Preformulation Studies of Rapid Dissolving Films Containing Granisetron Hydrochloride, Journal of Drug Delivery and Therapeutics. 2019; 9(4-A):511-515

http://dx.doi.org/10.22270/jddt.v9i4-A.3524

***Address for Correspondence:**

Manish Kumar Gupta, Associate Professor, School of Pharmaceutical Sciences, Jaipur National University, Jaipur, India

1. INTRODUCTION:

The humble tablet, and its alter ego, the two piece hard gelatin capsule, remains at the forefront in terms of oral dosage form. Present situation that may be seen somewhat surprising considering the production, made over hundred year ago, suggesting that tablets have had their day, and will pass away to make room for something else.

Thus, the appeal of these of dosage form remains high, providing a clear indication that choice may well be influenced by a need to:

- Create a delivery system that is relatively simple and inexpensive to manufacture.
- Provide a dosage form that is convenient, from the patient's perspective, to use.
- Utilize a technology that is relatively easy to adapt to changing need of the drug substance that will be incorporated into that particular dosage form.
- Utilize an approach that is unlikely to add complexity during the regulatory approval process.

1.1 Rapid (Fast) Dissolving Drug Delivery System

Rapid-dissolving solid drug delivery system for application into the oral cavity for the pediatric population seem to be very appropriate, especially in preterm and term infants. The delivery of drugs via the oral mucosa offers easy application, prevents drug degradation by gastrointestinal fluids, avoids first-pass metabolism and potentially improves bioavailability with rapid absorption and fast onset of action. Drug absorption through membranes depends on the following:

I. Drug concentration at the surface of the mucosa
II. Vehicle for drug delivery
III. Contact time with the mucosa
IV. Constitution of mucosal tissue
V. Degree of ionization of the drug

VI. pH of the absorption site

VII. Size of the molecule and the relative lipid solubility

These parameters have to be taken into account when formulating dosage forms for oral mucosal delivery. The drug concentration at the surface can be increased by varying the solubility of the drug. The drug partitioning can be influenced by environmental changes such as pH modifications. The permeability coefficient are often low, so the use of permeation enhancers is beneficial. The contact time at the mucosa may be prolonged by the use of mucoadhesive polymers such as chitosans, polyethylene glycol -tethered copolymers or alginates.

1.2 Rapid Dissolving Dosage Form:

Rapid-dissolving drug delivery systems have rapidly gained acceptance as an important new way of administering drugs. There are multiple fast-dissolving OTC and prescription products in the market worldwide, most of which have been launched in the past many years. There have also been significant increases in the number of new chemical entities under development using a rapid-dissolving drug delivery technology.

A rapid-dissolving drug delivery system, in most cases, is a tablet that dissolves or disintegrates in the oral cavity without the need for water or chewing. Most rapid-dissolving delivery system films must include substances to mask the taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients.

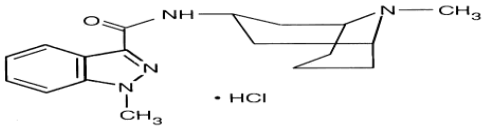
1.3 Classification of Rapid Dissolve Technology:

For ease of description, rapid-dissolve technologies can be divided in to three broad groups:

- Lyophilized systems,
- Compressed tablet-based systems,
- Oral thin film strips.

2. EXPERIMENTAL WORK:

Table 2.1 Profile of Granisetron Hydrochloride

Parameters	Description
A. Analytical profile	
CAS number	107007-99-8
Chemical structure	
Chemical formula	$C_{18}H_{24}N_4O_1 \cdot HCl$
Chemical name	N-(9-methyl-9-azabicyclo [3.3.1] non-3-yl)-1-methyl-1H-indazole-3-carboxamide hydrochloride
Molecular weight	Average: 348.9g/mol
pKa	9.4
B. Pharmaceutical profile	
Appearance	A whitish, crystalline powder
Melting point	298°C
Solubility	Freely soluble in water, sparingly soluble in methylene chloride, slightly soluble in methanol
Storage	Store between 15ºC - 30ºC. Keep container closed tightly. Protect from light
C. Pharmacodynamic profile:	
Mechanism of action	Granisetron is a selective inhibitor of type 3 serotonergic (5-hydroxytryptamine, 5-HT3) receptors, with little or no affinity for other serotonin receptors. Granisetron possesses antiemetic activity due to its binding to 5-HT3 receptors, resulting in blockage of serotonin stimulation.

3. PREFORMULATION STUDIES

Analyte Name: Granisetron hydrochloride (GSH)

3.1 Melting Point:

The melting point of GSH was determined using melting point apparatus.

3.2 Scanning of the Drug (Granisetron hydrochloride):

Granisetron hydrochloride was scanned in the following solvent and buffers-

i) Distilled water

ii) Acid buffer, pH 1.2

iii) Phosphate buffer, pH 6.8

i) Scanning of the drug in distilled water:

50 mg of drug was dissolved in distilled water in 100 ml in volumetric flask, and volume was made to 100 ml with distilled water. 2 ml of this stock solution was further diluted to 100 ml to get concentration of 10µg/ml. This solution was scanned in UV-spectrophotometer.

ii) Scanning of the drug in acid buffer, pH 1.2:

50 mg of drug was dissolved in acid buffer, pH 1.2 in 100 ml in volumetric flask, and volume was made to 100 ml with same solvent. 2 ml of this stock solution was further diluted to 100 ml to get concentration of 10µg/ml. This solution was scanned in UV-spectrophotometer.

iii) Scanning of the drug in phosphate buffer, pH 6.8:

50 mg of drug was dissolved in phosphate buffer, pH 6.8 in 100 ml in volumetric flask, and volume was made to 100 ml with same solvent. 2 ml of this stock solution was further diluted to 100 ml to get concentration of 10µg/ml. This solution was scanned in UV-spectrophotometer.

3.3 Standard Plots:

Standard plot of Granisetron HCl was prepared in following solvent and buffers-

i) buffer, pH 6.8

ii) **i) Standard** Distilled water

iii) Acid buffer, pH 1.2

Phosphate **plot of Granisetron hydrochloride in distilled water**

50 mg of Granisetron hydrochloride was dissolved in distilled water and volume was made up to 100 ml by same solvent. This gave the concentration of 500 µg/ml (stock solution). 1, 2, 3, 4, 5 and 6 ml of this stock solution was further diluted to 100 ml to get different concentrations (µg/ml): 5, 10, 15, 20, 25 and 30. Absorbances were measured at the wave-length of 302 nm.

ii) Standard plot of Granisetron hydrochloride in acid buffer, pH 1.2

50 mg of Granisetron hydrochloride was dissolved in acid buffer, pH 1.2 and volume was made up to 100 ml by same solvent. This gave the concentration of 500 µg/ml (stock solution). 1, 2, 3, 4, 5 and 6 ml of this stock solution was further diluted to 100 ml to get different concentrations (µg/ml): 5, 10, 15, 20, 25 and 30. Absorbances were measured at the wave-length of 302 nm.

iii) Standard plot of Granisetron hydrochloride in phosphate buffer, pH 6.8

50 mg of Granisetron hydrochloride was dissolved in phosphate buffer, pH 6.8 and volume was made up to 100 ml by same solvent. This gave the concentration of 500 µg/ml (stock solution). 1, 2, 3, 4, 5 and 6 ml of this stock solution was further diluted to 100 ml to get different concentrations (µg/ml): 5, 10, 15, 20, 25 and 30. Absorbances were measured at the wave-length of 302 nm.

3.4 Interpretation of IR Spectra:

The IR spectrum of pure drug (GSH), Pullulan, METHO K3P, METHO E3P, METHO E15P and POLYOX WSR N10 were recorded in potassium bromide using Shimadzu FTIR – 8400 S(CE).

3.5 Solubility Studies:

Solubility of Granisetron hydrochloride was determined using shake flask method. Solubility of Granisetron hydrochloride was determined in following solvents/ buffers:

i) Distilled water

ii) Acid buffer, pH 1.2

iii) Phosphate buffer, pH 6.8

4. RESULT AND DISCUSSION

4.1 Preformulation Studies: Granisetron hydrochloride (GSH)

4.2 Melting Point:

The melting point of GSH was found to be 288^0 C – 292^0 C, which is same as documented (291^0 C).

4.3 Scanning of the Drug (Granisetron hydrochloride)

Granisetron hydrochloride was scanned in the following solvent and buffers-

iv) Distilled water

v) Acid buffer, pH 1.2

vi) Phosphate buffer, pH 6.8

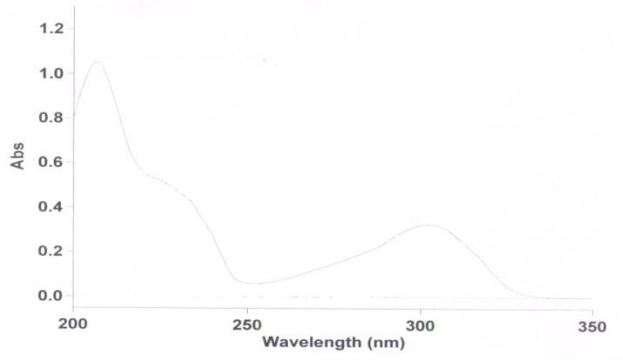


Fig.-1: UV spectrum of GSH in distilled water

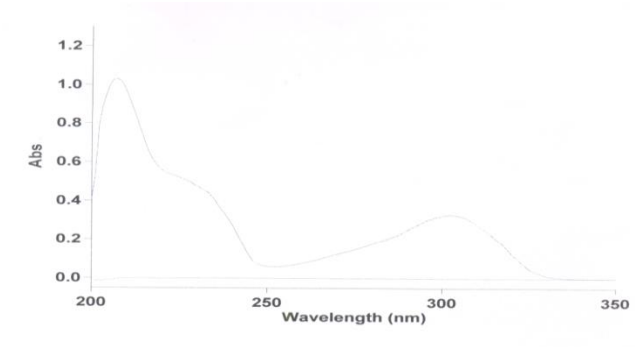


Fig.-2: UV spectrum of GSH in acid buffer, pH 1.2

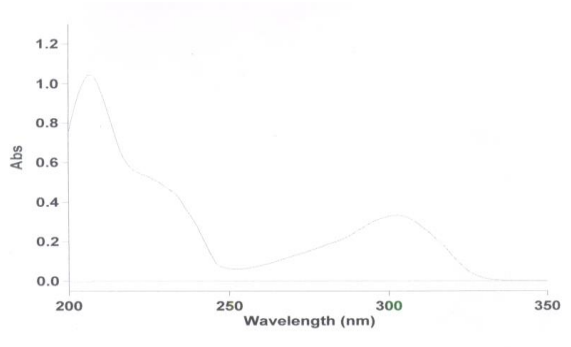


Fig.-3: UV spectrum of GSH in phosphate buffer, pH 6.8

Table 4.1: Summary of scanning of Granisetron hydrochloride in various solvents

S. No.	Amount of Granisetron hydrochloride (mg)	Solvent used to make up volume	Final volume (ml)	Conc. of stock solution (µg/ml)	Conc. of scanning solution (µg/ml)	Scanning range (nm)	Characteristic peak, λmax (nm)
1	50	Distilled water	100	500	10	200 nm – 400 nm	302
2	50	Acid Buffer, pH 1.2		500	10		302
3	50	Phosphate Buffer, pH 6.8		500	10		302

4.4 Standard Plots:

Standard plot of Granisetron Hydrochloride was prepared in following solvent and buffers-

i) Distilled water

ii) Acid buffer, pH 1.2

iii) Phosphate buffer, pH 6.8

4.5 Standard Plot of Granisetron hydrochloride in distilled water:

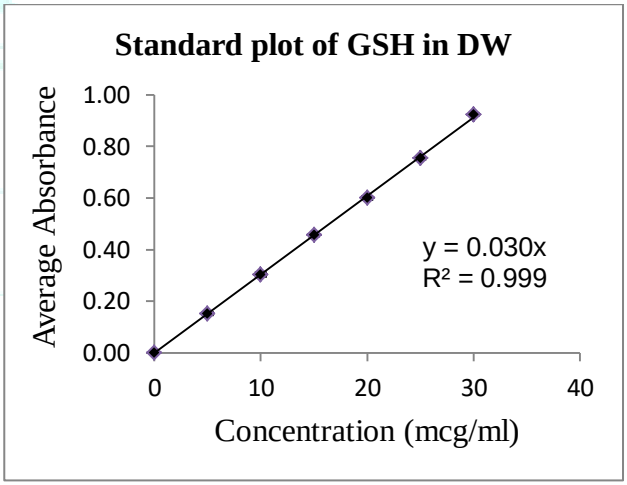
Concentration of stock solution = 500 µg/ml, Drug = Granisetron hydrochloride

Maximum wave-length (λ_{max}) = 302 nm, Solvent = distilled water

Table 4.2: UV Absorbance of Granisetron hydrochloride in distilled water

S. No.	Conc. of Drug (µg/ml)	Absorbance (Mean ± S.D.*)
1	0	0.000±0.000
2	5	0.152±0.006
3	10	0.303±0.009
4	15	0.456±0.006
5	20	0.600±0.008
6	25	0.753±0.005
7	30	0.923±0.007

* S. D. = Standard Deviation (n=3)



(Fig.-4: Average UV-absorbance of Granisetron hydrochloride in distilled water±S.D. (n=3))

4.6 Standard Plot of Granisetron hydrochloride in Acid buffer, pH 1.2:

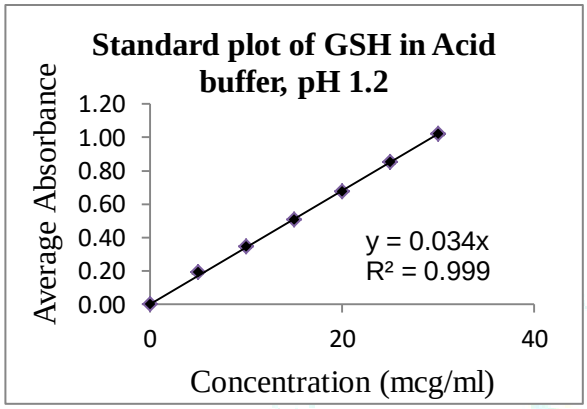
Concentration of stock solution = 500 µg/ml, Drug = Granisetron hydrochloride

Maximum wave-length (λ_{max}) = 302 nm
Solvent = Acid buffer, pH 1.2

Table 4.3: UV Absorbance of Granisetron hydrochloride in acid buffer, pH 1.2

S. No.	Conc. of Drug (µg/ml)	Absorbance (Mean ± S.D.*)
1	0	0.000±0.000
2	5	0.1920.007
3	10	0.3440.006
4	15	0.5090.006
5	20	0.6770.007
6	25	0.8510.007
7	30	1.0200.008

* S. D. = Standard Deviation (n=3)



(Fig.-5: Average UV-absorbance of Granisetron hydrochloride in acid buffer pH, 1.2±S.D. (n=3))

4.7 Standard Plot of Granisetron hydrochloride in Phosphate buffer, pH6.8:

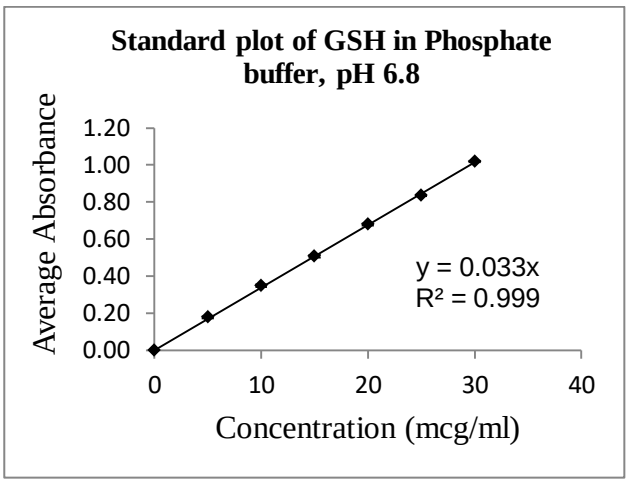
Concentration of stock solution = 500 µg/ml, Drug = Granisetron hydrochloride

Maximum wave-length (λ_{max}) = 302 nm,
Solvent = Phosphate buffer, pH 6.8

Table 4.4: UV Absorbance of Granisetron hydrochloride in phosphate buffer, pH 6.8

S. No.	Conc. of Drug (µg/ml)	Absorbance (Mean ± S.D.*)
1	0	0.000±0.000
2	5	0.177±0.006
3	10	0.348±0.006
4	15	0.508±0.007
5	20	0.678±0.007
6	25	0.835±0.008
7	30	1.019±0.008

* S. D. = Standard Deviation (n=3)



(Fig.-6: Average UV-absorbance of Granisetron hydrochloride in phosphate buffer pH, 6.8±S.D. (n=3))

5. CONCLUSION:

Granisetron hydrochloride is used as an antiemetic agent. The drug was scanned in the distilled water, Acid buffer, pH 1.2 and Phosphate buffer, pH 6.8. The IR spectrum of pure drug (GSH), Pullulan, were recorded in potassium bromide using Shimadzu FTIR – 8400 S(CE). Solubility of Granisetron hydrochloride was determined using shake flask method. Standard Plot of Granisetron hydrochloride were prepared in distilled water, Acid buffer, pH 1.2 and Phosphate buffer, pH 6.8. all the parameter obtained were satisfactory, which will be used further for formulation of rapid dissolving film.

6. REFERENCES:

1. Serra, L., Domenech, J., Peppas, N.A., **2006**. Design of poly(ethylene glycol)-tethered copolymers as novel mucoadhesive drug delivery systems. Eur. J. Pharm. Biopharm. 63, 11-18.
2. Gupta, M.K., Gupta, R., Khunteta, A., Swarnkar, S.K., **2018.** An Overview of Novel Techniques Employed in Mouth Dissolving Drug Delivery System. International Journal of Engineering Science and Generic Research. 4(3), 09-27.
3. Juliano, C., Gavini, E., Cossu, M., Bonferoni, M.C., Giunchedi, P., **2004.**Mucoadhesive alginate matrices containing sodium carboxymethyl starch for buccal delivery: in vitro and in vivo studies. J. Drug Deliv. Sci. Tec. 14, 159-163.
4. Ponchel, G., **1993**. Formulation of oral mucosal drug delivery systems for the systemic delivery of bioactive materials. Adv. Drug Deliv. Rev. 13, 75-87.
5. Mishra, R., Amin, A., **2007.** Quick API delivery. Pharm. Techn. Eur. 19, 35- 39.
6. Gupta, M.K., Gupta, R., **2013.** Designing, Optimization, Fabrication and Evaluation Mouth Dissolving Film of Montelukast Sodium. Journal of Drug Discovery and Therapeutics. 1(1), 53-69.
7. Sandri, G., Bonferoni, M.C., Franca, F., Rossi, S., Caramella, C., **2006**. Differentiating factors between oral fast-dissolving technologies. Am. J. Drug Deliv. 4, 249-262.
8. Slowson, M., Slowson, S., **1985**. What to do when patients cannot swallow their medications. Pharm. Times. 51, 90-96.
9. Doheny, K., **1993**. You really expect me to swallow those horse pills? Am. Druggist. 208, 34-35.
10. Das, N.G., Das, S.K., **2004**. Development of mucoadhesive dosage forms of buprenorphine for sublingual drug delivery. Informa Healthcare. 11(2), 89-95.
11. Gupta, M.K., Gupta, R., Khunteta, A., Swarnkar, S.K., **2017.** An Overview of Mouth Dissolving Films: Formulation Aspects. International Journal of Pharmaceutical and Biological Science Archive. 5(5), 01-18.