International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 230-237 www.ijprajournal.com ISSN: 2456-4494

# Formulation and Evaluation of Omeprazole Raft Forming System for the Treatment of Gastro Esophageal Reflux Disease

Ankit Bansal, Neelam Jain
*Oriental College of Pharmacy, Oriental University, Indore*

Submitted: 25-10-2022 Accepted: 05-11-2022

**ABSTRACT: Aim:** To formulate and evaluate omeprazole raft forming system for the treatment of gastro esophageal reflux disease.

**Materials and Methods:** Omeprazole drug was used in this research . The procured sample of omeprazole was characterized by melting point, IR, UV and DSC . The formulations were evaluated for various properties of solution such as drug content, pH, in-vitro gelling capacity, in-vitro floating, in-vitro drug release studies..

**Results and Discussion:** It was found that F-12 was the best formulation. All the evaluation parameters were successfully evaluated. The raft forming system of omeprazole was formulated. Based on the combined effects of, drug quality and cumulative drug release formulations , in-vitro gelation, drug content, pH ,in-vitro drug release.

**Keywords**: Raft forming systen, omeprazole, gastroesophageal reflux disease,

## I. INTRODUCTION:

Risk factors include obesity, pregnancy, smoking, hiatal hernia, and taking certain medicines. Medications that may cause or worsen the disease include benzodiazepines, calcium channel blockers, tricyclic antidepressants, NSAIDs, and certain asthma medicines. Acid reflux is due to poor closure of the lower esophageal sphincter, which is at the junction between the stomach and the esophagus. Diagnosis among those who do not improve with simpler measures may involve gastroscopy, upper GI series, esophageal pH monitoring, or esophageal manometry.

Treatment options include lifestyle changes, medications, and sometimes surgery for those who do not improve with the first two measures. Lifestyle changes include not lying down for three hours after eating, lying down on the left side, raising the pillow/ bed head height, losing weight, avoiding foods which result in symptoms, and stopping smoking. Medications include antacids, $H_2$ receptor blockers, proton pump inhibitors, and prokinetics.

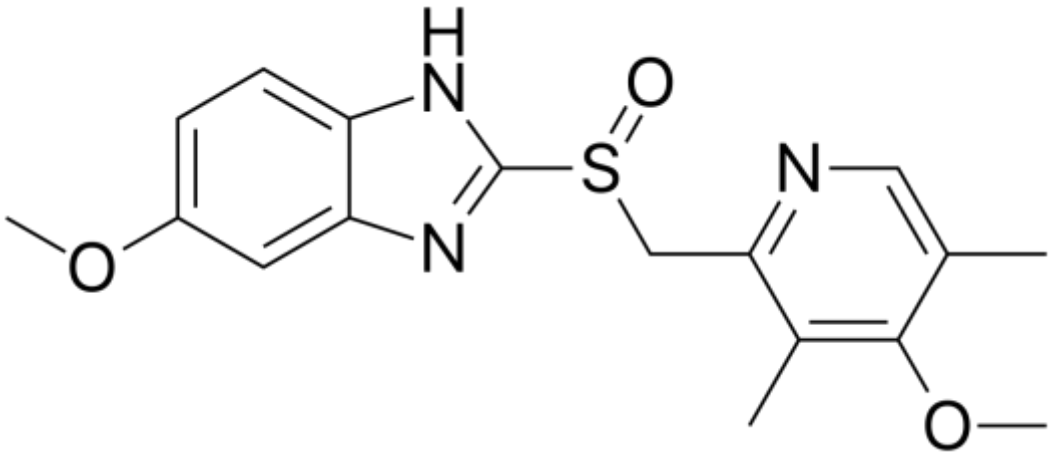


**Figure 1: Structure of Omeprazole**

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 230-237 www.ijprajournal.com ISSN: 2456-4494

## II. MATERIALS AND METHODS

**2.1 Materials:** Omeprazole drug sample was a generous gift by Schon Pharmaceuticals Limited. (Indore). All other chemicals used were of analytical grade and procured from local market.
A Shimadzu-1700 UV-Visible spectrophotometer with 1 cm matched silica cells were used for spectrophotometric analysis.

**2.2 Estimation of nimesulide:**

**2.2.1 UV spectrophotometric analysis of nimesulide:**
20µg/ml solution of drug was scanned in demineralised water on a double-beam UV-visible spectrophotometer (Shimadzu® 1700) between wavelength ranges of 200 nm to 400 nm. U.V spectrum was recorded in figure 2.

**2.2.2 IR analysis of drug sample:**
The infrared spectroscopy of omeprazole was performed for identification of drug. About 1-5 mg of the sample was triturated with approximately 300 mg of dry, finely powdered potassium bromide IR and compressed as pellet and spectra was recorded on FTIR spectrophotometer (Shimadzu 8400S). The IR spectrum is presented in figure 3.

**2.2.3 Preparation of calibration curve of omeprazole in 0.1 N HCl:** 100 ug/ml stock solution of drug was prepared in 0.1 N HCl and suitable dilutions were made i.e.10µg/ml, 20µg/ml, 30µg/ml, 40µg/ml and 50µg/m1 respectively. The sample was scanned at $\lambda_{max}$ in 275 nm. The absorbance of samples of different concentration at the previously measured $\lambda_{max}$ (at 275 nm). The graph was plotted between the absorbance and concentration. The graph obeyed the Beer-Lambert's law in the selected concentration range.

**2.2.4. Partition coefficient-** Partition coefficient is defined as the ratio of un-ionised drug distributed between the organic and aqueous phase at equilibrium.Partition coefficient was determined the following procedure. 50mg of drug was dissolved in 50ml of water which was taken in separating funnel and 50ml of octanol was added to it. Funnel was shaked for 30 min and stand for 5 min aqueous layer was separated and centrifuged for 1hour at 2000 rpm.1ml of this taken and diluted up to 10ml. The aqueous phase is assayed before ($\Sigma c$) and after partitioning ($C_w$) [the aqueous concentration] by using UV-visible spectrophotometer and $K_{o/w}$ calculated by using formula

**2.3 Solubility studies:** Equilibrium solubility of the drug in various selected solvents was determined Like water, methanol, ethanol and DMSO. Excessive quantity of drug was dissolved in 5.0ml of solvents in volumetric flask and kept in a shaker for the period of 5 hours. The resulting saturated solutions were kept aside for 24 hours, filtered through sintered glass filter and was analyzed by UV.

**Table.1: Solubility data of drug in different solvents**

| S. No. | Solvent systems | Solubility (mg/ml) |
|---|---|---|
| 1. | DMSO | 30 |
| 2. | Methanol | 10 |
| 3. | Water | 0.359 |
| 4. | Ethanol | 5.0 |

**2.4. Method of Preparation of raft forming system of omeprazole**

The preparation of raft forming system will be done in 9 different batches 0f formulation [F-1, F-2, F-3,F-4,F-5,F-6,F-7,F-8 and F-9}]. All the additives used in the preparations were passed from a No. 60 sieve (250 microns). Required ingredients for the preparation, like sodium alginate, HPMC K15 M, sodium bicarbonate, and sodium citrate, were accurately weighted as per the formulation chart depicted in Table 1. HPMC K4M was dissolved using 40 ml of deionized water. The

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 230-237 www.ijprajournal.com ISSN: 2456-4494

required quantity of sodium bicarbonate and sodium citrate were incorporated in it while stirring to attain complete homogenous dispersion. Sodium alginate was dissolved using deionized water (30 ml) taken in a beaker pre-heated to around 60° C on a hot plate (Whirlmatic Spectra Lab, Mumbai, India) with continuous stirring. The sodium alginate solution was cooled to 40 ◦C and added to the HPMC K 15 M solution. The total amount of the preparation finally reached 100 mL, making use of distilled water after adding methyl paraben as a preservative and mixed thoroughly

**Table 2: Formulation composition of Omeprazole batch**

| S.No | Ingredients | F-1 | F-2 | F-3 | F-4 | F-5 | F-6 | F-7 | F-8 | F-9 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1. | Omeprazole | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 2. | Sodium Alginate (g) | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 |
| 3. | HPMC K 15 M | 1 | 1 | 1 | 1.5 | 1.5 | 1.5 | 2 | 2 | 2 |
| 4. | Sodium bicarbonate (%) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 5. | Sodium citrate (%) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 6. | Methyl Paraben | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 |

## III. RESULTS AND DISCUSSION:

### 3.1Drug Characterization:

**3.1.1 UV spectrophotometric analysis of omeprazole :**The omeprazole drug sample exhibited a peak at 275 nm which was comparable to the value reported in the literature.

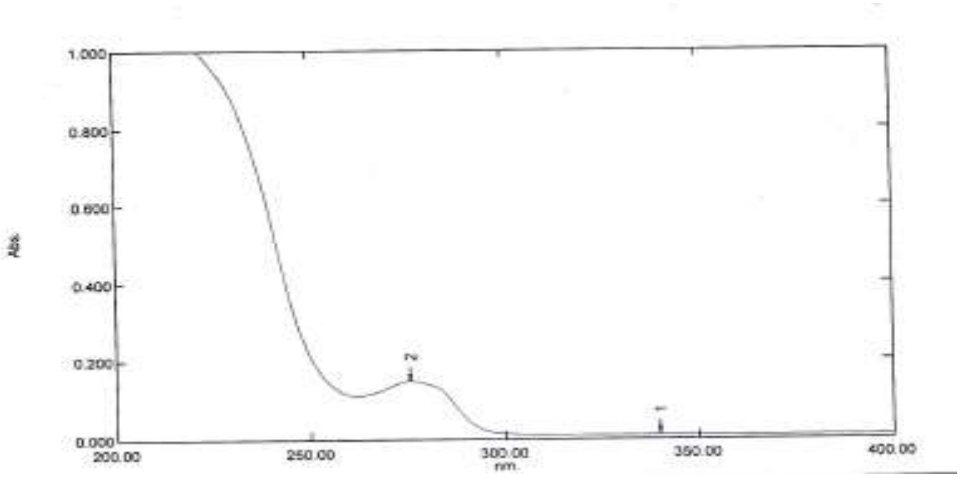


**Figure 2: U. V. spectra of Omeprazole**

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 230-237 www.ijprajournal.com ISSN: 2456-4494

**3.1.2.IR analysis of drug sample:**The FTIR spectrum of drug sample had shown identical peaks as reported in reference sample of omeprazole

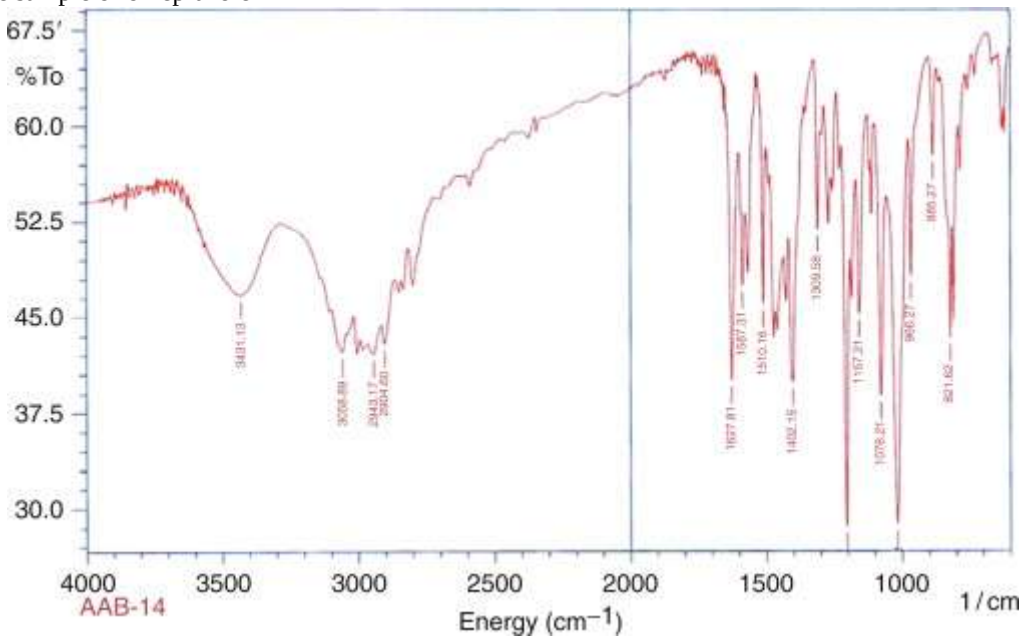


**Figure 3: IR spectrum of Omeprazole.**

**3.2 Preformulation studies:**

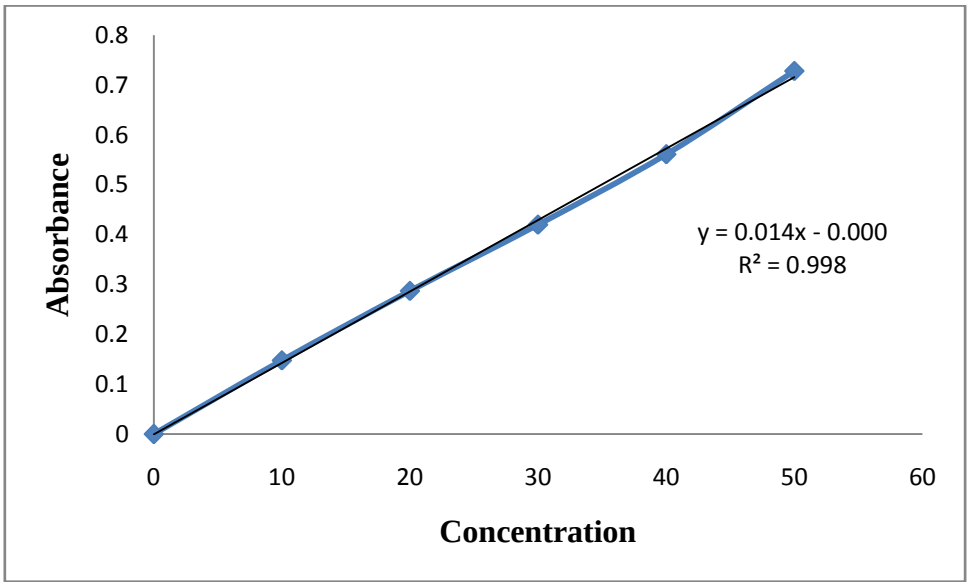


**Figure.4 :Calibration curve of omeprazole in 0.1 N HCl**

**3.3 Evaluations of raft forming system**

**3.3.1 Drug Content Determination** The required quantity of the solid dispersion formulation was measured, which was equivalent to 100 mg of the drug, and was placed in a volumetric flask of 100 mL. The drug content was measured at the absorption maxima of 275 nm using a UV-visible spectrophotometer (UV-1800, Shimadzu, Japan)

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 230-237 www.ijprajournal.com ISSN: 2456-4494

**Table-3: Drug content of different batches**

| Formulation | Drug Content |
|---|---|
| F-1 | 98. 7 |
| F-2 | 99.3 |
| F-3 | 97.8 |
| F-4 | 97.4 |
| F-5 | 98.8 |
| F-6 | 99.2 |
| F-7 | 97.8 |
| F-8 | 98.4 |
| F-9 | 97.7 |

**3.3.2. Determination of pH**

All the developed formulations were tested for pH using a previously calibrated digital pH meter) by placing the sensor end in the prepared formulation. The study was conducted at room temperature**.**

**Table-4: pH of different formulation batches**

| Formulation | pH |
|---|---|
| **F-1** | **7.2** |
| **F-2** | **7.8** |
| **F-3** | **7.8** |
| **F-4** | **7.1** |
| **F-5** | **7.4** |
| **F-6** | **7.3** |
| **F-7** | **7.1** |
| **F-8** | **7.2** |
| **F-9** | **7.2** |

**3.3.3. In Vitro Gelling Capacity** -In vitro gelation of the prepared formulations was measured as per the method reported in our previously published work [7]. One mL of the precisely measured colored formulation was placed in a test containing 5 mL of 0.1 N HCL with a pH 1.2 and was maintained at body temperature (37 ± 0.5 ◦C) with slight stirring to avoid breaking the formed gel. Based on the gelation time, stiffness of the gel formed, and the gel stability in a test tube, the gelling capacity was categorized as follows: no gelation (−), gelation after a few min following quick dispersion (+), instant gelation retained for few hours (++), and instant gelation retained for a longer period of time (+++).

**Table-5: In-vitro gelation capacity of different formulation batches**

| Formulation | In-vitro Gelation |
|---|---|
| **F-1** | +++ |
| **F-2** | +++ |
| **F-3** | +++ |
| **F-4** | +++ |
| **F-5** | +++ |
| **F-6** | +++ |
| **F-7** | +++ |
| **F-8** | +++ |
| **F-9** | +++ |

**3.3.4.. In Vitro Floating Study** -The study was performed by placing 10 mL of the prepared formulation in a beaker containing 0.1N HCL (900 mL) with a pH of 1.2 (determined used digital pH meter), and the temperature was maintained at 37 ± 0.5 ◦C. The beaker was placed to avoid turbulence or any disturbance. The length of time for the liquid formulation to float on the surface of the specified

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 230-237 www.ijprajournal.com ISSN: 2456-4494

medium was noted as the floating lag time, and the total time required by the formed gel to float on the medium was termed the floating duration. In addition, the floating lag time and floating duration were determined for all the formulations (F1– F8)

**Table-6: In-vitro floating study of different formulations**

| Formulation | Floating Lag time (in mins) |
|---|---|
| **F-1** | 2.4 |
| **F-2** | 3.1 |
| **F-3** | 6.2 |
| **F-4** | 30 |
| **F-5** | 42 |
| **F-6** | 49 |
| **F-7** | 74 |
| **F-8** | 86 |
| **F-9** | 89 |

**3.3.5. In Vitro Drug Release Study-** The OPZ release study was carried out in triplicate using a USP Type II (paddle type) dissolution apparatus (model). The stirring speed of 50 rpm was fixed, which is believed to simulate the mild agitation in vivo and avoid breaking the formation of the in situ gel. Five mL of the prepared formulation was incorporated into 900 mL dissolution medium of pH 1.2 (0.1N HCl) and the temperature was maintained at 37 ± 0.5 ◦C. About 5 mL of the samples were withdrawn at 1, 2, 4, 6, 8, 10, and 12 h and replaced by an equal volume of fresh dissolution medium immediately, which was maintained at the same temperature to maintain sink condition. The aliquot samples were filtered using a 0.45 µ membrane filter and analyzed using a UV-visible spectrophotometer (UV-1800, Shimadzu, Kyoto, Japan) at 275 nm after suitable dilutions.

**Table-7: In-vitro drug release study of different formulation batches**

| Formulation | % Drug Release *(6 hr) | % Drug Release* (12 hr) |
|---|---|---|
| F-1 | 65.2 | 87.54 |
| F-2 | 73.1 | 99.89 |
| F-3 | 58.3 | 84.32 |
| F-4 | 70.2 | 84.33 |
| F-5 | 45.6 | 74.31 |
| F-6 | 30.2 | 55.44 |
| F-7 | 42.3 | 69.91 |
| F-8 | 34.2 | 59.16 |
| F-9 | 29.4 | 50.73 |

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 230-237 www.ijprajournal.com ISSN: 2456-4494

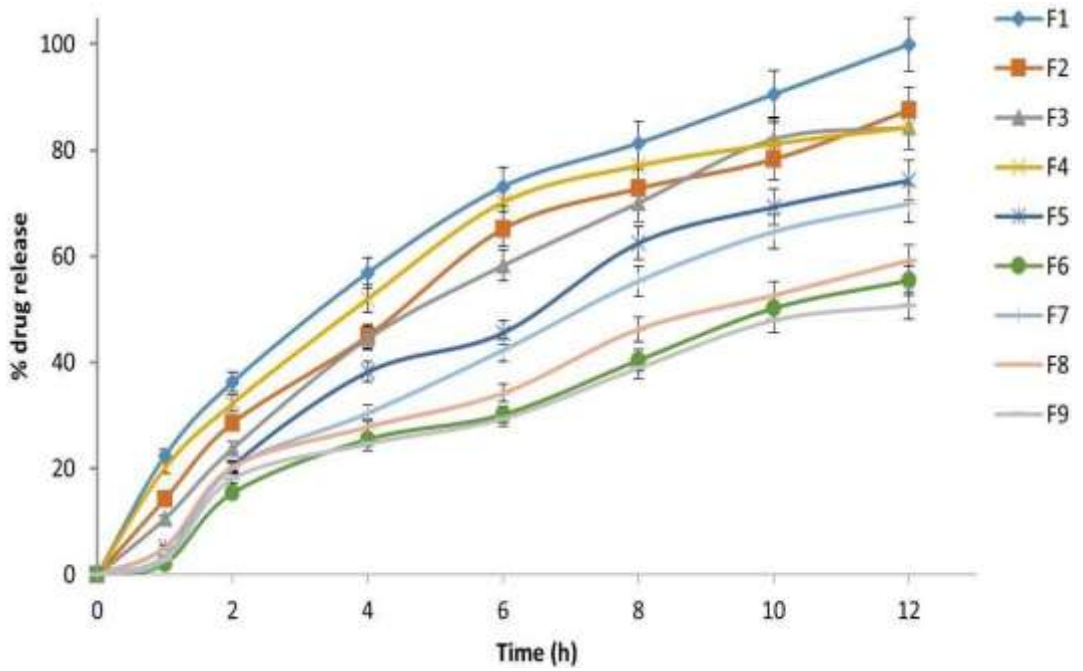


**Figure.5: In –vitro drug release study**

## IV. SUMMARY AND CONCLUSION:

New age of novel drug delivery the study on the formulation of the method is aimed at increasing the safety and effectiveness of existing drug molecules through novel drug delivery concepts. This work was aimed at preparing raft forming system of omeprazole. The main objective was to prepare and evaluate raft forming system of omeprazole for the treatment of gastro-oesophageal reflux disease. Preformulation tests were performed to validate the drug sample, such as organoleptic properties analysis, solubility analysis, partition coefficient. Infrared spectroscopy, UV spectroscopy, and melting point calculation were used to verify the drug sample. According to common references, all operations were carried out. The raft forming system of omeprazole was formulated. Based on the combined effects of, drug quality and cumulative drug release formulations , in-vitro gelation, drug content, pH ,in-vitro drug release. The findings showed that F2 formulation is the best formulation.

## REFERENCES:

[1]. Patti, M.G., "Gastroesophageal Reflux Disease", Available from https://emedicine.medscape.com/article/176595-overview. [Last accessed on 2019 April 22].

[2]. Binoy, B., Jayachandran, N.C.V., J drug dev .2012,1( 3) ,18.

[3]. "Treatment of GERD", International foundation for functional gastrointestinal disorders, January 2014, Available from: http://www.aboutgerd.org/site/about-gerd/treatment. [Last accessed on 2019 April 29].

[4]. "Heartburn, Gastroesophageal Reflux (GER), and Gastroesophageal Reflux Disease (GERD)", NIH Publication No.070882, May2007, Available from: http://www.digestive.niddk.nih.agov/ddiseases/pubs/gerd/index.asp x#1. [Last accessed on 2019 May 02].

[5]. Santoskar, R.S., Bhandarkar, S.D., Ainapure, S.S., Pharmacology and Pharmacotherapeutics, Popular Prakashan, Mumbai 2003.

[6]. Mituli, P., Priya, T., Bhavin, B., Upendra, P., Int J Pharm Res Biosci . 2014, 3(2), 580-597.

[7]. Badoni, A., Ojha, A., Gnanarajan, G., Kothiyal, P., Pharma Innov. 2012, 1(8), 32–42.

[8]. Shukla, S., Patidar, A.A., Biol. Arch. 2011, 1561–1568.

[9]. Gupta, G., Singh, A.A., Int J PharmTech Res. 2012, 4(4), 1527- 1545.

[10]. Thete, G., Mahajan, V.R., Int J Pharm Tech Res. 2014, 6(3), 1054- 1063.

[11]. Bramhankar, D.M., Jaiswal, S.B., Biopharmaceutics and Pharmacokinetics

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 230-237 www.ijprajournal.com ISSN: 2456-4494

A Treatise,Vallabh Prakashan, Delhi 2002.
[12]. Kanabar, V.B, Patel V.P., Doshi, S.M., Eur J Pharm Med Res. 2015, 2(4), 185-203.
[13]. Soni, H., Patel, V.A., Int J Sci Res. 2016. 5(4), 181- 186 .
[14]. Bhavsar, D.N, Varde, N., Sini Surendran, M.C., Shah, V.H., Upadhyay U.M., J Drug Deliv Ther. 2012, 2(5), 123-128.
[15]. Dixit N., J Curr Pharm. Res. 2011, 7(1), 6-20.
[16]. Yadawad M., Kavitha, K., Int J Res Pharm Biomed Sci. 2011, 2(1), 44-51.
[17]. Pandey, A., Kumar, G., Kothiyal, P., Barshiliya, Y., Asian J Pharm. Med Sci. 2012, 2(4), 60–77.
[18]. Garg, R., Gupta, G.D., Trop J Pharm. Res. 2008, 1055–1066.
[19]. Vinod, K.R., Santhosh, V., Anbuazaghan, S., David, B., Int J Appl Biol Pharm Tech. 2010, 1(2), 589-601.
[20]. Siegel, R.L.; Miller, K.D.; Jemal, A. Cancer statistics, 2020. CA Cancer J. Clin. **2020**, 70, 7–30. [CrossRef] [PubMed]
[21]. Hani, U.; Begum, M.Y.; Wahab, S.; Siddiqua, A.; Osmani, R.A.M.; Rahamathulla, M. Correction to: A Comprehensive Review of Current Perspectives on Novel Drug Delivery Systems and Approaches for Lung Cancer Management. J. Pharm. Innov. **2021**. [CrossRef]
[22]. Kolak, A.; Kamińska, M.; Sygit, K.; Budny, A.; Surdyka, D.; Kukiełka-Budny, B.; Burdan, F. Primary and secondary prevention of breast cancer. Ann. Agric. Environ. Med. **2017**, 24, 549–553. [CrossRef]
[23]. Kenchegowda, M.; Rahamathulla, M.; Hani, U.; Begum, M.Y.; Guruswamy, S.; Osmani, R.A.M.; Gowrav, M.P.; Alshehri, S.; Ghoneim, M.M.; Alshlowi, A.; et al. Smart Nanocarriers as an Emerging Platform for Cancer Therapy: A Review. Molecules **2021**, 27, 146. [CrossRef]
[24]. Jackisch, C.; Barcenas, C.H.; Bartsch, R.; Di Palma, J.; Glück, S.; Harbeck, N.; Macedo, G.; O'Shaughnessy, J.; Pistilli, B.; Ruiz-Borrego, M.; et al. Optimal Strategies for Successful Initiation of Neratinib in Patients with HER2-Positive Breast Cancer. Clin. Breast Cancer **2021**, 21, e575–e583. [CrossRef]
[25]. Rahamathulla, M.; Alam, N.; Hani, U.; Ibrahim, Q.; Alhamhoom, Y. Development and in vitro evaluation of effervescent floating matrix tablet of neritinib: An anticancer drug. Pak. J. Pharm. Sci. **2021**, 34, 1297–1303.
[26]. Rahamathulla, M.; Alsahhrani, S.M.; Al Saqr, A.; Alshetaili, A.; Shakeel, F. Effervescent floating matrix tablets of a novel anti-cancer drug neratinib for breast cancer treatment. J. Drug Deliv. Sci. Technol. **2021**, 66, 102788. [CrossRef]
[27]. Hani, U.; Krishna, G.; Shivakumar, H.G. Design and optimization of clotrimazole–hydroxypropyl-β-cyclodextrin bioadhesive vaginal tablets using Anacardium occidentale gum by 32 factorial design. RSC Adv. **2015**, 5, 35391–35404. [CrossRef]
[28]. Saisivam, S.; Rahamathulla, M.; Shakeel, F. Development of floating matrix tablets of losartan potassium: In vitro and in vivo evaluation. J. Drug Deliv. Sci. Technol. **2013**, 6, 611–617. [PubMed]
[29]. Rahamathulla, M.; HV, G.; Veerapu, G.; Hani, U.; Alhamhoom, Y.; Alqahtani, A.; Moin, A. Characterization, Optimization, In Vitro and In Vivo Evaluation of Simvastatin Proliposomes, as a Drug Delivery. AAPS PharmSciTech **2020**, 13, 129. [CrossRef] [PubMed]
[30]. Prajapati, V.D.; Jani, G.K.; Khutliwala, T.A.; Zala, B.S. Raft forming system-an upcoming approach of gastroretentive drug delivery system. J. Control. Release **2013**, 10, 151–165. [CrossRef] [PubMed]