ISSN: 0975-833X

Available online at http://www.journalcra.com

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

International Journal of Current Research
Vol. 13, Issue, 08, pp.18533-18537, August, 2021

DOI: https://doi.org/10.24941/ijcr.42024.08.2021

RESEARCH ARTICLE

DESIGNING OF CAPTOPRIL CONTROL RELEASE TABLETS BY USING DIFFERENT DRUG TO POLYMERS RATIO

Syed Muhammad Younas, *Ghulam Razaque, Noman Ul Haq, Nisar Ahmed Shahwani, Muhammad Arsalan, Ghulam Mustafa Shahwani, Abdullah, Raseed Ahmed and Waheed Ahmed Shah

Faculty of Pharmacy and Health Sciences, University of Baluchistan, Quetta, Pakistan
Department of Chemistry, University of Baluchistan, Quetta, Pakistan

ARTICLE INFO

Article History:
Received 28th May, 2021
Received in revised form
25th June, 2021
Accepted 19th July, 2021
Published online 31st August, 2021

Key Words:

Captopril, Controlled Released, Eudragit, Xanthan Gum, Physiochemical Test.

****Corresponding author:***
Ghulam Razaque

ABSTRACT

The aim of Controlled drug release system is to achieve a delivery profile that result in a high blood level of the drug for a long period of time, while in a conventional drug delivery system the drug level in blood flow rises after each administration of the drug and then falls before the next administration. Different drug to polymer ratios were combined and formulated CR captopril. F1, F2, F3 F4, F3, F5 and F6 prepared six separate formulations and tested their physicochemical properties. Preformulation studies Hausner's ratio, compressibility index, solubility studies and post formulation studies Hardness, thickness, weight variation, friability, disintegration and dissolution test were conducted. The flow properties were found to be within acceptable limits. The solubility studies done by using different solvents with different temperatures (pH 6.8, 7.4 with 25^0,37^0 and 40^0) it was found with near to the standards. The results of Physical tests were done and found within the acceptable limits. The dissolution of all formulations were checked according to the standard procedure and it was found that all the formulations were acceptable range. It is concluded that the formulations developed of controlled released captopril by using combination of polymers Eudragit, Xanthan Gum and formulation of controlled released of tablets were analyzed. The physical characteristics of tablets were checked accordingly which were within the limits specified. The dissolution of all formulations controlled released captopril showed more than 100% released within specified time. So it is recommended that in future control released tablets of different others drugs may be formulated in same combination of polymers to enhance the patient compliance.

Citation: Syed Muhammad Younas, Ghulam Razaque, Noman Ul Haq, Nisar Ahmed Shahwani, Muhammad Arsalan et al. "Designing of captopril control release tablets by using different drug to polymers ratio*", 2021. International Journal of Current Research, 13, 08, 18533-18537.*

INTRODUCTION

The non- invasive oral (through the mouth), nasal, inhalation, and rectal routes are the most common methods of delivery. Many drugs, however, cannot be administered via these channels due to risk of deterioration. Injection is needed for many protein and peptide drugs. Many immunizations depend on the administration of protein drugs, which is frequently by done by injection (Patel, 2012). Drug design is a method for discovering drugs based on their biological targets. Targeted drugs are molecules that are involved in a metabolic or signaling pathway that is unique to a disease or pathology, as well as the infectivity and survival of microbial pathogens (Kalyaanamoorthy, 2011). The aim of Controlled drug release system is to achieve a delivery profile that result in a high blood flow in which the level rises after each administration of the drug and then falls before the next administration (Langer, 1998). Matrix system that controls the excretion of the drug and has various solubility properties, the drug is dispersed and soluble hydrophilic substances, an insoluble matrix of rigid non soluble hydrophobic materials, and excretes the drug in a bounteous manner through both dissolutions-controlled as well as diffusion-controlled mechanisms. This material, which includes both hydrophobic and hydrophilic polymers, is widely used in the preparation of matrix systems. Xanthan gum, sodium alginate, poly (ethyl oxide), and cross-linked homo polymers copolymers of acrylic acid (HPMC), hydroxyl propyl cellulose (HPC), hydroxyl ethyl cellulose (HEC), hydroxyl ethyl cellulose (HEC), hydroxyl ethyl cellulose (HEC), hydroxyl ethyl cellulose (HEC), hydroxyl ethyl. Since small particle size is important

for the rapid formation of the gelatinous layer on the tablet surface, it is typically supplied in micronized form (Truog, 2006). Polymer is a large molecule made of repeating units. It is used as solubilizes, stabilizer, emulsifier, preservatives, flavoring agents, coloring agents, sweetening agents and mechanical supports for sustain released of drug. Polymers are macromolecules which refer to any large molecule. So polymer are consider to be a subset of macromolecules (Farokhzad, 2009). Polymers are used as a tablet binder and to regulate the movement of a controlling agent in a liquid. Suspension and emulsion are two different types of suspension. It can be used as a film coating to make a drug's test more uncomfortable, as well as to improve drug stability and alter drug release stability. The serve as prolong drug availability if medicines are formulated as hydrogels or micro particles, in polymers favorable changes bio distributions, if formulated into dense nanoparticles and it transport a drug to its accessible of action if formulated as gene medicines (Farokhzad, 2009). Carbapol is a powder or liquid made up of high molecular weight acrylic acid chains that are normally cross connected. In the cosmetic manufacturing Carbapol used as thickening agent in lotions, creams and gels. It is also used to stabilized suspend and control the release of pharmaceuticals products. Magnesium citrate is a magnesium preparation in salt form containing citric acid in a 1:1 ratio. The term magnesium is vague and may apply to other slats such as tri-magnesium citrate or magnesium stearate. It's used as a saline laxative and to fully clear the bowl before major surgery or a colonoscopy, among other things, and it's also used as pill form as magnesium dietary supplementary (Panzade, 2010). Captopril is an oral drug and membrane of classification of a drug is known as ACE inhibitors. High blood pressure and heart failure are treated with ACE inhibitors. Captopril's mechanism of action isn't fully understood. It has a beneficial effect in hypertension and heart failure, and it appears to be the product of rennin angiotensin aldosterone system self-control (Goodfriend, 1996). Captopril's mechanism of action has yet to be fully understood.

The inhibition of the rennin angiotensin aldosterone system appears to be the main cause of its beneficial effects in hypertension and heart failure. However, there is no clear relationship between rennin after oral administration of a therapeutic dose of captopril and rapid absorption, which occurs with a peak blood level at about one hour. Since the presence of food in the gastrointestinal tract (GIT) reduces absorption by around 30-40%, captopril should be taken before a meal. According to carbon -14 marking, the average minimum absorption is about 75%. Within a 24-hour cycle. The remainder of the absorption dose is excreted in the urine, with 40-50 percent being unchanged drug and the other being a disulfide dimer of captopril –cysteine disulfide. A quarter to a third of the drug is bound to plasma protein. Total radioactivity in blood has an apparent removal half-life of less than 3 hours (Wijesekara, 2010)

.

Keywords: Control Release, Captopril, Eudragit, Xanthan gum, Microspheres

MATERIALS AND METHODS

The chemicals were used without any further purification and were of analytical grade. Captopril chemical was gifted by Zafa Pharmaceutical, Pakistan, Eudragit RS 100.

Chemical Glassware: HPMC, Xanthan Gum, Carbapol, Avocil, Magnesium Citrate, Acetonitrile, Phosphoric Acid, N-Hexane, Tri-methyl-amine, Captopril.

Equipments: Centrifuge Machine, Shaking Water Bath, Sonicator, Micropipette, HPLC, Dissolution Apparatus, UV Spectroscopy, Single punch tabulating Machine, Friabilator, Hardness taster.

Pre-Formulation Studies: Following Pre-formulations were conducted as per described Procedures.

Standard Curve of Captopril: Phosphate Buffer solution having pH of 6.8 and then 7.4 were prepared before construction of standard curve of the captopril drug by dissolved 100mgof active drug and five (Farokhzad, 2009) different dilutions were prepared from stock solutions accordingly as per standard procedure and analyzed the absorbance by spectrophotometrically (Srividya *et al*., 2018).

Preparation of stock solution: Standard curve of the captopril was performed by dissolving 25mg in distilled water 25mg of the captopril was exactly weighed and transferred in to 100ml volumetric flask and five different dilutions were made. Then those solutions were kept for 30 minutes in Sonicator. After all those dilutions were kept in stability chamber at different temperatures in different time intervals i.e.25^0C, and 37^0C and 40^0C for 24 hours, after 24 hours reading of these solution were noted by using UV visible spectrophotometer at 227nm (Srividya, 2018).

Preparation of 6.8 and 7.4 PH Buffer Solution: Standard curve of the small quantity of phosphate buffer solution 6.8 pH and 7.4 pH were made by adding 50ML stock solution and then added Buffer solution, after that these solutions were kept for 30 minutes in five different volumetric flasks. After well dilution the solution were transferred into stability chamber for three different temperatures 25^{o}C, 37^{o}C and 40^{o}C for 24 hours. For 24 hours. After 24 hours take reading of these solutions on UV visible Spectrophotometry absorption was 227nm.

Solubility study of Captopril: Solubility study of captopril were perfumed by using distilled water with previous temperature at two different buffers solutions 6.8 pH and 7.4 pH were performed for 24 hours. In a 100ML volumetric flask, 100mg of captopril was applied to 100ML solvent and shaken. The shaker was maintained in accordance with the circumstances. After that, 5 mL samples were stockpiled and analyzed using spectrophotometry at a wavelength of 227nm.

Flow Properties: The flow properties of captopril granules and powders were investigated.

- Uniform feed from the storage container into tablet dies, allowing the uniform particles filling that maintains the weight uniformity of the captopril powder.
- Excess entrapped air inside the captopril powder may cause capping/lamination of the tablets due to the captopril powder flow.

Bulk Density of the Captopril: The bulk density of the powdered captopril was done. The collection of inter particulate transparent volume is included in the captopril volume. The bulk density is determined by the density of the powder particles as well as their spatial arrangement in the bed powder.

Table No. 1. Solubility studies chart with different solvents and temperature

No	Solvent	Drug used	Temperature
1	Buffer solution pH 6.8	Captopril 100mg	25°c
2	Buffer solution pH 6.8	Captopril 100mg	37°c
3	Buffer solution pH 6.8	Captopril 100mg	40°c
4	Buffer solution pH 7.4	Captopril 100mg	25°c
5	Buffer solution pH 7.4	Captopril 100mg	37°c
6	Buffer solution pH 7.4	Captopril 100mg	40°c

Since the calculation is done with a cylinder, the bulk density is expressed in gram per milliliter and kilogram per cubic meter (1 g/ml=1000 kg/m3).

CR Tablets Fabrication

Control Released tablets contain captopril were developed by method of direct compression and used variable concentration of polymers, magnesium stearate and filler were incorporated shown in tablets 2 (Reddy, 2011). The entire ingredient was precisely measured and passed through a sieve with a mesh size of No.60. Previously, all ingredients were evenly blended together for 20 minutes with the exception of magnesium stearate, using a mortar and pestle. As a post lubricant, 1 percent magnesium stearate was added after the active ingredient was thoroughly mixed with the other excipients. All of the components were re-mixed for 5-8 minutes. A single tableting machine was used to compress the blended mixture.

The impact of the drug-to-polymer ratio: The drug-to-polymer ratio was varied in the formulations, and the effect of the polymer ratio on drug release kinetics was investigated using various kinetic models. As the drug amount in all formulated controlled released matrices and the polymer amount of is increased as the drug polymer increased (Patel, 2012).

Physical Properties of the Tablets: Pharmaceutical tablets must meet certain criteria in order to be labelled as high-quality drugs. Potency, effectiveness, stability, patient acceptability, and regulatory enforcement are the key requirements for determining the consistency of any medication in dosage form. Physical properties are considered during the product design and formulation stages. Chemical and biological specifications that the drug product must meet in order to meet Quality Control standards must be determined, and a quality goal must be set (Ölmez, 2009).

Friability Test: A roach Friabilator can be used in the lab to assess the friability of tablets. For this experiment, 20 tablets were weighed and placed in a Friabilator, which was then spun at 25 rpm for four minutes. The tablets were disgusted and measured, and the difference between the two weights was used to measure friability, which was expressed as a percentage. And then use the formula below to figure it out.

Friability = (I w – F w) I w × 100%

Where I w = the total initial weight of the tablets, and F w is the total weight of the tablets after friability. According to the USP, traditional compressed tablets that lose less than 0.5 percent to 1% of their weight (after revolution) are usually considered suitable (Ölmez, 2009).

Thickness of the Tablets: Thickness tests of tablets were analyzed with Vernier caliper which was evaluating the degrees of compaction during the punches of the tablets. Within a ±5% variation of the standard, thickness should be regulated (Ahmed, 2019).

Hardness Test: Selected the 20 tablets randomly weighed them then Placed the tablets in Hardness tester. The pressure was applied for the breakdown of the tablet and the results were tabulated (Wijesekara, 2010).

Weight Variations Test: According to the USP, the weight variation test were performed by weighed 20 tablets individually and measured the average weights and the percentage value of the weight variance test. The formula is as follows.

Weight variation = (I W – Aw) Aw × 100%

Where I W = denotes the individual weight of a tablet and Aw denotes the average weight of tablets (Abbirami, 2013).

Disintegration Test: The disintegration of all various brands were assessed, compared, and tabulated. All of the tablets tested were compared with the USP's specifications, which is officially less than 15 minutes (Uddin, 2018)

RESULTS AND DISCUSSION

Angle of repose, compressibility index, and Hausner's ratio are the results: Captopril's flow properties were rated as excellent, with a 31-degree angle of repose, a compressibility index of 10, and a Hauser's ratio of 1.10. Both of the results of the Angle of repose, Compressibility index, and Hausner's ratio tests were within reasonable limits. Physical evaluation of the captopril tablets were studies. Hardness, thickness, weight variations and friability were performed as per the official standard procedure and found in acceptable limits according to the official standards. The weight variations of all formulations were tested and it was found that all the formulations were within acceptable range. The friability test was performed accordingly and the results showed that all the formulations were slightly difference between each other but were with-in the limits specified as in USP standards. The thickness results revealed that there was a small difference between these tablets that were under the USP's norm set limits and those that were 3% thicker and met the USP's requirements. The diameters of the tablets were measured individually using a Vernier Caliper and found within acceptable limits. All formulations' hardness was measured and compared with each other. It was discovered that there was a 5% discrepancy between these tablets that were under the USP specifications.

Disintegration: Disintegration times of all the formulations were checked accordingly with the given standard procedure and it is found that all the formulations were within the limits i.e. less than 15 minutes.

Dissolution test: The dissolution results were tabulated for 24 hours in different time intervals. The CR formulation F1 the D:P ratio was 10:2 which contained polymer Eudragit RL 100 and the release was104.982% , in F2 D:P ratio was 10:3 which contained polymer Eudragit RL 100,the release showed 100.883%, F3 D:P ratio was 10:4which contained polymer Eudragit RL 100 and the release was 103.695%, F4 which contained polymer HPMC and xanthan gum. Drug Polymer ratio was 10:2 the release was 103.199%, F5 D:P ratio was 10:3 which contained polymer HPMC and xanthan gum and the release was 103.596% and F6 drug polymer ratio was 10:4 which contained polymer HPMC and xanthan gum and the release was 105.180%the author confirms the findings. It shows that all the tablets formulated were within the limits (Abdel-Mottaleb, 2011).

Table No. 2. CR Captopril 100 mg by using the Polymer Carbapol and Eudragit

S.NO	Drug to polymer ratio	Drug captopril	Polymer Eudragit RL100	Mg St	Filler Avocil	Total
F1	10:2	30mg	6mg	0.5mg	63.5mg	100mg
F2	10:3	30mg	9mg	0.5mg	60.5mg	100mg
F3	10:4	30mg	12mg	0.5mg	57.5	100mg

Table No.3. CR of Captopril 100 mg by using the Polymer Xanthan Gum and HPMC

S. No	Drug/polymer ratio	Drug Captopril	Polymer HPMC Xanthan Gum	Mg stearate (lubricant)	Avocil (Filler)	Total
F4	10 :2	50mg	10mg	0.5%	39.5mg	100mg
F5	10:3	50mg	15mg	0.5%	34.5mg	100mg
F6	10:4	50mg	20mg	0.5%	29.5mg	100mg

Table No 4. Result of Solubility of captopril by using 6.8 PH buffer

S.NO	Solvent used	Temperature	Absorbance	wavelength
1	6.8 pH buffer	25^0C	2.240	227.00
2	6.8 pH buffer	37^0C	2.624	224.50
3	6.8 pH buffer	40^0C	2.613	222.00

Table No 5. Result of Solubility of captopril by using 7.4 pHbuffers

S.NO	Solvent used	Temperature	Absorbance	Wavelength
1	7.4 pH buffer	25^0C	2.315	226.50
2	7.4 pH buffer	37^0C	2.315	226.50
3	7.4 pH buffer	40^0C	2.315	226.50

Table No 6. Result of Valuable of angle compressibility index of Hausner's ratio

FlowProperty	Angleofreposeinly degree	Compressibility Index(%)	Hausner'sratio
Reference standards	25-30	<10	1.00-1.11
Results of Captopril	31ly	10	1.10

Table No 7. Result of Physical Characteristics of Formulation F1 to F6

S.NO	Weight variations(grams)	Friability test (%)	Thickness(mm)	Diameter (mm)	HardnessKg/cm^2
F1	1.36	0.2	9.1	16.5	7.34
F2	1.44	0.1	9.2	16.4	8.185
F3	1.25	0.7	9.1	16.5	7.859
F4	1.42	0.2	9.4	16.2	7.215
F5	1.4	0.3	9.1	16.5	7.765
F6	1.42	0.9	9.1	16.5	7.815

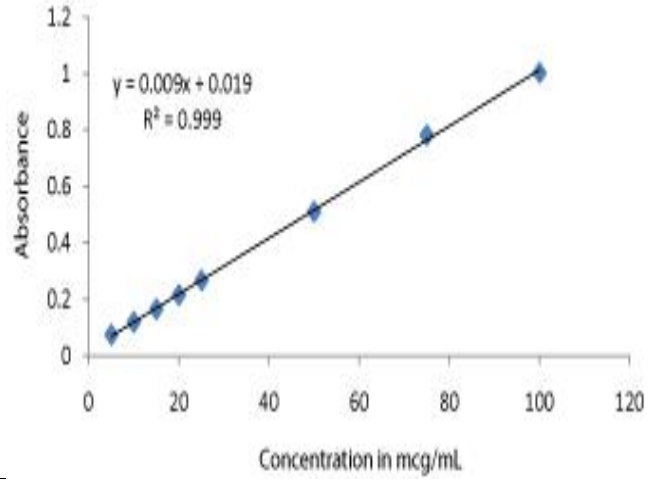

Figure No 1. Standard Curve of Captopril

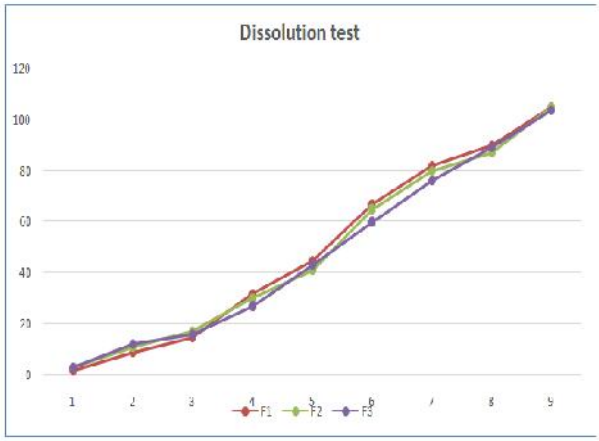

Figure No 2. Dissolution of CR formulation of Captopril F1, F2 and F3 with different drug to polymer ratio

Table No. 8 Results of Disintegration of all formulations

Formulation	Disintegration time (minutes)
F1	12
F2	11
F3	13
F4	12
F5	13
F6	12

Table No.9. Results of Dissolution test

S.N0	Formulation y	Drug Polymer Ratio	Dissolution %age
1	F1	10:2	104.982%
2	F2	10:3	104.883%
3	F3	10:4	103.695%
4	F4	10:2	103.199%
5	F5	10:3	103.596%
6	F6	10:4	105.180%

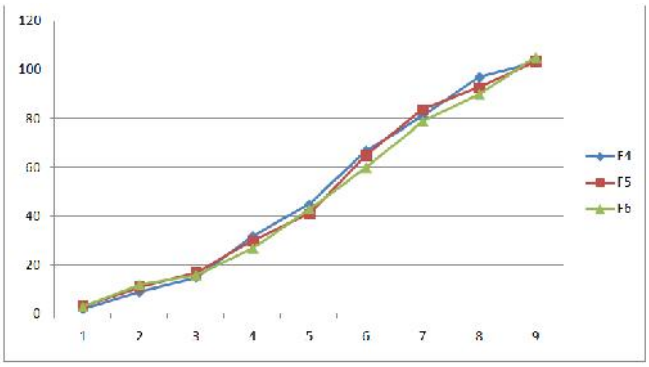

Figure No 3. Dissolution of CR formulation of Captopril F4, F5 and F6 with different drug to polymer ratio

Conclusion

The formulations developed of controlled released tablets of captopril by using combination of polymers Eudragit, Xanthan Gum and their different physical and chemical parameters were analyzed. The physical characteristics of CR tablets were checked accordingly which were within the limits specified. The dissolution of these controlled released tablets of captopril showed more than 100% released in 24 hours. So it is recommended that in future control released tablets of different others drugs may be formulated in same combination of polymers to enhance the patient compliance.

REFERENCES

Patel, D., Chaudhary, S. A., Parmar, B., & Bhura, N. 2012. Transdermal drug delivery system: a review. *The pharma innovation*, *1*(4, Part A), 66.

Kalyaanamoorthy, S., & Chen, Y.-P. P. 2011. Structure-based drug design to augment hit discovery. *Drug discovery today*, *16*(17-18), 831-839.

Langer, R. 1998. Drug delivery and targeting. *Nature*, *392*(6679 Suppl), 5-10.

Truog, P. 2006. 4-phenylbutyric acid controlled-release formulations for therapeutic use: Google Patents.

Farokhzad, O. C., Jon, S., & Langer, R. S. 2009. Controlled release polymer nanoparticle containing bound nucleic acid ligand for targeting: Google Patents.

Panzade, P., & Puranik, P. K. 2010. Carbopol Polymers: A Versatile Polymer for Pharmaceutical Applications. *Research Journal of Pharmacy and Technology*, *3*(3), 672-675.

Goodfriend, T. L., Elliott, M. E., & Catt, K. J. 1996. Angiotensin receptors and their antagonists. *New England Journal of Medicine*, *334*(25), 1649-1655.

8. Wijesekara, I., & Kim, S.-K. 2010. Angiotensin-I-converting enzyme (ACE) inhibitors from marine resources: Prospects in the pharmaceutical industry. *Marine drugs*, *8*(4), 1080-1093.

Srividya, G., Jain, M., Mahalakshmi, K., Gayathri, S., Raman, R., & Angayarkanni, N. 2018. A novel and less invasive technique to assess cytokine profile of vitreous in patients of diabetic macular oedema. *Eye*, *32*(4), 820-829.

Reddy, S. N. 2011. *Development and evaluation of controlled release matrix tablets containing perindopril in the treatment of hypertension.* RGUHS.

Ölmez, S. S., & Vural, İ. 2009. Advantages and quality control of orally disintegrating tablets. *FABAD J Pharm Sci*, *34*(3), 167-172.

Ahmed, F. R., Shoaib, M. H., Yousuf, R. I., Ali, T., Geckeler, K. E., Siddiqui, F., Qazi, F. 2019. Clay nanotubes as a novel multifunctional excipient for the development of directly compressible diclofenac potassium tablets in a SeDeM driven QbD environment. *European Journal of Pharmaceutical Sciences*, *133*, 214-227.

Abbirami, V., Sainithya, P., Shobana, A., Devi, D. R., & Hari, B. V. 2013. Review on In-vitro Bioeqivalence Studies and its Methodologies. *Int J Chem Tech Res*, *5*(5), 2295-2302.

Uddin, A. 2018. Comparative Dissolution and Disintegration Study of Different Brands of Linezolid 600 mg Tablets Available in Karachi, Pakistan. *Pharm Anal Acta*, *9*, 602.

Abdel-Mottaleb, M. M., & Lamprecht, A. 2011. Standardized in vitro drug release test for colloidal drug carriers using modified USP dissolution apparatus I. *Drug development and industrial pharmacy*, *37*(2), 178-184.

****