Journal of Social Research

JOSR: Journal of Social Research
Desember 2022, 2 (1), 126-133

p-ISSN: 2827-9832 e-ISSN: 2828-335x

Available online at http:// https://ijsr.internationaljournallabs.com/index.php/ijsr

Literature Review Article: Drug Delivery System held in the Stomach (*gastroretentive*)

Nurhalifah, Prayoga Daffa Sundawan, Santika Citra Veronita, Shella Imka Puji Destria, Siti Nuryamah, Nia Yuniarsih

Faculty of Pharmacy, Buana Perjuangan Karawang University

fm19.nurhalifah@mhs.ubpkarawang.ac.id, fm19.prayogasundawan@mhs.ubpkarawang.ac.id, fm19.santikaveronita@mhs.ubpkarawang.ac.id, fm19.shelladestria@mhs.ubpkarawang.ac.id, fm19.sitinuryamah@mhs.ubpkarawang.ac.id, nia.yuniarsih@ubpkarawang.ac.id

Received: November 29, 2022
Revised : Desember 01, 2022
Accepted: Desember 03, 2022

Abstract (Indonesia)

Latar Belakang: Obat merupakan suatu subtansi yang melalui efek kimianya membawa perubahan dalam fungsi biologi. Sistem penghantaran GRDDS merupakan suatu system penghantaran obat tertunda (sustained) yang dapat menahan obat agar berada di dalam lambung dalam waktu yang lebih lama. Keuntungan dari GRDDS antara lain dapat meningkatkan bioavailabilitas, meningkatkan kelarutan obat yang kurang larut dalam pH tinggi, dapat mengontrol level terapi sehingga mengurangi terjadinya fluktuasi, dapat memperpanjang waktu paruh sehingga frekuensi pemberian obat dapat dikurangi.

Tujuan: Penelitian ini betujuan untuk menguraikan tipe-tipe sediaan GRDDS. Variasi tersebut disebabkan adanya kombinasi dari perbedaan mekanisme dan teknologinya.

Metode: Rancangan dalam penelitian ini menggunakan systematic review tinjauan litelatur review yang mengidentifikasikan, menilai dan menginterprestasi seluruh temuan-temuan pada suatu topik penelitian.

Hasilnya: Sistem *floating* dapat menggunakan bahan polimer yang dapat mengembang seperti HPMC dan chitosan. Mekanisme *floating* diawali dengan adanya kontak cairan lambung dengan tablet yang menyebabkan polimer mengalami hidrasi membentuk lapisan gel yang dapat menahan gas CO2 yang terbentuk akibat interaksi natrium bikarbonat dengan asam sitrat sehingga tablet dapat mengembang dan dapat mengapung**.** Rute penghantaran obat oral merupakan rute yang paling banyak disukai karena mudah untuk digunakan. Absorpsi obat oral sebagian besar terjadi di lambung dan di usus.

Kesimpulan: Maka dari itu, perlu adanya sistem penghantaran obat yang dapat memperpanjang waktu kontak

dengan lambung, yakni Gastroretentive Drug Delivery System (GRDDS).

Keywords: obat, GRDDS, system *floating*

Abstract (English)

Background: *Medicine is a substance that through its chemical effects brings about changes in biological functions. The GRDDS delivery system is a sustained drug delivery system that can hold drugs back in the stomach for a longer time. The advantages of GRDDS include being able to increase bioavailability, increase the solubility of drugs that are poorly soluble in high pH, can control of therapeutic levels to reduce the occurrence of fluctuations, can extend the half-life so that the frequency of drug administration can be reduced.*

Objectives: *This study aims to describe the types of GRDDS preparations. The variation is due to a combination of differences in mechanisms and technology.*

Method: *The design in this study uses a systematic review of the review process that identifies, assesses, and interprets all findings on a research topic.*

Result: *Floating systems can use expandable polymeric materials such as HPMC and chitosan. The floating mechanism begins with the contact of gastric juices with tablets which causes the polymer to hydrate to form a gel layer that can withstand CO2 gas formed due to the interaction of sodium bicarbonate with citric acid so that the tablets can expand and can float**.*** *The oral drug delivery route is the most preferred because it is easy to use. Absorption of oral drugs mostly occurs in the stomach and the intestines.*

Conclusion: *Therefore, it is necessary to have a drug delivery system that can extend the contact time with the stomach, namely the Gastroretentive Drug Delivery System (GRDDS).*

Keywords: *drug, GRDDS, floating system*

**Correspondent Author: Nurhalifah*
Email: fm19.nurhalifah@mhs.ubpkarawang.ac.id

INTRODUCTION

Medicine is an ingredient that aims to be used in determining diagnosis, preventing, reducing, and curing diseases or symptoms of diseases, wounds, or abnormalities of the body and spiritually in humans or animals, improving the body or parts of the human body (Wardani, 2021).

According to (Martien et al., 2012) medicine is a substance that through its chemical effects brings changes in biological functions. Drug molecules interact with special molecules in biological systems that act as regulators in this case receptors. To chemically interact with its receptors, the drug molecule must have the appropriate size, shape of the electric charge, and atomic composition. Currently, many considerations underlie the development of technology for pharmaceutical therapy consisting of three main factors, namely effectiveness, suppressing the effects of harm on the system if applied (safety), and acceptability to patients (acceptability).

In the process of discovering new pharmaceuticals, pharmaceutical preparation formulation technology and drug delivery systems played an important role. The main factors that are generally considered in this field include molecular and physicochemical considerations such as molecular equilibrium, hydrophilic-lipophilic equilibrium, biopharmaceutical processes, metabolism and biodegradation, drug-receptor affinity, physiological considerations, and biocompatibility (Martien et al., 2012). This delivery system serves to direct the drug molecules to the desired target. This encourages the development of drug delivery systems, especially in terms of formulations to optimize the use of additives to obtain a drug preparation with a good delivery system and meet the therapeutic effect.

The oral drug delivery route is the most preferred because it is easy to use. Absorption of oral drugs mostly occurs in the stomach and the intestines. Imperfect absorption in the stomach is caused by the Gastro Residence Time (GRT) factor. The presence of gastric emptying time causes the drug to not be in the stomach for a long time so it is necessary to increase GRT. The longer the drug stays in the stomach, the more absorption of the drug so that the bioavailability of the drug also increases. Therefore, it is necessary to have a drug delivery system that can extend the contact time with the stomach, namely the Gastroretentive Drug Delivery System (GRDDS). There have been many studies on GRDDS formulations, including Nifedipine and Nilotinib formulations to increase bioavailability, antibiotics to increase the effectiveness of drugs against H. pylori treatment, ofloxacin as a delayed release drug delivery system, increasing the solubility of verapamil drugs, furosemide, propranolol, and others (Annisa, n.d.-a).

The GRDDS delivery system is a sustained drug delivery system that can hold drugs back in the stomach for a longer time. The advantages of GRDDS include being able to increase bioavailability, increase the solubility of drugs that are poorly soluble in high pH, can control of therapeutic levels to reduce the occurrence of fluctuations, can extend the half-life so that the frequency of drug administration can be reduced. However, this system is not suitable for use in drugs that irritate the stomach, are unstable in gastric pH, or experience significant first-pass effects. There are several systems in the GRDDS formulation, namely floating, aggressive, high density, superiors, expandable, raft forming, and magnetic (Annisa, n.d.-b). This study aims to describe the types of GRDDS preparations. The variation is due to a combination of differences in mechanisms and technology.

RESEARCH METHODS

This research is by using the Literature Review design where a literature review is a writing method looking for literature from international or national, this literature can be obtained based on journals, books, the internet, or from other library sources, the design in this study uses systematic review reviews of review documents that identify, assess and interpret all findings on a topic research, to be predetermined later as an effort made by the researcher in finding information related to the problem under study.

Criterion	Inclusion	Conclusion
Timeframe and population	10-year journal, i.e. year (2012-2022)	International and national journals whose year span is below 2012
Language	Journals took in Indonesian (National) and English (International)	International journals with languages other than English such as Arabic, Chinese, etc.
Subject	Journal with drug delivery system material	Journal with material on the delivery system of drugs held in the field
Journal Content Theme	Discharged drug delivery system (GRDDS)	Route of delivery of the drug through the stomach
Types of Journals	Fulltext research journal	Journals are not full-text research

(Table 1. Inclusion and Exclusion Criteria)

RESULTS AND DISCUSSION

Based on searching for data sources, information was obtained about several descriptions of the drug delivery system that was withheld in the drug. Shown in Table.2

No	Reference	Article title	Method	Result	Data based
1.	Mohammad Zulfikhar A.1, Dwi Nurahmanto2, Lusia Oktora R.K.S, 2019	*HYDROXYPROPYL METHYLCELLULOSE* OPTIMIZATION AND *CHITOSAN ON FLOATING-MUCOADHESIVE* TABLETS CIMETIDINE BY FACTORIAL DESIGN METHOD	Research method with Powder making for *floatingmucoadhesive* tablets cimetidine.	Creation of *floating* tablet systems Cimetidine is made using the method *effervescent* with the addition of *gas generating systems* i.e. citric acid and sodium bicarbonate. Drug *floating* system in hull can be made using making air-filled chambers or inert gases that	Google Scholar

				formed as a result of *gas-generating* interactions *a system* with gastric juices	
2.	Eva Setyorini, Eka Deddy Irawan, Lusia Oktora Ruma Kumala Sari, 2021	Optimization of *Hydroxypropyl Methylcellulose* and *Xanthan Gum* on *Floating-Mucoadhesive Gliclazide* Tablets Factorial Design Method (*Optimization of Hydroxypropyl Methylcellulose and Xanthan Gum on Floating-Mucoadhesive Gliclazide Tablet using Factorial Design*)	The study is conducted by the method of factorial design. The optimized factor is amount of polymer HPMC K4M and *xanthan gum* Complete formula arrangement	Floatability parameters what was tested in this study was *floating lag time* and *floating duration time*. Requirement *The floating lag time* chosen is between 10-600 seconds with the goal that the tablet can floats right in the hull and gives good buoyancy. *Floating* requirements The duration time chosen is no less of 12 hours. The response is generated later processed using *software design expert* version 9.0.6.	Google Scholar
3.	Vivianne Annisa, 2021	Review: Gastroretentive Drug Delivery System (GRDDS)	Literature Method Review	there are many types of GRDDS preparations. The variation is due to a combination of differences in mechanisms and technology. Each type of system has its advantages and disadvantages. Several types of GRDDS preparations have been produced by the pharmaceutical industry and marketed. The most widely applied systems by the	Google Scholar

				pharmaceutical industry are floating and bioactive systems. Examples of trademarks that have been marketed are Zanocin, Riomet, Cifran, Madopar, Prolopa, Valrelease, Xifaxan, Cytotec, Conviron, and many more	

(Table 2. Data source Overview of Nutritional Status in tuberculosis Patients)

1. *Effervescent* with the addition of *gas-generating systems*, namely citric acid and sodium bicarbonate. The *floating* system of the drug can be made by creating a space filled with air or inert gases formed due to the interaction of *generating system* gases with gastric juices**).** Floating systems can use expandable polymeric materials such as HPMC and chitosan. The *floating* mechanism begins with the contact of gastric juices with tablets which causes the polymer to hydrate to form a gel layer that can withstand CO2 gas formed due to the interaction of sodium bicarbonate with citric acid so that the tablets can expand and can float**.** Table 5 shows the floating *lag* time capability of formula AB> A> (1)>B, while for *floating duration time* all formulas give the same result that they can float for more than 12 hours. Based on the results of testing the ability to float lag time tablets in table 5, it shows that the use of HPMC with a high-level concentration in formula A compared to formula (1) and formula AB compared to formula B can prolong the floating lag time, while the use of *chitosan* at high levels in formula AB compared to formula A can prolong the *floating lag time* Tablets. The use of low levels of HPMC and chitosan can speed up the floating lag time of tablets, but in formula (1) low levels of chitosan produce a longer *floating lag time* than the use of high levels of *chitosan* in formula B. Coded factor equations from *software design expert* version 11 of HPMC polymers and *Chitosan* shows positive values in the floating lag time response, this shows the use of both polymers can increase *the floating lag time*. HPMC and *chitosan* are hydrophilic hydrocolloid polymers that can form *barrier* gels with high viscosity, to slow down the penetration rate of gastric juices and result in fewer and fewer *gas-generating agents* in contact with gastric juices to increase *floating lag time* tablets.

2. Obtaining uniformity of gliclazide powder in the mixture of powder and tablet content shows that all formulas meet the range of % content of active ingredient *gliclazide* (85.0-115.0%) and CV <6% so that it can be said to be a uniform sample [10]. Testing the mechanical strength of tablets aims to avoid the influence of other variables that may result from the physical properties of tablets. The results of the tablet's mechanical strength test showed that all yield formulas met the criteria of 10-20 kg hardness [11] and the brittleness (<1%) [12]. The floatability parameters tested in this study are floating *l* time and *floating duration time*. The selected *floating lag ti* requirement is between 10-600 seconds with the aim that the tablet can float right in the hull and provide good buoyancy. The *selected floating duration time* requirement is not less than 12 hours. The resulting response is then processed using *software design expert* version 9.0.6 from Equation 1, it is known that the use of HPMC K4M polymers and *xanthan gum* gives positive values indicating a slowdown in *floating lag time.* The effect of the HPMC K4M factor and *the effect of the xanthan* factor gives negative values indicating an acceleration of *floating lag time.* The results of the great *mucoadhesive* strength test

on the AB formula with the results of the AB>A>B> (1) formula. The test results can be seen in Table 3. The *mucoadhesive* strength response was further analyzed with *software design expert* version 9.0.6. Equation 2, shows that the effect of the HPMC K4M factor and the *effect of the xanthan g* factor gives a positive value that there is an increase in mucoadhesive strength and the interaction effect gives a negative value that there is a decrease in *mucoadhesive* strength. Determination of the parameters of DE720 is aimed at obtaining an idea of the percentage of drugs released in plasma. The DE720 response value is then analyzed with *software design exper*t version 9.0.6 Equation 3, it shows that the factor effect of HPMC K4M, *xanthan g, um,* and the interaction of the two gives a positive value. The effect of HPMC K4M and *xanthan g* interaction factors gave the greatest DE720 response value compared to the single-factor effect. The magnitude of the response value resulting from the effect of the interaction factor HPMC K4M and *xanthan gum* shows a dominant influence on the DE720 value of tablets, namely increasing the DE720 response that there is an increase in DE720 Table 4. indicates that r2 in formulas A, B and AB is high so that formulas A, B, and AB denote zero-order discharge models. While the value of r2 in formula (1) follows the *Higuchi* model.

3. The development of a sustained-release drug delivery system, namely GRDDS has the potential to increase bioavailability because it can extend GRT. In addition, GRDDS can also control drug delivery so that the plasma concentration of drugs can be controlled within a certain period. The GRDDS approach can go through various means, such as floating, aggressive, high-density, super porous, expandable, raft forming, and magnetic systems. Floating systems can go through two manufacturing mechanisms, namely effervescent and non-effervescent. The development of GRDDS has been carried out by the pharmaceutical industry and has been widely marketed. The application of GRDDS has the potential to be developed in other drugs that have low absorption problems in the upper gastrointestinal tract or have a short half-life

CONCLUSION

The oral drug delivery route is the most preferred because it is easy to use. Absorption of oral drugs mostly occurs in the stomach and the intestines. Therefore, it is necessary to have a drug delivery system that can extend the contact time with the stomach, namely the Gastroretentive Drug Delivery System (GRDDS). The GRDDS delivery system is a sustained drug delivery system that can hold drugs back in the stomach for a longer time. The advantages of GRDDS include being able to increase bioavailability, increase the solubility of drugs that are poorly soluble in high pH, can control of therapeutic levels to reduce the occurrence of fluctuations, can extend the half-life so that the frequency of drug administration can be reduced.

BIBLIOGRAPHY

Annisa, V. (n.d.-a). *Sistem Penghantaran Obat Gastroretentif (GRDDS)*.

Annisa, V. (n.d.-b). *Sistem Penghantaran Obat Gastroretentif (GRDDS)*.

Martien, R., Adhyatmika, A., Irianto, I. D. K., Farida, V., & Sari, D. P. (2012). Perkembangan teknologi nanopartikel sebagai sistem penghantaran obat. *Majalah Farmaseutik*, *8*(1), 133–144.

Wardani, B. K. (2021). Pengaruh Pelayanan Kefarmasian Terhadap Kepuasan Pasien Di Apotek Berkah Santosa Klaten. *IJMS-Indonesian Journal on Medical Science*, *8*(2).