IJMPR 2024, 8(3), 10-15

International Journal of Modern Pharmaceutical Research
www.ijmpronline.com

ISSN: 2319-5878
IJMPR
Review Article
SJIF Impact Factor: 5.273

COMPREHENSIVE REVIEW ON COLON TARGETED DRUG DELIVERY

Dnyanai P. Dafar, Gaurav M. Wadhankar, Devesh A. Nagphase, Mrunal M. Choudhary, Samiksha P. Dafar, Vaibhav P. Uplanchiwar and Renuka K. Mahajan*

Nagpur College of Pharmacy, Wanadongri, Hingna, Nagpur (MH) - 441110.

Article Received on: 29/12/2023
Article Revised on: 19/01/2024
Article Accepted on: 09/02/2024

***Corresponding Author**
Renuka K. Mahajan
Nagpur College of Pharmacy, Wanadongri, Hingna, Nagpur (MH) - 441110.

ABSTRACT

Colon medicines can focus specific pharmaceuticals or peptides to the colonic area for the treatment of a variety of disorders. While ignoring systemic absorption and any negative effects. In order for new pharmaceutical formulations to reach the colon, a thorough understanding of natural and synthetic or semisynthetic polymers is required. Colon drug administration is critical for the local treatment of a wide range of bowel disorders such as ulcerative colitis, Crohn's disease, amoebiasis, colonic malignancy, local therapy of colonic pathologies, and systemic delivery of protein and peptide medicines. Colonic medication administration is beneficial in the treatment of natural asthma, angina, and arthritis. Direct medication administration to the colon is more effective for the treatment of colonic disorder. . such as endorectal cancer and ulcerative colitis Drug that demolishes the acidic region of the stomach and is absorbed by the impacted in the colon. The purpose of this article is to provide insight into the design and assessment of medication delivery systems. The architecture and physiology of the lower gastrointestinal tract are described in this article. This review article contains a thorough examination of colon disorders, variables influencing medicine absorption, and various colon methods.

KEYWORDS: Oral Administration, Colon Targeted Drug Delivery, Nano system, Oral Peptide Therapy.

INTRODUCTION

Colon delivery is mentioned as a method of delivering medications into the lower gastrointestinal system.[1] These medications are found in the big intestine. For example, colon medication administration in the bottom section of the GIT. There is a strong option for localised therapy. Inflammatory bowel disease, Crohn's disease, and ulcerative colitis are examples of colonic illnesses. Colon cancer with irritable bowel syndrome. The colon is thought to be a good absorption site for peptides and protein drug reasons are **Digestive enzymes** are less diverse and intense **The comparative** proteolytic activity of colon mucosa is less than that of small intestine mucosa. CTDDS protects peptide pharmaceuticals from hydrolysis and enzymatic degradation in the duodenum and jejunum, and in the end, it must be capable of safeguarding the medication through route to the colon.[2,3] Colon has a lengthy residence duration of roughly 5 days and is quite sensitive to absorption enhancers. The oral route is the most frequent and preferred approach for CODS, however alternative routes for CDDS may be employed, such as rectal administration, which gives the shortest path for attacking medicines reaching the colon. Rectal administration makes it harder to reach the approximal section of the colon.[4] Rectal administration is sometimes unpleasant for patients, and complins may be inadequate Intrarectal medications are available in the form of liquids, foam, and suppositories. Colonic medication administration has grown in popularity for the treatment of local illness.[5,6] Colonic drug delivery is a possible venue for systemic distribution of therapeutic proteins and peptides that are injected.[7]

Anatomy and physiology of colon

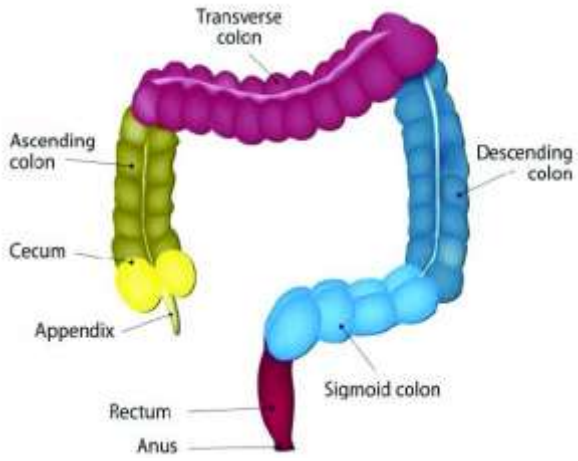

Figure 1: Anatomy of colon.

Colon drug delivery is the targeted administration of a medication into the lower regions of the GI tract,

primarily the large intestine.[8] These deliveries allow the drug to release from the delivery system once it reaches the colon when taken orally. Generally, a colonic drug is a solid oral dose from which their medication is designed to release in the lower area of G.I.T.[9] where circumstances of G.I.T. would benefit from the creation of such modified release technologies. The medicine should be able to enter the colon via the colon drug delivery system. Colon has a lengthy residence duration of 72 hours and a high-water content. It may increase bioavailability by promoting the absorption of poorly absorbed medicinal molecules.[10,11] The colonic medication delivery system is used to achieve goals are - **It provides** prolonged administration in order to lessen dose frequency. **It postpones** medication administration to attain high concentration in the treatment of distal gastrointestinal illness. **Also, postpones** medication administration to the acute period of therapy**.** The colon is approximately 5 feet (150 cm) length and is split into 5 primary parts. The gastrointestinal system is split into three sections: the stomach, the small intestine, and the large intestine.[12,13] The long intestine runs from the ileocecal junction to the anus and is divided into three sections: The colon, rectum, and anal canal are all parts of the digestive tract. The ascending and descending colon supported the perinatal folds known as mesentery. The right colon is made up of the sigmoid, descending colon, and splenic flexure.[14] The rectum is the final anatomic section before the anus. Villi, lymph, muscular nerves, and vessels are all found in the colon tissue. The colon has a large absorptive capacity; around 2000ml of fluid enters the colon via the ileocecal valve, from which 90 fluids are absorbed.[15] The adult colon is dominated by at least eight different epithelial cell types, including columnar or absorptive cells, deep crypt, secretory cells, vacuolated cells, unidentate crypt cells, multivesicular or caveated cells, goblet cells, and a variety of endocrine cells (Fig.1).

Need for medicine delivery to the colon

Targeted medication delivery to the colon ensures that the medicine is delivered directly to the colon. Targeted drug delivery device for oral administration of peptide and protein drugs. A special formulation for the colon can be employed to extend medication delivery.[16] A medicine delivery system tailored to the colon is thought to be effective in the treatment of colon illness. It is a successful and safe treatment for various colonic disorders that employs a site-specific medication delivery mechanism.[17] Colon tailored medication delivery is beneficial in the treatment of illnesses since there are less systemic adverse effects and the amount may be reduced. Colon tailored medication administration is appropriate for polar drugs that are vulnerable to chemical and enzymatic degradation in the upper gastrointestinal tract. Hepatic metabolism has a significant impact.[18,19] If medications were directed specifically to the colon, major colon disorders may be treated more successfully. Colon cancers, for example, are similar to colorectal cancer. The colon is a venue for both local and systemic medication delivery. A number of additional important colon disorders, such as colorectal cancer, may be treated more successfully if medications targeting the colon are developed.[20,21]

Benefits of a colon-targeted medication delivery system

Colon target drug delivery system reduces the unfavourable effects of colonic illness therapy such as ulcerative cells, colorectal cancer, Crohn's disease, and so on. It creates a 'friendlier' environment for peptides and proteins than the upper gastrointestinal tract. It reduces steroid's extended initial pass metre ballism. It alleviates stomach discomfort caused by NSAIDS used orally. It causes the release of medications used to treat angina, asthma, and rheumatoid arthritis.[22,23,24]

Limitations of the colon target medication delivery system

The colon target drug delivery system is difficult to reach. medications require effective transport before they can be insulated in the colon, but the fluid environment in the colon is lower and more viscous than it is in the upper G.I.T., which is a limiting factor for poorly soluble medications. Lower surface area and relative tightness. The relative tightness of tight junctions and the reduced surface area of the colon can prevent drug transport over the mucosa into the systemic circulation.[25] Colon provides a near-natural PH at the location of medication administration as well as decreased enzyme activity. For improved medication delivery results, it should be in solution state before entering the colon. The colon's fluid content is lower delayed.[26]

Advantages: Medication administration occurs in the lower section of G.I.T tract, which is useful for the treatment of various colonic diseases, most significant disease id inflammatory bowel diseases, irritable bowel diseases, irritable bowel syndrome, colon cancer. most helpful and beneficial in treatment of nicotinic addiction.[27] it is advantageous for delivery of protein and peptides through injection. It is used in the treatment of aliments directly at the location. the colon have high water absorption capacity, colon content are quietly viscous, so that availability of most drugs to absorptive membrane is low.[28] Azoreduction and enzymatic cleavage are metabolic process which obtained in the colon and responsible for many medications metabolism.
Disadvantages: The single unit of colon targeted drug delivery system suffers from interetional breakdown of formulation due to manufacturing flaws or atypical stomach physiology. Due to several biological hurdles, developing a colon-specific medication is challenging. The colon mucosa has a lesser affinity for the cytochrome class of drug metabolising enzymes.[29,30]

Factors governing the colon drug delivery

Factor which influences colon drug delivery are physiological and pharmaceutical factors.

Physiological parameters

Gastrointestinal Transit: Gastrointestinal motility is the quickest stage and progresses through four phases over a period of 2-3 hours. The eating state disrupts the typical pattern due to irregular contractive activity.

Small Intestinal Transit: Small intestinal transit is unaffected by physical state, dose form size, or the presence of food in the stomach. The average transit duration of the dose form to the junction is around.

Colonic Transit: The colonic transit time can have a significant impact on the bioavailability of the medicine released from the dose. The colonic transit time is influenced by several elements such as gender and dose form size, as well as physiological conditions such as stress, food present, and sick status. Small particles and solutions move slowly in the proximal colon, and males have lower colonic transit times than women. The colonic transit time of a capsule in humans is 20-25 hours, and it is independent of capsule density and volume. 3-4 hours, and the time period is constant.

Gastric Emptying: Gastric emptying is the quickest and most consistent method. Emptying might take anywhere from 5-10 minutes to 2 hours. Depending on the phase of the stomach at the time of medication delivery, fed condition can significantly impede gastric emptying.

Stomach and Intestinal PH: Gastric and intestinal PH regulate the release and absorption of orally administered drugs (Table 1).[31-35]

Table 1: Stomach and Intestinal P_H.

Sr no	PH	Organ
1	1.5-2.0 (Fastel state) 2.0-6.0 (Fed state)	Stomach
2	5.4-5.9	Right colon
3	6.1-7.5	Left colon
4	6.7	Mid colon
5	6.6-7.5	Small intestine

Pharmaceutical Factors

Drug molecule represents drug that has limited absorption from the stomach or intestine, such as peptide medicines are well suited for drug delivery systems in the colon. Sulphonate and are common medications used to treat various disorders.

Drug transporter are the carrier for a certain medication candidate is chosen based on the pharmacological nature of the medicine as well as the disorders for which the system is to be employed. The chemical composition, stability, and partition coefficient of the medication, as well as the type of absorption enhancer used, all have an impact on carrier selection.

Targeting Approaches to Colon includes colon specific drug delivery system to treat illnesses and the oval delivery of protein and peptide medicines. Mechanisms are used for colon targeted medication delivery are **Coating** with polymers that are PH dependant, **System** of osmatic control, **system** for delivering pressure, **applying** a PH-independent biodegradable polymer coating, **delivery technique** based on intestinal bacteria's metabolic activities, **medicine** delivery device that pulses, **time system** that is regulated or dependant.

Colonic medicine Delivery CIT's are solid dosages that are meant to release their medicine in the higher regions of the (G.I.T). Drug administration is dependent on the metabolic activity of microflora which includes: Prodrug's, Hydrogel's, Pulsating drug delivery, Time control/dependent system, Clinical education tests, High frequency capsule method.[36,37,38]

Prodrugs are frequently designed with limited bioavailability, reduced site specificity, and chemical stability in mind. Aseptic compounds, such as undesired drug proteins prodrugs, are now often targeting a specific transporter membrane or an enzyme. These have a broad potential for medication delivery, particularly for colon colonel chemotherapy. Sulphasalazine for example, is used to treat ulcerative colitis and Crohn's disease.[39]

Hydrogels, a drug delivery technology that has been proposed to deliver the medicine to efficient therapy. Acidic comonomers and enzymatically degradable aco-aromatic cross linkages make up the hydrogels. The regulated release of active antimicrobial agents from the polymerise matrix has been well described for hydrogels such as amoxicillin, metronidazole, oxytetracycline, and tetracycline-HCL.[40]

Pulsing Drug Delivery is the system in which the medicine is delivered rapidly and often over a predetermined period of time. The permeation primarily monitors the extended time duration to rupture. The mechanical characteristics of the polymer covering and the swelling behaviour of the swelling layer are therefore affected. There are 5 methods for pulsating drug delivery: Capsular system, Osmotic system, Solubilisation, Rupture of membrane, Erosion of membrane.[41,42,43]

Time/Control Dependent Systems are important for medication administration that is synchronised. Transit time via the small intestine is unrelated to formulation time. These diverse effects on gastric resident time may be reduced by employing a system that is protected in the stomach and drug related can be focused on the colon by utilising formulation that releases drug after specified gastric emptying. The time-controlled formulation was likewise created by combining water-insoluble ethyl cellulose with swellable polymers.[44]

Clinical Evaluation Tests i.e. Colonoscopy and intubation are used to regulate medication absorption from the colon. Gamma scintigraphy and high frequency

capsules are now the most often utilised procedures for evaluating colon medication delivery systems.[46]

High Frequency Capsule Method: This method is used to test the absorption qualities of a medicine in the colon. High frequency capsules can be used to assess the relative bioactivity of a colonic medication. It has an advance is from any frequency site and drug can be evacuated by high frequency and drug may be released numerous G.I.T. sites with the same item. Now, look at the brief table to thoroughly grasp the move.[47]

Table 2: Formulation and dosage of marketed drug's.

Sr no	Trade name	Dose	Drug	Formulation	referance
1.	Asacal	8-2.49/day	Mesalamine	Eudrogit coated tablets	53
2.	selatac	1-4g/day	Mesalamine	Eudrogit coated tablets	53
3.	salazopyrin	1-2g/day	sulfasolacin	S-ASA linked to sulfopyridine as tablet	53
4.	Entocort	9g/day	Budenoside	Eudrogit-L- coated tablet	53
5.	Pentaza	1.5-4g/day	Mesalamine	Controlled release enteric coated tablet	53
6.	Dipentan	1g/day	Osalacine	S-ASA dinner as capsule & tablet	53
7.	Uoversal	1-2g/day	Mesalamine	Eudrogit-L- coated tablet	53

CONCLUSION

Drug delivery is useful to give drugs to the sick colon. Less dose of drug delivery is necessary and maintain drug in its intact form or dose as feasible to target site to reduce systemic adverse effect. Good colonic delivery might be produced by shielding the medicine from absorption and environment of upper GI tract and released into proximal colon, which is the place for the colon target medication. All of this above give the permission for treatment of local disease which related with colon as well as synthetic absorption of poorly absorbed drug. The colon has a wide range of microflora that can be used to target drug secreted in colon.

Conflict of interest

The authors have no conflict of interest.

Abbreviations

CTDD: Colon target drug delivery, GIT: Gastrointestinal tract.

REFERENCES

1. Khan AK, Piris J, Truelone SC. An experiment to determine the active therapeutic moiety of sulphasalazine. *Lancet*, 1977; 2: 895-896.
2. Friend DR, Chang GW. A colon-specific drug-delivery system based on drug glycosides and the glycosidases of colonic bacteria. *J Med Chem.*, Mar., 1984; 27(3): 261-266. 10.1021/jm00369a005
3. Friend DR, Chang GW. Drug glycosides: potential prodrugs for colon-specific drug delivery. *J Med Chem.*, Jan. 1985; 28(1): 51-57. 10.1021/jm00379a012
4. Hergenrother RW, Wabewr HD, Cooper SL. The effect of chain extenders and stabilizers on the in vivo stability of polyurethanes. *J Appl Biomater*, 1992; 3: 17-22.
5. Park K, Shalaby WS, Park H, eds. Biodegradation In: Biodegradable hydrogels for drug delivery, USA: Technomic publishing company, 1993; 13-34. 0.1002/jab.770030104
6. Peters R, Kinget R. Film-forming polymers for colonic drug deliver: Synthesis and physical and chemical properties of methyl derivatives of Eudragit S. *Int J Pharm.*, 1993; 94: 125-134. 10.1016/0378-5173(93)90016-9
7. Mackay M, Tomlinson E. Colonic delivery of therapeutic peptides and proteins, In: Biek PR, editors. Colonic drug absorption and metabolism. New York: Marcel Dekker, 1993; 159-176.
8. Gazzaniga A, Iamartino P, Maffino G, Sangalli ME. Oral delayed release system for colonic specific drug delivery. *Int J Pharm.*, 1994; 108: 77-83. 10.1016/0378-5173(94)90418-9
9. Rubinstein A. Approaches and opportunities in colon-specific drug delivery. *Crit Rev Ther Drug Carrier Syst*, 1995; 12(2-3): 101-149.
10. Hita V, Singh R, Jain SK. Colonic targeting of metronidazole using azo aromatic polymers, development and characterization. *Drug Deliv.*, 1997; 4: 19-22. 10.3109/10717549709033183
11. Kinget R, Kalala W, Vervoort L, van den Mooter G. Colonic drug targeting. *J Drug Target*, 1998; 6(2): 129-149. 10.3109/10611869808997888
12. Reddy SM, Sinha VR, Reddy DS. Novel oral colon-specific drug delivery systems for pharmacotherapy of peptide and nonpeptide drugs. *Drugs Today (Barc)*, Jul., 1999; 35(7): 537-580.
13. Fukui E, Miyamura N, Uemura K, Kobayashi M. Preparation of enteric coated timed-release press-coated tablets and evaluation of their function by in vitro and in vivo tests for colon targeting. *Int J Pharm.*, Aug., 2000; 204(1-2): 7-15 10.1016/S0378-5173(00)00454-3
14. SarasijaS, Hota A. Colon specific drug delivery systems. Indian journal of pharmaceutical sciences, 2000; 62(1): 1-8.
15. Bussemer T, Otto I, Bodmeier R. Pulsatile drug-delivery systems. *Crit Rev Ther Drug Carrier Syst*, 2001; 18(5): 433-458. Vyas S.P., Roop K.Khar, "Controlled Drug Delivery Concepts and Advances", Vallabh Prakashan, 1st ed., Delhi, 2002, 218-22 Vyas S.P., Roop K.Khar, "Controlled Drug Delivery Concepts and Advances", Vallabh Prakashan, 1 sted., Delhi, 2002, 218-225Vyas S.P., Roop K.Khar, "Controlled Drug Delivery Concepts

and Advances", Vallabh Prakashan, 1st ed., Delhi, 2002; 218-225. Vyas S.P., Roop K.Khar, "Controlled Drug Delivery Concepts and Advances", Vallabh Prakashan, 1st ed., Delhi, 2002, 218-225 Vyas S.P., Roop K.Khar, "Controlled Drug Delivery Concepts and Advances", Vallabh Prakashan, 1st ed., Delhi, 2002; 218-225.

16. Basit A, Bloor J. Prespectives on colonic drug delivery, Business briefing. Pharmtech, 2003; 185-190.
17. Chourasia MK, Jain SK. Pharmaceutical approaches to colon targeted drug delivery systems. *J Pharm Pharm Sci.*, Jan-Apr, 2003; 6(1): 33-66.
18. Liu L, Fishman ML, Kost J, Hicks KB. Pectin-based systems for colon-specific drug delivery via oral route. *Biomaterials.*, 2003; 24(19): 3333–43. doi: 10.1016/S0142-9612(03)00213-8
19. Jain, N.K.; *Advances in controlled & Novel Drug Delivery*, CBS Publishers, 2005; 89.
20. Philip AK, Dubey RK, Pathak K. Optimizing delivery of flurbiprofen to the colon using a targeted prodrug approach. *J Pharm Pharmacol*, May. 2008; 60(5): 607-613. 10.1211/jpp.60.5.0006
21. Vyas SP, Khar RK; Basis of targeted Drug Delivery. In Targeted and controlled Drug Delivery, CBS Publishers and Distributors Reprint, 2008; 42-46, 74.
22. Singh R, Lillard Jr JW. Nanoparticle-based targeted drug delivery. Experimental and molecular pathology, Jun 1, 2009; 86(3): 215-23.
23. Yassin AE, Alsarra IA, Alanazi FK, Al-Mohizea AM, Al-Robayan AA, Al-Obeed OA. New targeted-colon delivery system: in vitro and in vivo evaluation using X-ray imaging. *J Drug Target.*, 2010; 18(1): 59–66. doi: 10.3109/10611860903165022.
24. hilip AK, Philip B. Colon targeted drug delivery systems: a review on primary and novel approaches. *Oman Med J.*, 2010; 25(2): 79–87. doi: 10.5001/omj.2010.24. [
25. Vinaykumar K.V, Sivakumar T, Tamizhmani T. Colon targeted drug delivery system: A review on recent approaches, Int J Pharm Biomed Sci., 2011; 2(1): 11-19.
26. TarakJayraj Mehta et al., Need of colon specific drug delivery system: Review on primary and novel approaches, Int J Pharm Research Dev., 2011; 3(1): 134-153.
27. Garala RJ, Shirolkar SV, Deshpande AD, Kulkarni AD. Colon Targeted Drug Delivery System of Prednisolone by Press Coating Technique: Effect of Different Grades of Hydroxyethylcellulose in Coat. Research Journal of Pharmacy and Technology, 2011; 4(3): 405-10.
28. Jangde R. Magnetically modulated Drug Delivery Systems: An Overview. Research Journal of Pharmacy and Technology, 2011; 4(11): 1649-57.
29. Gupta M, Sharma V; Targeted drug delivery system: A Review. Research Journal of Chemical Sciences, 2011; 1: 134-138.
30. Sethi S, Harikumar SL, Nirmala Review on advances in colon targeted drug delivery system. Int J Pharm Sci Res., 2012; 3(9): 2989–3000.
31. Huanbutta K, Sriamornsak P, Luangtana-Anan M, Limmatvapirat S, Puttipipatkhachorn S, Lim LY, et al. Application of multiple stepwise spinning disk processing for the synthesis of poly(methyl acrylates) coated chitosan-diclofenac sodium nanoparticles for colonic drug delivery. *Eur J Pharm Sci.*, 2013; 50(3–4): 303–11. doi: 10.1016/j.ejps.2013.07.010
32. Bhimavarapu R, Devi RR, Nissankararao S, Devarapalli C, Paparaju S. Microsponges as a Novel Imperative for Drug Delivery System. Research Journal of Pharmacy and Technology, 2013; 6(8): 842-8.
33. Gujral SS, Khatri S; A Review on Basic Concept of Drug Targeting and Drug Carrier System. International Journal of Advances In Pharmacy, Biology and Chemistry, 2013; 2(1): 134-136.
34. Beloqui A, Coco R, Memvanga PB, Ucakar B, des Rieux A, Preat V. pH-sensitive nanoparticles for colonic delivery of curcumin in inflammatory bowel disease. *Int J Pharm.*, 2014; 473(1–2): 203–12. doi: 10.1016/j.ijpharm.2014.07.009.
35. Kadiyam R, Muzib YI. Colon specific drug delivery of tramadol HCl for chronotherapeutics of arthritis. *Int J Pharm Investig*, 2015; 5(1): 43–9. doi: 10.4103/2230-973X.147232.
36. Thakur A, Roy A, Chatterjee S, Chakraborty P, Bhattacharya K, Mahata PP. Recent trends in targeted drug delivery. *SMGroup*, 2015.
37. Thakur A, Roy A, Chatterjee S, Chakraborty P, Bhattacharya K, Mahata PP. Recent trends in targeted drug delivery. *SMGroup*, 2015.
38. Shukla A. Niosomes: an approach towards targeted drug delivery system. *Int J Pharm Pharm Sci*., 2016; 6(6): 40–46.
39. Kıvılcım O, Hakan E, Sema Ç. Novel advances in targeted drug delivery. *J Drug Target*, 2017. doi: 10.1080/1061186X.2017.1401076
40. Rosenblum D, Joshi N, Tao W, Karp JM, Peer D. Progress and challenges towards targeted delivery of cancer therapeutics. *Nat Commun*, 2018; 9: 1410. doi: 10.1038/s41467-018-03705-y
41. Rav S, Maina SS, Malviya R, Kushwah MG, Khan MG, Yezdani U. Novel approach of targeted drug delivery system and its application. *ARC J Public Health Commun Med*., 2019; 4(4): 1–4.
42. Narayanaswamy R, Torchilin VP. Hydrogels and their applications in targeted drug delivery. Molecules, Jan, 2019; 24(3): 603.
43. Priya K, Kumar V, Damini VK, et al. Somes: a review on composition, formulation methods and evaluations of different types of "somes" drug delivery system. *Int J App Pharm*, 2020; 12(6): 7–18.
44. Akhtar M, Jamshaid M, Zaman M, Mirza AZ. Bilayer tablets: a developing novel drug

delivery syste. *J Drug Deliv Sci Technol*, 2020; 60: 102079. doi: 10.1016/j.jddst.2020.102079

45. Malviya V. Preparation and Evaluation of Emulsomes as a Drug Delivery System for Bifonazole. Indian journal of pharmaceutical education and research, Jan. 1, 2021; 55(1): 86-94.
46. Jodh R, Tawar M, Burange P, Malviya V. A Pharmacological Review on Orchid Dactylorhiza hatagirea (D. Doon) Soo. Asian Journal of Pharmacy and Technology, May 25, 2022; 12(2): 141-5.