A Review on Encapsulated Colon Patch: Novel Drug Delivery System

[1]Ms. Pratiksha Sarjerao kumbharkar, [2]Dr Rajashree S. Chavan, [3]Prof.Nilesh R. Bhosale,

[4]Sakshi M. Rananaware, [5]Sejal S. Dorage

[1]Student, [2]Principal, [3]HOD Pharmaceutics Dept., [4]Student, [5]Student

PDEA's Seth Govind Raghunath Sable College of Pharmacy, Saswad, Pune

Abstract

The main aim of the research is to develop and assess a budesonide colon patch-based colon targeting system using several polymers, including chitosan for binding and adhesion, HPMC as a matrix, Eudragit L100 pH-sensitive polymer, and pectin enzyme-triggered polymer. This polymer was used to create the hydrogel plug that sealed the capsule body containing the EudragitL100 pH-sensitive covering. These designs included layers that are helpful for delivering drugs to the colon in a targeted manner. Mucoadhesive elements found in the layers allow the patch to stick to the colon's mucosal surface. In vitro drug release experiments were conducted in 0.1NHCL for two hours, pH 6.8 phosphate buffer for three hours, and pH 7.4 phosphate buffer for six to twelve hours.When the hydrogel plug comes into touch with water, it swells and releases the medication at the colon's site of action. Numerous physiochemical characteristics of the colon patches were investigated. Weight consistency, thickness, folding endurance, surface pH, swelling index, mucoadhesive strength, mucoadhesive duration, and drug content.

KeyWords:-Mucoadhesive polymer, EudragitL100pH sensitive coating, HPMC matrix forming polymer, Pectin enzyme triggered polymer, Hydrogel plug, colon targeted delivery.

Introduction

These design contained layers that are useful in targeted delivery of drug to the colon. The layers contain Mucoadhesive materials by which the patch gets adhered to the mucosal surface in the colon. The drug get loaded in the Mucoadhesive layer uniformly and spread in the patch. It contains a backing membrane, when the colon patch is administered the patch get adhered to the mucous membrane of the large intestine and the drug get slowly released by Mucoadhesive layer of the patch. The

backing layer prevent drug loss and premature drug released in stomach and small intestine. The release of the drug can be achieved by using pH sensitive polymer, mucoadhesive polymer, enzyme-triggered polymer.The colon patch which are encapsulated in capsule body ,when administered as a patch adhering to colon mucosa and releasing the drug locally at the site of inflammation. The patch adhering to colon mucosa and releasing the drug locally at the site of inflammation.(1)

Meachanism of action:-

Adhesive layer:- to adhere or secure patch to colon and faciliate the controlled drug relase.(2)

Backing layer:-prevent drug loss and premature drug relsae in stomach and small intenstine.(3)

pH sensitive layer:-Helps to anlyzed and response to pH of colon and faciliate targeted drug delivrery at inflammed site of colon.(4)

Drug relase:-The changed in polymer matrix,such as swelling membrane brusting or rupture allowing encapsulated drug diffused out.(5)

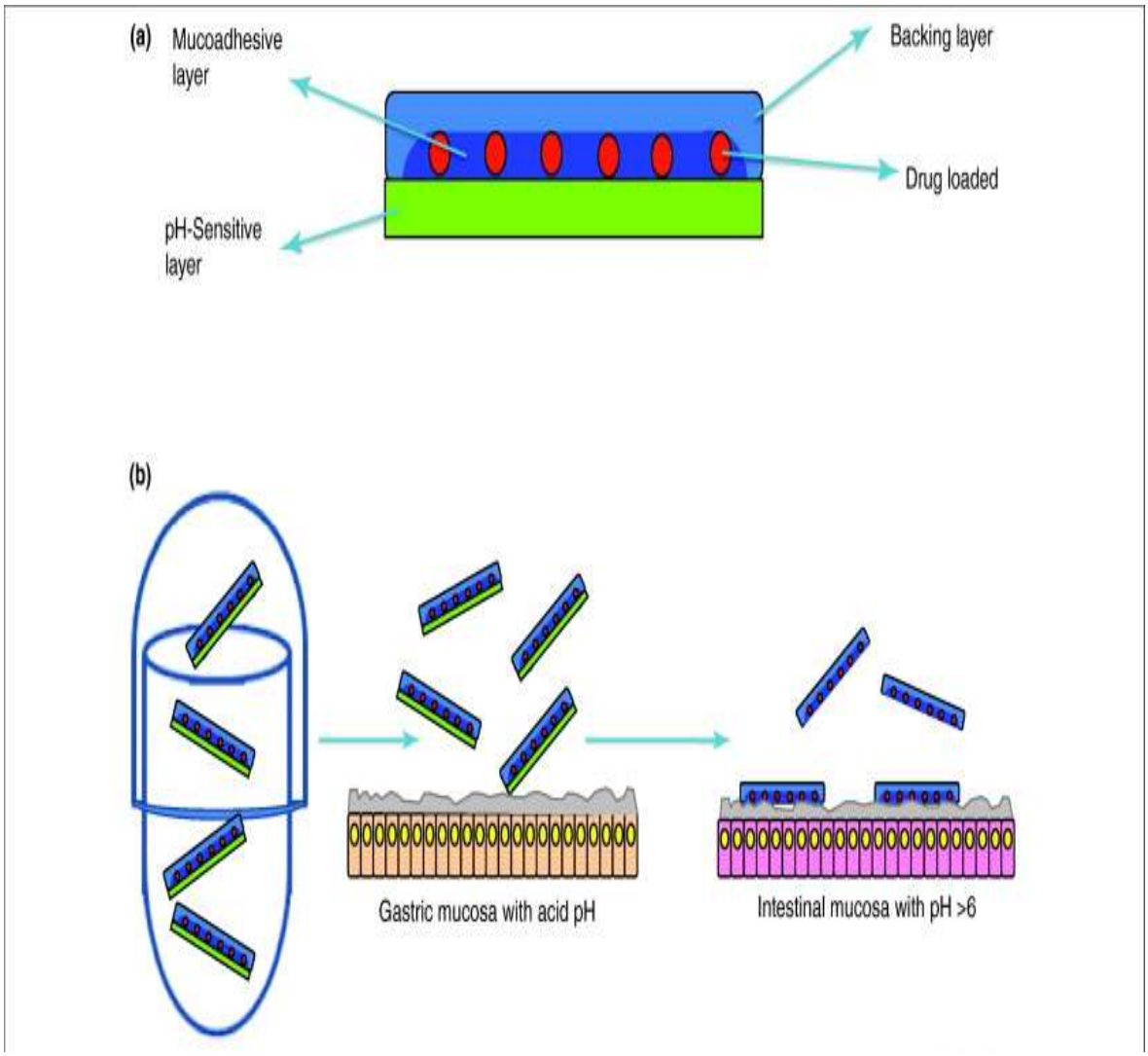

(a)
Mucoadhesive layer
Backing layer
Drug loaded
pH-Sensitive layer
(b)
Gastric mucosa with acid pH
Intestinal mucosa with pH >6

Fig.1

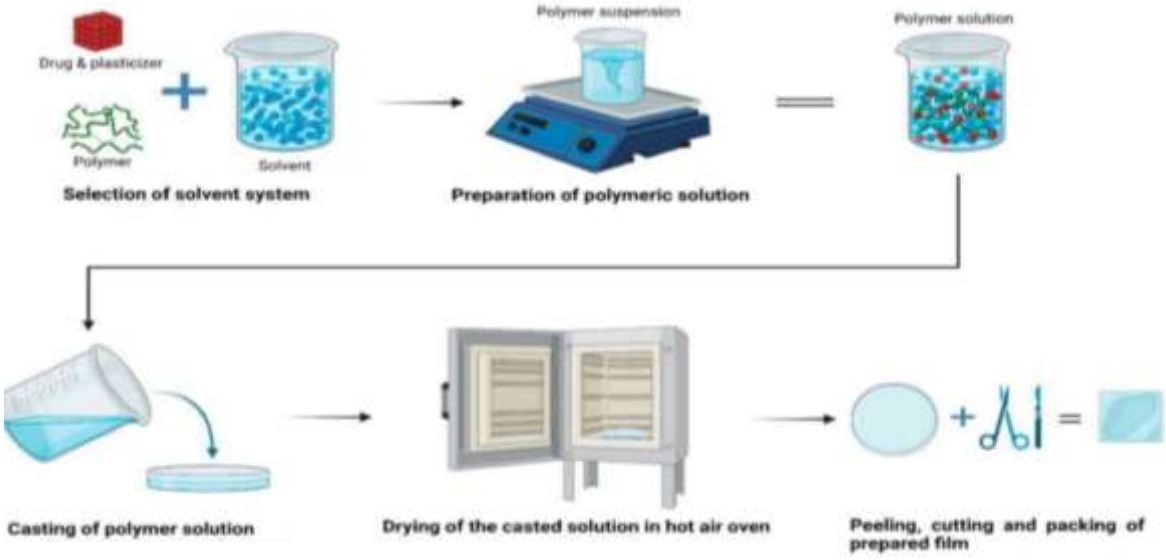
(6)

Method of Preparation for Encapsulated Colon Patch:-

1) Solvent casting
2) Semi solid casting
3) Hot melt extrusion
4) Solid dispersion extrusion

1) Solvent casting:-

1. Colon patches were prepared by Solvent casting method the polymers such (Chitosan/pectin/sodium alginate) was taken in a ratio of 1:1 and are dissolve first in the 10ml of water and kept a side for swelling of the polymer solution.
2. Add drug to polymer solution and stir to get a uniform dispersion.
3. Add plasticizer glycerin or PEG400 to improve flexibility.
4. Pour the mixture into petri plate, dry at 40-50c in hot air oven for 24hr
5. After drying ,cut patches into appropriate sizes 2-4cm
6. Then the patch is folded and kept in the capsule body and the capsule body is coated with the eudragit enteric coating solution and it also contains a hydrogel plug, upon contact with the water the hydrogel plug swells and patch is adhering colon mucosa and releasing the drug locally at the site of inflammation.(7)



2)Semi-solid casting:- First of all, a solution of water soluble patches forming polymer is prepared in semi-solid casting method. Then resulting solution is added to insoluble polymer like cellulose acetate butyrate, cellulose acetate phthalate etc., prepared in sodium or ammonium hydroxide. Then add accurate amount of

plasticizer to get gel mass. Finally cast gel mass into patches by using heat controlled drums. The thickness of the patch is about 0.015-0.05.(8)

3) Hot melt extrusion:-The medication is combined with carriers to create the first bulk, which is then solidified and dried. The extruder is then filled with dry granular material. The extruder is separated into four zones, each of which has a temperature of 800°C (zone 1), 1150°C (zone 2), 1000°C (zone 3), and 650°C (zone 4). To ensure that the mass is adequately melted, the extruder screw speed should be adjusted at 15 rpm. This will process the granules inside the extruder barrel for about 3–4 minutes. To create a film, the extrudate (T = 650°C) is subsequently compressed into a cylindrical cylinder.(9)

4) Solid dispersion extrusion:-

In order to load the drug, a solid dispersion of the drug is integrated into a melted polymer solution. In order to obtain the solid dispersion, the medication is dissolved in an appropriate liquid solvent and the resulting solution is added to a suitable polymer melt that can be achieved below 70°C without the liquid solvent being removed. Ultimately, dyes are used to form the resulting solid dispersions into films.(10)

Advantages:-

1) Patches provide localization and adherence to the region of inflammatory colon mucosa, prevent drug form degradation, and enable targeted drug distribution to the colon.
2) Adhesion guarantees that the patch remains in position.
3) A patch with mucoadhesive, pH-sensitive, and enzyme-triggered polymers for drug localization and targeted delivery at the colon's irritated mucosa.
4) Less systemic absorption because the medication mostly affects locally at the colon's inflammatory location.
5) Less frequent doses if the patch is left on for a longer time; sustained release.(11)

Sr. No.	List of Excipients	Role
1)	Budesonide	API
2)	Ethanol/Chloroform/Acetone	Organic solvent
3)	Water	Vehicle
4)	Chitosan/Pectin/Sodium alginate	Binding and adhesion
5)	Hydroxypropyl methylcellulose(HPMC)Polyvinyl pyrrolidine(PVP)	Act as hydrophilic polymer and matrix forming polymer. Protect drug from premature release in stomach and small intestine.
7)	Xanthum gum/Eudragit L100	Resistance to enzymatic degradation
8)	PEG400/Glycerin	Act as plasticizers to maintain flexibility of patch and prevent cracking of patch
9)	Polysorbate(Tween80) Sorbiton(Span20)	Act as penetration enhancers

List of Excipients and Role:-

Evaluation of Encapsulated Colon Patch:-

1) Weight uniformity of patch:-

Ten 1 cm patches were obtained, each of which was weighed separately, and the average was determined.(13)

2) Thickness of patch:-

Each patch's thickness was measured using a screw gauge. The patch removed, and their thickness was measured at five different locations using a screw gauge. This average was computed.(14)

3) Folding Endurance:-

By repeated folding of the patch at the same place of one patch and the time taken for the patch to fold up to the point where the patch was broken on repeated folding was considered. The test was done on the 5 patches where the number of times the patch could be folded gives the value of folding endurance.(15)

4) Surface pH:-

The patch was taken and placed in Petri plates moistened with the 0.5ml distilled water and room temperature and leaved for 30s. The pH was determined by placing the electrodes in contact with the patch surface and pH was determined using pH meter. (16)

5) Swelling index:-

The patch of size 3x3mm was taken and weighed on a placing the patch on the cover slip and was weighed. Then the patch was placed in the buffer solution of pH 6.8 after 5min the cover slip from the buffer was removed and weighed till 30min. swelling of the patch is due to the absorption of buffer to the patch. The difference in the weight gives the weight increased due to absorption of the buffer to the swelling of patch. (17)

$$\frac{\text{Weight of individual patch-Average weight of patch}}{\text{Average weight of patch}} \times 100$$

6) Drug content uniformity:-

The drug content was determined by dissolving the colon patch in 100ml of the 6.8 phosphate buffer solution for about 12hr and then it is sonicated for about 30min. t hen the solution was filtered through Whatman filter paper and measured spectrophotometrically by UV-Visible spectrophotometer at 274nm with the blank. And the calibration cure was determined.(18)

7) Fourier transform infrared spectroscopy (FTIR):-

FTIR helps to verify that the polymers, drugs, and excipients compatibility used in the patch or encapsulation matrix are present.
FTIR was used to record the infrared spectra of drug using potassium bromide (KBr) pellets. The range of 400 to 4000cm-1.(19)

8) Scanning Electron Microscopy (SEM):-

A focused electron beam scans the surface and produces detailed 3D-like images of surface morphology.

Resolution: - Typically 1–10 nm (high-resolution SEM can go below 1 nm).(20)

9) Mucoadhesive strength:-

The Mucoadhesive strength of the Colon patches was determined by measuring the time it took for the patch to separate from the pan after it was affixed to the bottom of the pan using glue or plaster. Weights were then placed one after the other on the opposite side of the pan.(21)

Applications:-

1) Targeted delivery of drug at inflammation site of colon in ulcerative colitis.(22)
2) Reduced systemic side effects by limiting exposure of drug to the rest of the body.(23)
3) Deliver anti- inflammatory drugs at local site of inflammation in the colon.(24)
4) Provide Localized, sustained drug release to inflammation site of colon.(25)

Conclusion:-

The drug has strong physiological qualities and a favorable dissolving study when combined with various mucoadhesive polymers, such as sodium alginate and carbopol. Ethyl cellulose and HPMC K100M are examples of hydrophobic and hydrophilic polymers that can be successfully used to control drug release and water penetration into capsule contents before the plug material completely erodes. The pH sensitive polymer coating to the capsule body helps in reaching the patch for colon

targeting. Which possess poor oral bioavailability, self-regulated release, mucoadhesion, drug protection, unidirectional release and cell specific targeting provides additional smart characteristics to this innovative therapeutic platform. The formulation were prepared and succeeded in targeting to colon. Combination of polymer can be successfully employed for better results. The prepared formulations can be successfully commercialized after establishing the safety and efficacy studies for in-vivo after healthy human volunteers.

References:-

1. Patel VM, Prajapati BG, Patel MM. Designed and characterized chitosan-containing mucoadhesive buccal patches of propranolol hydrochloride. Acta Pharm, 2007; 57: 61–72. doi: 10.2478/v10007-007-0005(1)

2. Khairnar A, Jain P, Baviskar D, Jain D.Eavaluations of in-vitro and formulation of Mucoadhesive buccal patches containing aceclofenac. Int J Pharma Sci, 2009; 1(1): 91–95.

3. Patel VM, Prajapati BG, Patel MM. Mucoadhesive buccal patches design and Chitosan characterization of propranolol hydrochloride. Acta Pharma, 2007; 57: 61-72.

4. Vashmi Vishnu Y, Chandrasekhar K, Ramesh G, Madhusudan Rao Y. Mucoadhesive patches development for buccal administration of carvedilol, 2007; 4: 27-39.

5. V M., Prajapati B G., Patel, M M. Effect of hydrophilic polymer on baccoadhesive Eudragit patches of propranolol hydrochloride using factorial design. AAPS Pharmscitech, 2007; 8(2): article 45.DOI 1208/pt0802045.

6. Mackay M, Tomlinson E. Colonic delivery of therapeutic peptides and proteins. In: Colonic drug absorption and metabolism. Bieck, P. (Ed), Marcel Dekker, New York, 1993; 159-176.

7. Krishnaiah YSR, Veer Raju P, Dinesh Kumar B, Satyanarayana V, Karthikeyan RS, Bashkar P. Development of colon-targeted drug delivery system for mebendazole. J Control Release, 2001; 77: 87–95.

8. Jain SK, Rai Gopal, Saraf DK, Agarval GP. The preparation and evaluation albendazole microspheres for colonic delivery. Pharma Tech, 2004; 12: 66-71.

9. Theeuwes F, Guittard G, Wong P. Delivery of drugs to colon by oral dosage forms. US Patent 4904474, 1990. www.wjpr.net Vol 9, Issue 4, 2020.

10. Sinha VR, Kumria R. Microbial triggered drug delivery to the colon. Eur J Pharma Sci, 2003; 18: 3-18.

11. David R. Friend. New oral delivery systems for treatment of inflammatory bowel disease. Advanced Drug Delivery Reviews, 2005; 57: 247– 265

12. Rubinstein A, Radai R, Ezna M, Pathnack S. In vitro evaluation of calcium pectinate: a potential colon specific drug delivery carrier. Pharma Res, 1993; 10: 258–263.

13. Ashford M, Fell JT, Attwood D, Sharma HL, Woodhead PJ. Studies on pectin formulation for colonic drug delivery. J Control Release, 1994; 30: 225–232.

14. Wakerly Z, Fell JT, Attwood D, Parkins D. Pectin/ethylcellulose film coating formulations for colonic drug delivery. Pharm Res, 1996; 13: 1210–1212.

15. MacLeod GS, Fell JT, Collett JH, Sharma HL, Smith AM. Selective drug delivery to the colon using pectin: chitosan: hydroxypropyl methylcellulose film coated tablets. Int J Pharm, 1999; 187: 251-257.

16. Tozaki H, Komoike J, Tada C, Maruya Davaran S., Rashidi M., Khandaghi R., Hashemi M, Development of a novel prolonged-release nicotine transdermal patch. Pharmacol. Res, 2005; 51: 233–237.

17. Burkman R.T, The transdermal contraceptive system. Am. J. Obstet. Gynecol, 2004; 190: S49–S53.

18. Thomas B.J., Finnin B.C, The transdermal revolution. Drug Discov. Today, 2004; 9: 697–703.

19. Eaimtrakarn S., Itoh Y., Kishimoto J.I., Yoshikawa Y., Shibata N., Takada K, Rentention and transit of intestinal mucoadhesive films in the rat small intestine. Int. J. Pharm, 2001; 224: 61–67.

20. Eaimtrakarn S., Itoh Y., Kishimoto J.I., Yoshikawa Y., Shibata N., Takada K, Gastrointestinal mucoadhesive patch system (GI-MAPS) for oral administration of G CSF, a model protein. Biomaterials, 2002; 23: 145–152.

21. Eaimtrakarn S., Rama Prasad Y.V., Puthli S.P., Yoshikawa Y., Takada K, Possibilty of a patch system as a new oral delivery system. Int. J. Pharm, 2003; 250: 111–117.

22. Eaimtrakarn S., Rama Prasad Y.V., Puthli S.P., Yoshikawa Y., Takada K, Evaluation of gastrointestinal transit characteristics of oral patch preparation using

caffeine as a model drug in human volunteers. Drug Metab. Pharmacokinetic, 2002; 17: 284–291.

23. Shen, Z., Mitragotri, S, Intestinal patches for oral drug delivery. Pharm. Res, 2002; 19: 391–395. www.wjpr.net Vol 9, Issue 4, 2020. 494

24. Kathryn W., Zancong S., Samir M, Oral delivery of macromolecules using intestinal patches: application for insulin delivery. J. Contl. Release, 2004; 98: 37–45.

25. Girish S., Devendra K., Dhananjay M, Preparation and in-vitro evaluation of bilayer and floatingbioadhesive tablets of rosiglitazone maleate. Asian J. Pharm Sci, 2007; 2(4): 161-169.