Available online on 15.02.2022 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Review Article

A Review on Pharmacological and Therapeutical Insight of Satranidazole for Colon Targeting in the treatment of Colonic Diseases

Soumyadip Ghosh[1]*, Debgopal Ganguly[2], Subhabrota Majumder[1], Ananta Chowdhury[3]

[1] *Calcutta Institute of Pharmaceutical Technology and AHS, Uluberia, Howrah, West Bengal – 711316, India*

[2] *School of Pharmacy, Seacom Skills University, Bolpur, Birbhum, West Bengal –731236, India*

[3] *Faculty of Pharmaceutical Science, Assam down town University, Guwahati, Assam – 781026, India*

Article Info:

Article History:

Received 16 December 2021
Reviewed 14 January 2022
Accepted 06 February 2022
Published 15 February 2022

Cite this article as:

Ghosh S, Ganguly D, Majumder S, Chowdhury A, A Review on Pharmacological and Therapeutical Insight of Satranidazole for Colon Targeting in the treatment of Colonic Diseases, Journal of Drug Delivery and Therapeutics. 2022; 12(1-s):186-191

DOI: http://dx.doi.org/10.22270/jddt.v12i1-s.5348

*Address for Correspondence:

Mr. Soumyadip Ghosh, Calcutta Institute of Pharmaceutical Technology and AHS, Uluberia, Howrah, West Bengal – 711316, India

Abstract

Drugs targeting the colonic environment to treat various colonic diseases are the major challenges recently. Various drugs are available in the markets to targeting to the colonic region to treat diseases but due to premature drug releases, target specificity, the low concentration at the target site with high adverse effects which increase patients' compliance day by day. Satranidazole is a promising drug that is particularly targeting the colonic environment and can break down microorganism DNA to involve the treatment of several diseases such as inflammatory bowel diseases subdivided Ulcerative colitis, Crohn's disease, amoebiasis, chronic diarrhea, and reduction of pain due to inflammation. Conventional drug delivery of Satranidazole has some disadvantages such as target specificity, high dosing frequency, low therapeutic efficacy, and high adverse effects that can be overcome through targeted drug delivery systems. Satranidazole is successfully showing the efficacy against aerobic, microaerophilic as well as anaerobic bacterial and reduction of inflammation of inflammatory bowel diseases subdivided as Ulcerative colitis and Crohn's disease. It is a much more potent drug than metronidazole and has fewer adverse effects. Satranidazole is more convenient for oral administration compared to other routes of administration to show activity. Researchers are giving much more attention to targeted drug delivery systems of Satranidazole to show high therapeutic activity with fewer side effects. The current review focus on the pharmacological and therapeutical insight of Satranidazole in the treatment of colonic diseases and recent advancement and the future aspects of Satranidazole targeting various diseases.

Keywords: Satranidazole, Inflammatory bowel diseases, Ulcerative colitis, Crohn's disease, Amoebiasis, Targeted drug delivery system, Future advancement, Colonic drug delivery systems.

1. Introduction

The drug target to the colonic diseases in the colon region is a challenging task. Maximum colon-specific drugs are failed to maintain the concentration at the target site and show proper therapeutic activity with fewer side effects due to alternate pH conditions. The ideal drug with the proper carrier should have to such a way that the drug should be stable at alternative pH conditions and release at particular disease state in a controlled manner and show proper therapeutic activity. Colon-targeted drug delivery is much more suitable for target specificity, less enzymatic activity, suitable for local and systemic treatment, suitable for protein and peptide drug delivery, and enhancement of drug therapy can be seen which is more suitable for targeting the colon region [1,2].

The oral route is much more convenient for colon-specific drug delivery systems because of self-administration. Patient compliance can be reduced and drug interaction and painless administration compared to parenteral. Though the rectal route can provide painless administration but comparison with oral, it has less bioavailability and transfers the drug to the proximal area of the colon can't be reached [3,4].

Satranidazole is under the class of BCS class II, used in the treatment of protozoal infection (Entamoeba histolytica, Tenia vaginalis, Giardia), antibiotics, amoebicidal, and shows activity in the treatment of inflammatory bowel diseases subdivided as ulcerative colitis and Crohn's disease. Satranidazole is convenient to show activity towards colonic bacteria and protozoal diseases with higher plasma absorption with high residence time than marketed drugs to treat colonic disorders [5]. Satranidazole is also recommended for infections that occurred after surgery and infections involved in the liver, brain, heart caused by microorganisms. Satranidazole makes different from other marketed drugs to treat colon diseases as it has high physicochemical stability, high therapeutic efficacy, feasible analytical methods available to develop a proper dosage form, and low adverse effects with fewer adverse events. Satranidazole is active against parasites by damaging their DNA or any genetic materials to deactivate their activity without causing cell damages. In the treatment of periodontal treatment, Satranidazole plays an important role to reduce inflammation [6,7].

2. Chemical Name

Chemical name of Satranidazole is 1-(1-Methyl-5-nitro-1H-imidazole-2-yl)-3 (Methylsulfonyl) -2-imidazolidine.

Satranidazole has 6 hydrogen bond acceptor counts, 2 rotatable bonds, 19 heavy atoms with a molecular weight of 289.27 g/mol ana d boiling point of 505.2 ± 42°c, and a melting point is 189°c. Though Satranidazole is under the class of BCS II, as low solubility and high permeability, the solubility of Satranidazole can be seen in methanol, 1,4 – dioxane dimethylformamide, and insoluble in water. The dose of Satranidazole can be 300mg to 500mg twice daily in the treatment of Amoebiasis, Inflammatory Bowel Diseases and can be taken with or without food [8-9].

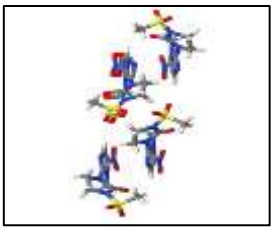

Figure 1: 3D image of Satranidazole structure.

3. Pharmacological Properties of Satranidazole

After human studies of Satranidazole, Satranidazole has a half-life of 14hrs with higher blood plasma concentration, and in comparison, with metronidazole, it has higher potency and good therapeutic activity with less adverse effects and elimination half-life of Satranidazole in the golden hamster (Mesocricetus auratus) shows of 1.01 hr. which is shortened than metronidazole half-life of 3.62 hrs. [10]. Satranidazole shows more rapidly absorbed than metronidazole and the oral route is preferentially better to treat colonic diseases it comes as a tablet administered with or without food and onset of action can be seen at 1-2 hrs. after administration [11].

Satranidazole is consist of a nitroimidazole ring a C-N linkage at the C2 position of the imidazole ring and can denature the microorganism DNA and physical damage to DNA such as viscometry, renaturation, denaturation of the protein present in the microorganism. Satranidazole has the greater amoebicidal activity as well as anti-inflammatory activity compared to metronidazole as ED50 values of Satranidazole is 19.5 mg/kg and metronidazole ED50 value is 45 mg/kg. All those data show that Satranidazole has higher plasma concentration and high intrinsic potency and has high therapeutic activity than other drugs present in the market [12-14].

Satranidazole has some major and minor side effects and some instructions to follow as Headache, Dizziness, Rash, Insomnia, Metallic taste, Dry mouth, Urinary tract infection. It is contraindicated to pregnant, and lactating women is not recommended to children who are less than 18 years of age [15].

4. Mechanism of Action of Satranidazole treating colonic diseases

Satranidazole is 5-Nitroimidazole containing C-N linkage at the C2 position of the imidazole ring particularly active against aerobic, microaerophilic, and anaerobic microorganisms by damaging their DNA as the destabilization of Helix and DNA stand breaking and shows activity [16-17].

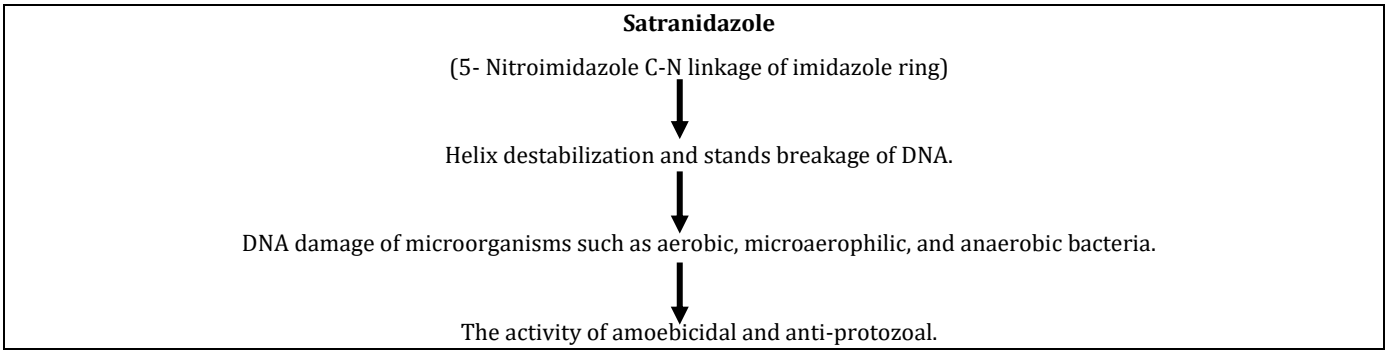

Figure 2: Flow chart representation mechanism of action of Satranidazole for colonic diseases.

5. Marketed Satranidazole for treatment of colonic diseases

Satranidazole is successfully showing the efficacy against aerobic, microaerophilic as well as anaerobic bacterial and reduction of inflammation of inflammatory bowel diseases subdivided as Ulcerative colitis and Crohn's disease. It is a much more potent drug than metronidazole and has fewer adverse effects. Satranidazole is more convenient for oral administration compared to other routes of administration to show activity.

Jitendra Jagtap, Mareswhwar Patil et al done formulation of satranidazole tablet with different polymers for the treatment of amoebiasis. Targeting the drug to the colon valuable treatment for colonic diseases that protects the drug in a different environment and allows release particularly to the colon region. Different polymers help to formulate matrix tablets such as guar gum, hydroxypropyl methylcellulose (HPMC) K4M in different ratios, and for enteric coating materials such as Eudragit S100 followed by wet granulation process. Studies reported that 79.21% of drugs release at the pH of 7.4 and 94.08% after 24hrs. Studies demonstrate that orally administrated Satranidazole matrix tablet is efficient delivery to show the activity of amebiasis [18].

Disha et al. did the preparation of Satranidazole tablet for targeting to colonic region. Tablet of Satranidazole is composed of polysaccharides like Guar, Xanthan gum used different 2 ratios as 1:1 and 2:1 and enteric-coated done by Pectin, Eudragit L, Eudragit S, and Eudragit RS. The report said that the S7 formulation showed the highest release rate up to 92% in the colonic region. To bypass the stomach acid several enteric-coated was done with the ratio of 4:16:5 with less quantity if plasticizer as PEG400 showed excellent stability at the different gastric environment. The formulation S7 was found to be optimum for targeting the colonic environment [19].

Harshal Ashok Pawar et al. was done developed and evaluated of taste-masked granular formulation of Satranidazole by the method of Meth Granulation Technique with different polymers as glyceryl monostearate, stearic acid, and cetyl

alcohol. The ratio of drug: stearic acid (1:2) was found to be optimum based on the result of in-vitro as it showed 87.65%. Formulated granules were found to be good flow properties and no interaction had not been found with drugs and excipients [20].

K. Bansal et al. researched the development of Satranidazole Mucoadhesive gel for the cure of Periodontitis using different gelling agents such as sodium carboxymethyl cellulose (SCMC), poloxamer 407, hydroxypropyl methylcellulose, and Carbopol 934P. The SC30 (containing sodium carboxymethyl cellulose 3% w/v) showed maximum mucoadhesive strength (167.72 ± 3.76 g) and adhesiveness (-46.23 ± 0.34 N mm) and moderate cohesiveness (0.87 ± 0.01). After 42 days clinical study of SC30 gel shows significantly reduce probing depth, plaque index, gingival index, calculus criteria, and bleeding index and with the comparison with metronidazole gel, it showed high efficacy and fewer adverse effects [21].

Gautami. S. Penmetsa et al., was done the preparation and evaluated of clinical efficacy of Satranidazole and Ornidazole gel to the treatment of Chronic Periodontitis. The study reported that Satranidazole gel and Ornidazole gel showed higher efficacy in the treatment of Chronic Periodontitis by reduction of inflammation and pain. The patients are subjected to non-surgical periodontal therapy to determine plaque index (PI), gingival index (GI), Bleeding index (BI), Probing pocket depth (PD), clinical attachment level (CAL). Results showed that Satranidazole and Ornidazole combination therapy successfully helped to reduce inflammation and pain sensation [22].

6. Satranidazole in targeted drug delivery systems

Targeted drug delivery is such a drug delivery that can be selectively targeted to organ or tissue without affecting non-targeted tissue or organ show proper therapeutic activity with less adverse effects and can be stable in the different physicochemical environments with in-vivo and in-vitro conditions and can be delivered with controlled as well as predictable rate. There are several reasons drugs are suitable for targeted drug delivery as pharmaceutical factors – Drugs are instability in conventional dosage form, dose frequency is more, drugs have problem insolubility as poorly soluble drugs are not suitable for conventional drug delivery to show therapeutic activity. Biopharmaceutical factors – Low absorption, biological instability, high membrane bounding which leads to showing low bioavailability. Pharmacokinetics/ Pharmacodynamic factors – Conventional drug delivery systems showed shorter half-life, low specificity towards the targeted region, and a large volume of distribution. Clinical factors – Low therapeutic index and having a high adverse effect with high adverse events can be seen.

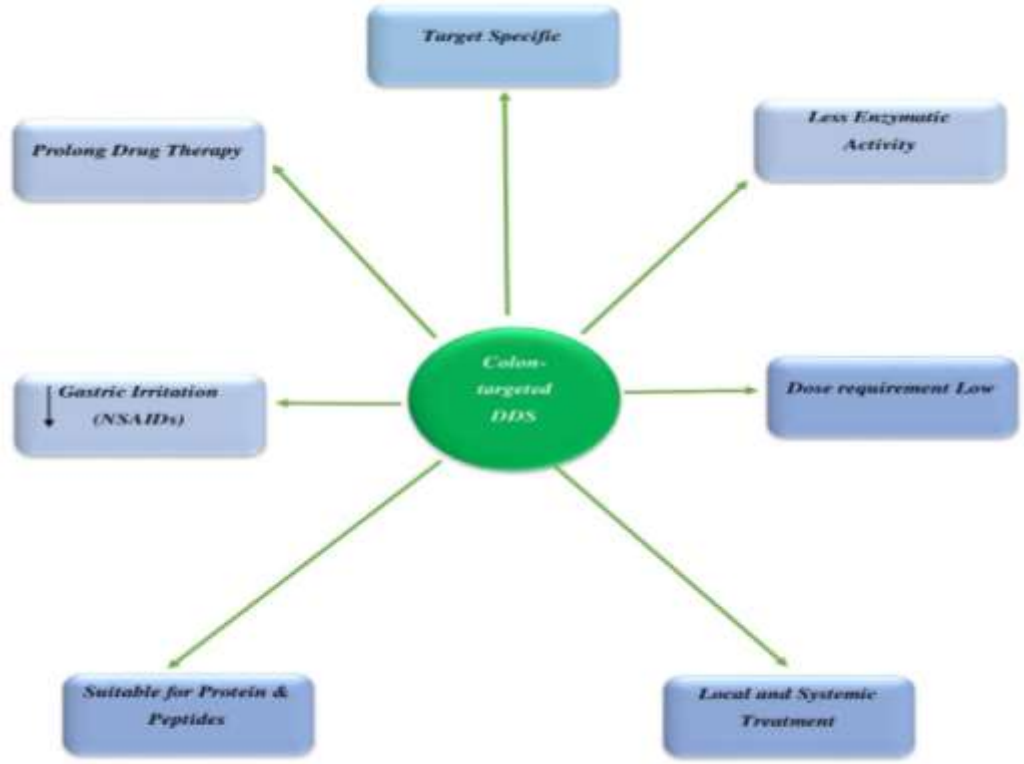

Figure 3: Importance of colon-targeted drug delivery systems

Satranidazole is under the class BCS II, due to the low solubility of the drug leads to a decrease the absorption and decrease the bioavailability. Orally administered drug of Satranidazole has the problem is target specificity, particularly to the colonic region, instability in the altered gastric environment and showed high adverse effects as well as less therapeutic efficacy. The engineered vectors as carriers help to reduce all problems to stabilize the Satranidazole in the colonic environment and showed efficacy towards colonic disorders. Particularly nanoparticles are the most convenient and promising drug delivery to the colonic environment because of increased bioavailability, reduce administration frequency, and promotes drug targeting. The nanoparticles have a small size range (10 - 1000 nm), are biochemically inert, non-toxic, non-irritant as well as non-immunogenic, stable in both in-vivo as well as in-vitro conditions, high drug loading capacity, controlled and predictable release, and target specific characteristics which are suitable to target particularly to the colonic environment [23].

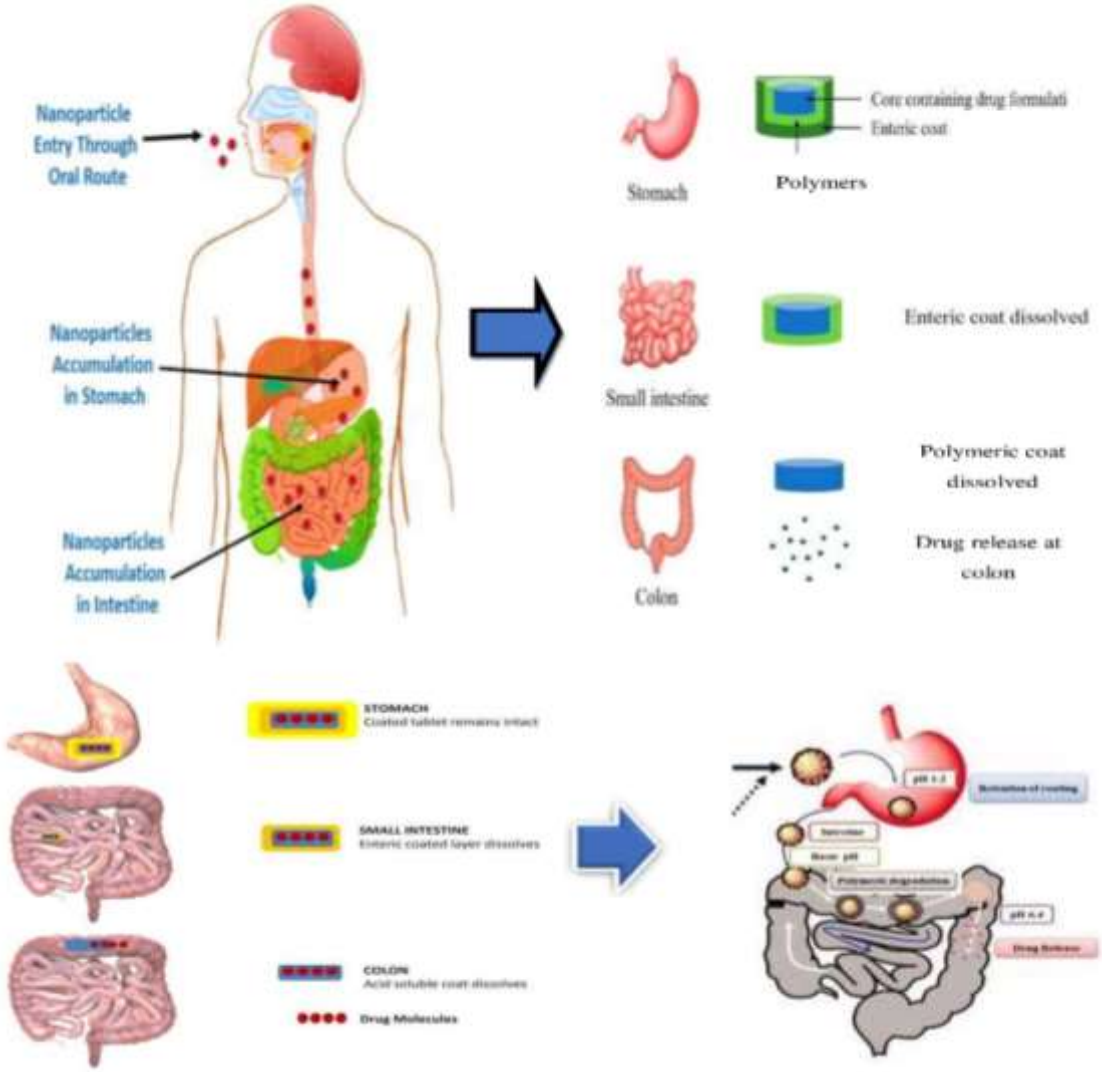

Figure 4: Diagrammatic representation of oral Nanoparticle formulation targeting colonic regions

K. Tirumala Devi et al., Done investigation on formulation and characterization of Satranidazole loaded polymeric nanoparticles for targeting to colonic region especially inflammatory bowel diseases subdivided as Ulcerative colitis and Crohn's disease using ionic gelation method. The research described Satranidazole loaded polymeric nanoparticles used chitosan as the primary polymer which is successfully showed stability in gastric environment and Enteric coating was done using Eudragit S100 to achieve high stability and degrade at particular pH region. Studies showed that particles size achieved within the 200 nm to 300 nm and stable zeta potential range and high entrapment efficiency and controlled and predictable rate of drug release at the colonic environment [24].

Dinesh Chandra et al., researched on formulation and evaluation of the Satranidazole microsphere for colon targeted drug delivery using pH-dependent polymers as enteric-coated polymers like Eudragit based microsphere. Eudragit based microsphere of Satranidazole was done oil in oil solvent evaporation technique using different emulsifiers to stabilize the solution. Research said that using the drug: polymer (1:1 to 1:5) with the proper stirring speed in the range of 1200 - 1400 rpm microsphere-based Satranidazole successfully formulated achieve the ideal range of particle size, zeta potential, in-vitro drug release, and high entrapment efficiency with controlled and predictable release at the colonic environment [25].

Mohammad Reza Saboktakin et al., synthesized and characterization of biodegradable inert and nontoxic chitosan beads as nanocarriers for local delivery of Satranidazole to design gastro- protective multiparticulate delivery system by incorporating hydrogel beads. N- Sulfonate-N, O-carboxymethyl chitosan used as biopolymer-based materials grafting with polymethacrylic acid. Results showed that nanocarriers are stable and achieve the ideal range of the evaluation parameters of nanoparticles [26].

Preeti Singh et al. did an investigation on the preparation and characterization of Poly (€- caprolactone) nanosuspension containing Satranidazole for colon targeting. Nanosuspension preparation was done using the nanoprecipitation method and done several evaluation parameters and achieved all the parameters followed ideal characteristics and showed proper release in a controlled and predictable manner to target the colonic environment [27].

7. Recent advancement and Future prospective of Satranidazole

Colon targeted drug delivery system is the drug targeting the colonic environment without premature drug release at the upper GI tract particularly effective towards colonic diseases with maintaining proper concentration and controlled and predictable release and showing proper therapeutic efficacy with less adverse effects. There are several drugs are available in the market to treat colonic diseases such as inflammatory

bowel disease subdivided as Ulcerative colitis and Crohn's disease, amoebiasis, colon cancer, chronic diarrhea, etc. But they do not achieve proper treatment as no proper therapeutic efficacy due to premature drug release in the colonic environment. Satranidazole is a wonderful drug targeting the colonic environment and is active against various microorganisms, particularly targeting inflammatory bowel diseases and amoebiasis. Several Marketed formulations of Satranidazole are available to treat diseases and can be administered with or without food intake [28].

Table 1: Different brands name available of Satranidazole in the markets

Brand Name	Dose (mg)	API	Uses
Satrogyl	300	Satranidazole	Treatment of Amoebiasis, diarrhea, vaginal and bacterial infections.
Satogyl O	200	Satranidazole + ofloxacin	Treatment of Diarrhea, Dysentery.
Satromax O	300	Satranidazole + Ofloxacin	Treatment of Diarrhea, Dysentery.
Satromax	300	Satranidazole	Treatment of Amoebiasis, diarrhea, vaginal and bacterial infections, antibiotics, and ulcerates.

Marketed Satranidazole in the category of conventional drug delivery system involved in the treatment of inflammatory bowel diseases as well as colonic diseases but due to target specificity, solubility problems, instability in the colonic environment, and premature drug release which leads to less therapeutic efficacy with a high adverse reaction [29]. This problem can be overcome by introducing nanocarriers to show proper target specificity with the enhancement of bioavailability by reduction of particles size and stabilizing the particles in the altered gastric environment. Researchers are involving and too much attention to formulate advanced technology with advanced carriers to achieve therapeutic effectiveness with less adverse effects [30].

8. Conclusion

The importance of colon-targeted drug delivery is the drug must release from the system and be sensitively acting in the colonic region and targeting the diseases. Drug targeting to the diseased colon is advantageous as shows therapeutic efficacy, reducing systemic side effects, lowering dosing frequency, maintaining the drug concentration to the target site. Satranidazole is a wonderful drug to treat diseases such as inflammatory bowel diseases, amebiasis, chronic diarrhea, and dysentery. The novel advancement of Satranidazole can be possible to reduce systemic side effects with high benefits in the treatment. There is a need to develop a novel approach that is specific for the colon targeting using natural materials which can be degraded particularly to the colonic environment in the presence of microflora or colonic bacterial enzymes. The motto of this review article is the development strategies of Satranidazole, various therapeutic as a well pharmacological aspects of Satranidazole in the treatment of colonic diseases.

9. Acknowledgment

Thanks to Dr. Subhabrota Majumder and Dr. Ananta Choudhury for guiding us to write the articles makes a proper format and collecting all related information. We are also grateful for all those who gave us a helping hand, morally and help to write this article.

10. Conflict of interest

No conflict of interest.

11. References

1. Philip AK, Philip B. Colon targeted drug delivery systems: a review on primary and novel approaches. Oman medical journal. 2010 Apr; 25(2):79-87. DOI: http:/doi.org/10.5001/omj.2010.24 https://doi.org/10.5001/omj.2010.24

2. Cui M, Zhang M, Liu K. Colon-targeted drug delivery of polysaccharide-based nanocarriers for the synergistic treatment of inflammatory bowel disease: A review. Carbohydrate Polymers. 2021 Nov 15; 272:118530. https://doi.org/10.1016/j.carbpol.2021.118530

3. Liu L, Fishman ML, Kost J, Hicks KB. Pectin-based systems for colon-specific drug delivery via the oral route. Biomaterials. 2003 Aug 1; 24(19):3333-3343. https://doi.org/10.1016/S0142-9612(03)00213-8

4. Nicholas ME, Panaganti S, Prabakaran L, Jayveera KN. Novel colon-specific drug delivery system: A review. International Journal of Pharmaceutical Sciences and Research. 2011 Oct 1; 2(10):2545-2561.

5. Pawar HA, Joshi PR. Development and validation of a discriminating in vitro dissolution method for oral formulations containing Satranidazole. International Journal of Spectroscopy. 2014:1-8. https://doi.org/10.1155/2014/624635

6. Zahoor A, Knight RC, Whitty P, Edwards DL. Satranidazole: mechanism of action on DNA and structure-activity correlations. Journal of Antimicrobial Chemotherapy. 1986 Jul 1; 18(1):17-25. https://doi.org/10.1093/jac/18.1.17

7. Gowrishankar R, Phadke RP, Oza SD, Tulwalker S. Satranidazole: experimental evaluation of activity against anaerobic bacteria in vitro and in animal models of anaerobic infection. Journal of Antimicrobial Chemotherapy. 1985 Apr 1; 15(4):463-470. https://doi.org/10.1093/jac/15.4.463

8. Rathi PB, Kale M, Jouyban A. Thermodynamic Modeling and Solubility Study of Satranidazole in Different Monosolvents at Different Temperatures. Journal of Chemical & Engineering Data. 2021 Sep 1; 66(10):3745-56. https://doi.org/10.1021/acs.jced.1c00385

9. Rose MF, Peruboina R, Hamid HE, Parthipan P. Development of new RP-HPLC method for the simultaneous estimation of Satranidazole and Oflaxacin pharmaceutical dosage form. Indian Journal of Research in Pharmacy and Biotechnology. 2017; 5(5):325-328.

10. Malathi DC, AnushaBommasani RP. Self-medicated, satranidazole induced fixed drug eruption: a case report. International Journal of Basic & Clinical Pharmacology. 2020 Dec; 9(12):1903-1905. https://doi.org/10.18203/2319-2003.ijbcp20205131

11. Dhat S, Pund S, Kokare C, Sharma P, Shrivastava B. Risk management and statistical multivariate analysis approach for design and optimization of satranidazole nanoparticles. European Journal of pharmaceutical sciences. 2017 Jan 1; 96:273-83. https://doi.org/10.1016/j.ejps.2016.09.035

12. Zahoor A, Knight RC, Whitty P, Edwards DL. Satranidazole: mechanism of action on DNA and structure-activity correlations. Journal of Antimicrobial Chemotherapy. 1986 Jul 1; 18(1):17-25. https://doi.org/10.1093/jac/18.1.17

13. Sanmukhani J, Shah V, Baxi S, Tripathi C. Fixed drug eruption with ornidazole having cross-sensitivity to secnidazole but not to other nitro-imidazole compounds: A case report. British journal of clinical pharmacology. 2010 Jun; 69(6):703-704. https://doi.org/10.1111/j.1365-2125.2010.03651.x

14. Parmar DM, Jadav SP. The concept of personal drugs in the undergraduate pharmacology practical curriculum. Indian Journal of Pharmacology. 2007 May 1; 39(3):165. https://doi.org/10.4103/0253-7613.33438

15. Krishna U, Gupta K, Vaidya AB, Desai J, Paul T, Sheth UK. Single dose therapy for trichomonal vaginitis with satranidazole (Go. 10213)-phase 2 study with a new antiprotozoal agent. J. Ob/Gyn India. 1986; 36:688-692.

16. Chandra D, Yadav IK, Jaiswal D, Ghosh N, Singh HP, Mishra A, Bhattacharya A, Bajpai M, Jain DA. Formulation and evaluation of satranidazole microspheres for colon targeted drug delivery. J Pharm Res. 2009 Jul; 2(7):1230-1233.

17. Tiwari A, Ramteke S, Dahima R, Shukla R. Preparation and characterization of satranidazole loaded calcium pectinate microbeads for colon specific delivery; Application of response surface methodology. Current Nanoscience. 2011 Aug 1; 7(4):608-15. https://doi.org/10.2174/157341311796196871

18. Jagtap J, Patil M, Patil V. Development and in-vitro evaluation of colon-specific satranidazole tablet for the treatment of amoebiasis. Asian Journal of Pharmaceutics (AJP): Free full text articles from Asian J Pharm. 2014 Aug 28; 7(2): 1-7. https://doi.org/10.4103/0973-8398.115952

19. Disha SN, Raju S, Govind RS, Dev JA. An Investigation on Colon Drug Delivery System for Satranidazole Tablet. International Journal of Research in Pharmacy & Science. 2013 Apr 1; 3(2): 161-182.

20. Pawar HA, Joshi PR. Development and evaluation of taste masked granular formulation of satranidazole by melt granulation technique. Journal of pharmaceutics. 2014; 8(6):78-84. https://doi.org/10.1155/2014/789676

21. Bansal K, Rawat MK, Jain A, Rajput A, Chaturvedi TP, Singh S. Development of satranidazole mucoadhesive gel for the treatment of periodontitis. Aaps Pharmscitech. 2009 Sep; 10(3):716-723. https://doi.org/10.1208/s12249-009-9260-z

22. Pradesh A et al. Comparative Evaluation of the Clinical efficacy of 3% Satranidazole and 1% Ornidazole (OrnigreatTM) gel through local drug delivery system in the treatment of Chronic periodontitis. Research J Pharm and Tech. 2020; 13(8): 3675-3680. https://doi.org/10.5958/0974-360X.2020.00650.2

23. Chandra D, Yadav IK, Jaiswal D, Ghosh N, Singh HP, Mishra A, Bhattacharya A, Bajpai M, Jain DA. Formulation and evaluation of satranidazole microspheres for colon targeted drug delivery. J Pharm Res. 2009 Jul; 2(7):1230-1233.

24. Tirumala K et al. Formulation and Characterization of Satranidazole Loaded Polymeric Nanoparticles. International Journal of Pharmacy and Biological Science. 2019; 9(2):360-370.

25. Chandra D, Yadav IK, Jaiswal D, Ghosh N, Singh HP, Mishra A, Bhattacharya A, Bajpai M, Jain DA. Formulation and evaluation of Satranidazole microspheres for colon targeted drug delivery. J Pharm Res. 2009 Jul; 2(7):1230-1233.

26. Saboktakin MR, Tabatabaie RM, Maharramov A, Ramazanov MA. Synthesis and characterization of biodegradable chitosan beads as nano-carriers for local delivery of satranidazole. Carbohydrate Polymers. 2010 Jul 7; 81(3):726-731. https://doi.org/10.1016/j.carbpol.2010.03.047

27. Singh PR, Kumar VI. Preparation and characterization of Poly (Ɛ-Caprolactone) Nanosuspension containing Satranidazole. World Journal of Pharmaceutical research. 2013 Oct; 3(1):1460-1472.

28. Priyanka N, Kalra N, Saquib S, Kudyar N, Malgaonkar N, Jain H, Pradeep AR. Clinical and microbiological efficacy of 3% satranidazole gel as a local drug delivery system in the treatment of chronic periodontitis: A randomized, controlled clinical trial. Contemporary clinical dentistry. 2015 Jul; 6(3):364-372. https://doi.org/10.4103/0976-237X.161891

29. Kaur S, Narang RK, Aggarwal G. Formulation and development of colon-targeted mucopenetrating metronidazole nanoparticles. Tropical Journal of Pharmaceutical Research. 2017 Jun 2; 16(5):967-973. https://doi.org/10.4314/tjpr.v16i5.1

30. Jadhav VY, Gandhi SV, Dhavale ND, Sabnis SS. RP-HPLC determination of nitazoxanide in bulk and different tablet formulations. Eurasian Journal of Analytical Chemistry. 2008; 3(3):318-323