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ROLE OF MINERAL OIL IN NOVEL DRUG DELIVERY SYSTEM: AN OVERVIEW

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ABSTRACT

Novel drug delivery systems are designed to achieve a continuous delivery of drugs at predictable and reproducible kinetics over an extended period of time in the circulation. Floating drug delivery system is the form of novel drug delivery system. That controls kinetic release rate of drug to a specific site for its pharmacological action. These are achieved by use of various oils including mineral oil. This delivery system prolongs the retention time of the drug in the stomach as compared to conventional dosage form. The present article highlights the use of mineral oil for the formulation of the floating drug delivery system especially with oil (mineral oil). The main goal of any drug delivery system is to achieve desired concentration of the drug in blood or tissue, which is therapeutically effective and non-toxic for a prolonged period. Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, patient compliance and flexibility in formulation etc. From immediate release to site specific delivery, oral dosage forms have really progressed.

KEYWORDS: Mineral oil, floating system, fermentation process.

INTRODUCTION

Gastric floating drug delivery system (GFDDS) is particularly useful for drugs that are primarily absorbed in the duodenum and upper jejunum segments. The GFDDS is able to prolong the retention time of a dosage form in the stomach, thereby improving the oral bioavailability of the drug. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestines. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients.[1]

Advantages of floating drug delivery system[30]

- In the treatment of peptic ulcer disease.
- Used for the delivery of drugs with narrow absorption window in the small intestine.
- Reduced dosing frequency.
- Improved bioavailability of the drug.
- Used for drugs which are unstable in intestinal fluids.
- Used to sustain the delivery of drug.
- Used for maintaining the systemic drug concentration within the therapeutic window.
- Site specific drug delivery is also possible.

Disadvantages of gastro retentive drug delivery system

- These require sufficiently high levels of stomach fluids, for the system to float and to work efficiently.
- Not suitable for drugs with stability or solubility problem in stomach.
- Drugs which undergo extensive first pass metabolism are not suitable candidates.
- Drugs with irritant effect also limit the applicability.[2]

List of Drugs Formulated as Single and Multiple Unit Forms of Floating Drug Delivery Systems.[3, 27, 28, 29]

Dosage forms	Drugs
Tablet	Chlorpheniramine maleate, Theophylline, Furosemide, Ciprofloxacin, Pentoxyfillin, Captopril, Acetylsalicylic acid, Nimodipine, Amoxycillin trihydrate, Verapamil HCl, Isosorbide di nitrate, Sotalol, Atenolol, Isosorbide mono nitrate, Acetaminophen, Ampicillin, Cinnarazine, Diltiazem, Fluorouracil, Piretanide, Prednisolone, Riboflavin- 5′ Phosphate
Capsules	Nicardipine, L- Dopa and benserazide, chlordiazepoxide HCl, Furosemide Misoprostal, Diazepam, Propranlol, Urodeoxycholic acid
Microspheres	Verapamils, Aspirin, griseofulvin, and p-nitro aniline, Ketoprofen, Tranilast Ibuprofen, Terfenadine
Granules	Indomathacin, Diclofenac sodium, Prednisolone
Powders	Cinnarizine
Films	Several basic drugs

Mineral Oil Used In Floating Drug Delivery System-
The aim of this work is tried to give to the role of mineral oil in the development of floating drug delivery system. The use of mineral oil is valuable based on proven biocompatibility and safety. Oils are generally employed in floating drug delivery system so as to target the delivery of drug to a specific region in the gastrointestinal tract i.e., stomach moreover these oils are safe and nontoxic.[4]

Mineral oil
Mineral oil is a liquid by-product of the distillation of petroleum to produce gasoline and other petroleum-based products from crude oil. Mineral oil is a substance of relatively low value, and it is produced in very large quantities. Mineral oil is available in light and heavy grades, and can often be found in drug stores.

Chemistry of Mineral oil-
A mineral oil in this sense is transparent, colourless oil composed mainly of alkanes and cyclic paraffins, related to petroleum jelly (also known as "white petrolatum"). It has a density of around 0.8 g/cm3.

Properties of mineral oil
Physical characteristics
Appearance slightly greasy
Odour dourless
Colour colourless
Density 0.8g/cm3
Solubilty Insoluble in water. Soluble in petroleum solvents.
PH 7-9

Application
Cosmetics and for medical purposes.[5,6,7]

Manufacture of mineral oil
They are manufactured from crude mineral oils in various refining steps including distillation, extraction and crystallization followed by purification through acid treatment and/or catalytic hydrogenation. The manufacturing process is designed to exclude substances with carcinogenic potential like polycyclic hydrocarbons (PAH) and to minimize the presence of aromatic compounds, referred to as 'MOAH' (mineral oil aromatic hydrocarbons), which are inevitably present in the crude mineral oil starting material.(min)

Advantages of mineral oil in floating drug delivery system
- Oil has low density resulting able to continuously float over the medium for more than 10 h.
- Incorporation of oil in to the fdds dosage form, floated for prolonged time over the surface of the dissolution medium.

Literature Review
Indira Muzib Y et al, Develop mineral oil emulsion alginate gel beads with sodium alginate, HPMC, mineral oil, through an ionotropic emulsion gelation process. The alginate beads with oil addition were able to continuously float over the medium for more than 10 h.[8]

Shashi kiran mishra et al, prepared gastro retentive controlled release system of loratadine was formulated to increase the residence time in stomach and to modulate the release behaviour of the drug. Oil entrapped floating micro beads prepared by the emulsion gelation method were optimized by 23 factorial design and a polymer ratio of 2.5:1.5 (pectin/sodium alginate) by mass, 15% (*m*/*V*) of oil (mineral oil or castor oil) and 0.45 mol L–1 calcium chloride solution as the optimized processing conditions for the desired buoyancy and physical stability. *In vitro* drug release in the fed state conditions demonstrated sustained release of loratadine for 8 h, which best fitted the Peppas model with $n < 0.45$.[9]

Singh et al, Alginate based mineral oil entrapped emulsion gel (MOEG) buoyant beads of domperidone were prepared by emulsion gelation technique. Effect of different oils (castor oil, olive oil and linseed oil) and oil concentrations (10%, 15% and 20%, w/w) on uniformity, homogeneity and integrity of the beads was also studied. Density of the formulated beads was found to be ranging between 0.101 and 0.182 g/cm3. The results of the in vitro drug release indicated that linseed oil showed to be good release retardant compared to castor oil and olive oil. Moreover, the beads formulated using 15%, w/w linseed oil were more uniform in shape, exhibited maximum buoyancy and minimal oil leakage.[10]

R.A. Fursule et al, The present work describes the formulation and evaluation of gastroretentive system of an antibacterial agent, amoxicillin trihydrate, based on the concept of altered density. Different formulations of oil entrapped floating gel beads were prepared by using sodium alginate as gelling agent. The prepared beads were evaluated for diameter, surface morphology and encapsulation efficiency. Percentage buoyancy of floating amoxicillin trihydrate gel beads was found satisfactory. Results demonstrate that the oil entrapped gel beads can be used as floating drug delivery system for local as well as systemic drug delivery.[11]

P K Choudhury et al, A new sustained release system of oil entrapped calcium alginate beads were designed and prepared by an emulsion gelation method and it's morphological and release characteristics were studied. The prepared beads were easy to prepare and the mean diameter of beads increased with increase in the amount of the oil phase. The pore size of oil-entrapped beads was affected by concentration of the oil. The beads showed excellent sustaining properties as compared to the conventional beads. Thus, oil entrapment technique can become a useful tool for the development of multiparticulate system even for a highly water-soluble drug like metformin hydrochloride.[12]

G Tripathi, S Singh et al, A gastroretentive pH sensitive system has been a frontier approach to release the drug in controlled manner in stomach and duodenum. The aim of this study was to develop buoyant beads of gellan based, wherein, the oil was entrapped, blended with hydroxypropyl methyl cellulose or carbopol 934 in order to evaluate its potential for targeted sustained delivery of clarithromycin in the gastric region. Buoyant beads of gellan was developed by inotropic gelation technique using calcium carbonate as gas forming agent and the drug polymer dispersion was emulsified with mineral oil.[13]

Ravindra A Fursule et al, A formulation was prepared without using mineral oil by conventional ionotropic gelation method. All other formulations of oil entrapped floating gel beads of propranolol hydrochloride were prepared by using emulsion gelation method in which sodium alginate was used as a gelling agent and mineral oil was used to impart buoyancy to the formulation Spherical gel beads were formed instantaneously. The prepared beads were evaluated for diameter, surface morphology, encapsulation efficiency and drug release.[14]

Shaik Firoz et al, The objective of the present study was to develop multiparticulate gastro retentive drug delivery system of Venlafaxine hydrochloride by Emulsion gelation method using sodium alginate as a polymer and liquid paraffin. Floating microcarriers of the Venlafaxine hydrochloride was developed to prolong the gastric residence time, increase therapeutic efficiency, reduce frequency of administration and improve patient compliance.[15]

Pornsak Sriamornsak et al, A new emulsion-gelation method to prepare oil-entrapped calcium pectinate gel (CaPG) beads capable of floating in the gastric condition was designed and tested. The gel beads containing edible oil were prepared by either being gently mixed or homogenized an oil phase and a water phase containing pectin, and then extruded into calcium chloride solution with gentle agitation at room temperature. The oil-entrapped calcium pectinate gel beads floated if a sufficient amount of oil was used.[16]

Mohammed Muqtader et al, buoyant delivery systems are promising dosage forms which could be a better alternative to the conventional oral dosage forms in order to improve bioavailability by increasing the gastric retention time of the drug.[17]

Maya Sharma et al, The aim of the research work was formulation and evaluation of sodium alginate beads containing voglibose for the effective use in the treatment of hyperglycemia. The gel beads containing mineral oil were prepared by gentle mixing or homogenizing oil and water phase, containing sodium alginate, which was then extruded into calcium chloride solution to produce gel beads. The oil entrapped calcium alginate gel beads showed sustained release.[18]

Arpa Petchsomrit et al, Oil entrapped floating alginate beads of curcumin were developed and characterized. Cremophor EL, Cremophor RH and Tween 80 were utilized to improve the solubility of the drug. The oil-loaded floating gel beads prepared by emulsion gelation method contained sodium alginate, mineral oil and surfactant. The drug content and % encapsulation declined as the ratio of surfactant was increased. The developed floating beads of curcumin powder with surfactant provided a superior drug release than those without surfactant. Floating beads based on oil entrapment containing the drug solubilized in surfactants is a new delivery system to enhance the dissolution of poorly soluble drugs.[19]

Khalifa my et al, The aim of this study was formulation and characterization of floating hydrogel beads of cefdinir for improving its bioavailability. Cefdinir is broad-spectrum, oral, third-generation cephalosporin antimicrobial agent active against Gram-positive and Gram-negative bacteria. The floating hydrogel beads of cefdinir were formulated with polymers such as sodium alginate and sodium carboxymethyl cellulose by emulsion gelation technique using olive oil/castor oil. The beads were evaluated for surface morphology, bead size, entrapment efficiency, floating characteristics, in vitro swelling, in vitro drug release, and stability studies. On the basis of evaluation, all the beads show good swelling up to 12 h in 0.1 N hydrochloric acid. The

swelling was followed by values in order of vegetable oil > mineral oil in case of emulsion gelation method.[20]

Inderbir Singh et al, Alginate based mineral oil entrapped emulsion gel (MOEG) buoyant beads of domperidone were prepared by emulsion gelation technique. The prepared beads were evaluated for particle size, surface morphology, buoyancy, actual drug content and entrapment efficiency. Effect of different oils (castor oil, olive oil and linseed oil) and oil concentrations (10%, 15% and 20%, w/w) on uniformity, homogeneity and integrity of the beads was also studied. Density of the formulated beads was found to be ranging between 0.101 and 0.182 g/cm^3. The results of the in vitro drug release indicated that linseed oil showed to be good release retardant compared to castor oil and olive oil. Moreover, the beads formulated using 15%, w/w linseed oil were more uniform in shape, exhibited maximum buoyancy and minimal oil leakage.[21]

Anurag Verma et al, Prepared floating alginate beads in which, Incorporation of type B gelatin (M7) or XG (M8 and M9) into floating beads although extended the drug release up to 7-8 hours.[22]

Ali J et al, The aim of the present study was to develop a delivery system wherein the retention of ofloxacin could be achieved for increased local action in gastric region against Helicobacter pylori infection. The formulation was optimized on the basis of in vitro buoyancy and in vitro release in citrate phosphate buffer (pH 3). The hydrodynamically balanced capsules were prepared by physical mixing of various grades of HPMC and poly(ethylene oxide) (PEO) alone as well as in combinations. Cellulose acetate pthalate, liquid paraffin, and ethyl cellulose were used as release modifiers so as to maintain release of drug over a period of 12 h.[23]

Jimenez-Castellanos et al, approaches and materials that have been reported are highly swellable hydrocolloids and light mineral oils, a mixture of sodium alginate and sodium bicarbonate, multiple unit floating pills that generate carbon dioxide when ingested, floating minicapsules with a core of sodium bicarbonate, lactose and polyvinyl pyrrolidone coated with hydroxypropyl methylcellulose (HPMC) and floating systems based on ion exchange resin technology, etc.[24]

Desai et al, developed controlled release floating moulded gel tablets of theophylline using agar and light mineral oil. The light mineral oil was essential for the floating property of the tablet. Additionally, it served to prevent the air entrapped within the gel matrix from escaping in the acidic environment of the stomach, due to its hydrophobicity.[25]

Kakkar AP et al, developed and characterized Ibuprofen loaded microspheres by ionotropic gelation technique. The preparation of microspheres was based on the dispersion of sodium alginate –ibuprofen mixture in liquid paraffin followed by calcium chloride as curing agent. Sodium alginate concentration influenced the mean diameter recovery encapsulation efficiency, wall thickness, size distribution and release characteristics of the microspheres.[26]

CONCLUSION

Mineral oil have been successfully used by many investigators for various approaches in floating drug delivery system. After through literature survey it have been concluded that crude oil like mineral oil play vital role in different formulation of floating drug delivery system along with better utilization and advantage over the natural oils.

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