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MICROSPHERES: A RECENT UPDATE

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ABSTRACT

Therapeutic alternative to conventional or immediate release single-unit dosage forms. With regards to the final dosage form, the multiparticulates are usually formulated into microspheres and filling them into hard gelatin capsules. Microspheres received much attention not only for prolonged release, but also for targeting of drugs. In future microspheres will find the central place in novel drug delivery, particularly in diseased cell sorting, diagnostics, genetic materials, targeted and effective drug delivery. Microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers having a particle size ranging from 1-1000 µm. The range of Techniques for the preparation of microspheres offers a Variety of opportunities to control aspects of drug administration and enhance the therapeutic efficacy of a given drug. There are various approaches in delivering a therapeutic substance to the target site in a sustained controlled release fashion. Microspheres has a drug located centrally within the particle, where it is encased within a unique polymeric membrane.

Keywords: Microspheres, Controlled release, Novel Drug Delivery, Therapeutic Efficacy

INTRODUCTION:

A well designed controlled drug delivery system can overcome some of the problems of conventional therapy and enhance the therapeutic efficacy of a given drug. To obtain maximum therapeutic efficacy, it becomes necessary to deliver the agent to the target tissue in the optimal amount in the right period of time thereby causing little toxicity and minimal side effects. There are various approaches in delivering a therapeutic substance to the target site in a sustained controlled release fashion. One such approach is using microspheres as carriers for drugs. Microspheres are characteristically free flowing powders consisting of protein or synthetic polymers which are biodegradable in nature and ideally having a particle size less than 200 μm. In contrast to drug delivery system, the word novel is searching something out of necessity. The drug has to be delivered for a prolonged period of time and many medicines have to be taken simultaneously in case of chronic patients. Frequent administration of drug is necessary when those have shorter half-life and all these leads to decrease in patient's compliance. In order to overcome the above problems, various types of controlled release dosage forms are formulated and altered, so that patient compliance increase through prolonged effect, adverse effect decreases by lowering peak plasma concentration. The controlled release dosage form maintaining relatively constant drug level in the plasma by releasing the drug at a predetermined rate for an extended period of time. One such in Microspheres as carriers of drug become an approach of controlled release do sage form in novel drug delivery system. Microspheres are defined as "Monolithic sphere or therapeutic agent distributed throughout the matrix either as a molecular dispersion of particles" (or) can be defined as structure made up of continuous phase of one or more miscible polymers in which drug particles are dispersed at the molecular or macroscopic level **[1]**. It has a particle size of (1-1000nm).Further, currently available slow release oral dosage forms, such as enteric coated/ double-layer tablets which release the drug for 12-24 hours still result in inefficient systemic delivery of the drug and potential gastrointestinal irritation.

Microencapsulation for oral use has been employed to sustain the drug release, and to reduce or eliminate gastrointestinal tract irritation. In addition, multiparticulate delivery systems spread out more uniformly in the gastrointestinal tract. This results in more reproducible drug absorption and reduces local irritation when compared to single-unit

dosage forms such as no disintegrating, polymeric matrix tablets. Unwanted intestinal retention of the polymeric material, which may occur with matrix tablets on chronic dosing, can also be avoided **[2]**. Thus, microencapsulation technique has been used to modify and retard drug release. There are various Marketed microsphere products available in market that are listed in **Table 1** and various patents described in **Table 2**.

REVIEW OUTCOME:

This paper focus on the various types of microspheres along with their method of preparation and basic technique to evaluate its efficiency with most important emphasizes on pharmaceutical application of microspheres by means of microspheres taken by various routes of system such as oral, trasnsdermal, parenteral *etc*. Radioactive labelled microspheres found to attain more medicinal importance for the treatment of disease with labelled isotope tagging. Beside this Fluorescent microspheres can be used for membrane based technology flow cytometry, cell biology, fluorescent linked immuno sorbent assay **[3]**. Isotope of Yttrium 90 can be used for primary treatment of cancer causing diseases and also used for pre transplant management of Hepato cellular Carcinoma with promising results.

Table 1: List of Marketed Microsphere Drug Products

Drug	Commercial Name	Company	Technology
Risperidone	RISPERDAL® CONSTA®	Janssen®/Alkermes, Inc.	Double emulsion (oil in water)
Naltrexone	Vivitrol®	Alkermes	Double emulsion (oil in water)
Somatropin	Nutropin®	Genentech/Alkermes	(Cryogenic spraydrying)
Triptorelin	Trelstar™	Pfizer	Phase separation

Table 2: Patents of Microspheres

S. No.	S. No. Patent No. Drug Used Reference	S.No Patent No. Drug Used
1	CN 201110142359	Ketoprofen
2	CN 201110313846	Paclitaxel
3	CN 201210025085	Fluorouracil
4	US08455091	Ganciclovir
5	EP19980924438	Cimetidine
6	EP20070808011	Risperidone
7	CA 2217462]	Cyclosporin

TYPES OF MICROSPHERES

Bioadhesive microspheres

Adhesion can be defined as sticking of drug to the membrane by using the sticking property of the water soluble polymers. Adhesion of drug delivery device to the mucosal membrane such as buccal, ocular, rectal, nasal etc. can be termed as bio adhesion. These kinds of microspheres exhibit a prolonged residence time at the site of application and causes intimate contact with the absorption site and produces better therapeutic action.

Carrier technology offers an intelligent approach for drug delivery by coupling the drug to a carrier particle such as microspheres, Nano spheres, liposomes, nanoparticles, etc., which modulates the release and absorption of the drug. Microspheres constitute an important part of these particulate drug delivery systems by virtue of their small size and efficient carrier capacity.

Magnetic microspheres

This kind of delivery system is very much important which localizes the drug to the disease site. In this larger amount of freely circulating drug can be replaced by smaller amount of magnetically targeted drug. Magnetic carriers receive magnetic responses to a magnetic field from incorporated materials that are used for magnetic microspheres are chitosan, dextran etc. The different types are therapeutic magnetic microspheres and diagnostic microspheres.

Therapeutic magnetic microspheres

It is used to deliver chemotherapeutic agent to liver tumor. Drugs like proteins and peptides can also be targeted through this system.

Diagnostic microspheres

It can be used for imaging liver metastases and also can be used to distinguish bowel loops from other abdominal structures by forming Nano size particles supramagnetic iron oxides **[4]**.

Floating microspheres

In floating types the bulk density is less than the gastric fluid and so remains buoyant in stomach without affecting gastric emptying rate. The drug is released slowly at the desired rate, if the system is floating on gastric content, increases gastric residence and fluctuation in plasma concentration. It also reduces chances of striking and dose dumping and produces prolonged therapeutic effect. One another way it produces prolonged therapeutic effect and therefore reduces dosing frequencies

Polymeric microspheres

The different types of polymeric microspheres can be classified as follows and they are biodegradable polymeric microspheres and synthetic polymeric microspheres.

Biodegradable polymeric microspheres

Natural polymers such as starch are used with the concept that they are biodegradable, biocompatible, and also Bio adhesive in nature.

Biodegradable polymers prolongs the residence time when contact with mucous membrane due to its high degree of swelling property with aqueous medium, results gel formation. The rate and extent of drug release is controlled by concentration of polymer and the release pattern in a sustained manner. The main drawback is, in clinical use drug loading

efficiency of biodegradable microspheres is complex and is difficult to control the drug release.

Synthetic polymeric microspheres

The interest of synthetic polymeric microspheres are widely used in clinical application, moreover that also used as bulking agent, fillers, embolic particles, drug delivery vehicles etc. and proved to be safe and biocompatible. But the main disadvantage of these kind of microspheres, are tend to migrate away from injection site and lead to potential risk embolism and further organ damage.

Radioactive microspheres

Radio embolization therapy microspheres sized 10-30 nm are of larger than capillaries and gets tapped in first capillary bed when they come across. They are injected to the arteries that lead to tumor of interest. So these radioactive microspheres deliver high radiation dose to the targeted areas without damaging the normal surrounding tissues. It differs from drug delivery system, as radio activity is not released from microspheres but acts from within a radioisotope typical distance and the different kinds of radioactive microspheres are αemitters, β emitters, γ emitters.

Mucoadhesive microspheres

Mucoadhesive microspheres which are of 1-1000 mm in diameter and consisting either entirely of a mucoadhesive polymer or having an outer coating of it and coupling of mucoadhesive properties to microspheres has additional advantages, *e. g.* efficient absorption and enhanced bioavailability of the drugs due to a high surface to volume ratio, a much more intimate contact with the mucus layer, specific targeting of drug to the absorption site achieved by anchoring plant lectins, bacterial adhesions and antibodies, etc. on the surface of the microspheres. Mucoadhesive microspheres can be tailored to adhere to any mucosal tissue including those found in eye, nasal cavity, urinary and gastrointestinal tract, thus offering the possibilities of localized as well as systemic controlled release of drugs.

ADVANTAGES

1. Microspheres provide constant and prolonged therapeutic effect.
2. Reduces the dosing frequency and thereby improve the patient compliance.
3. They could be injected into the body due to the spherical shape and smaller size.
4. Better drug utilization will improve the bioavailability and reduce the

incidence or intensity of adverse effects.

5. Microsphere morphology all owes a controllable variability in degradation and drug release.

LIMITATION

Some of the disadvantages were found to be as follows:

1. The modified release from the formulations.
2. The release rate of the controlled release dosage form may vary from a variety of factors like food and the rate of transit though gut.
3. Differences in the release rate from one dose to another.
4. Controlled release formulations generally contain a higher drug load and thus any loss of integrity of the release characteristics of the dosage form may lead to potential toxicity.
5. Dosage forms of this kind should not be crushed or chewed **[5]**.

ETHOD OF PREPARATION:

1. Spray Drying
2. Solvent Evaporation
3. Phase separation coacervation technique
4. Spray drying and spray congealing
5. Solvent extraction

SPRAY DRYING:

Concept of spray drying technique **(Figure 1)** depending upon the removal of solvent or the cooling of solution the two processes are spray drying & spray is congealing. Spray drying is the most widely used industrial process involving particle formation and drying. Therefore, spray drying is an ideal process where the end product must comply with precise quality standards regarding particle size distribution, residual moisture content, bulk density, and particle shape.

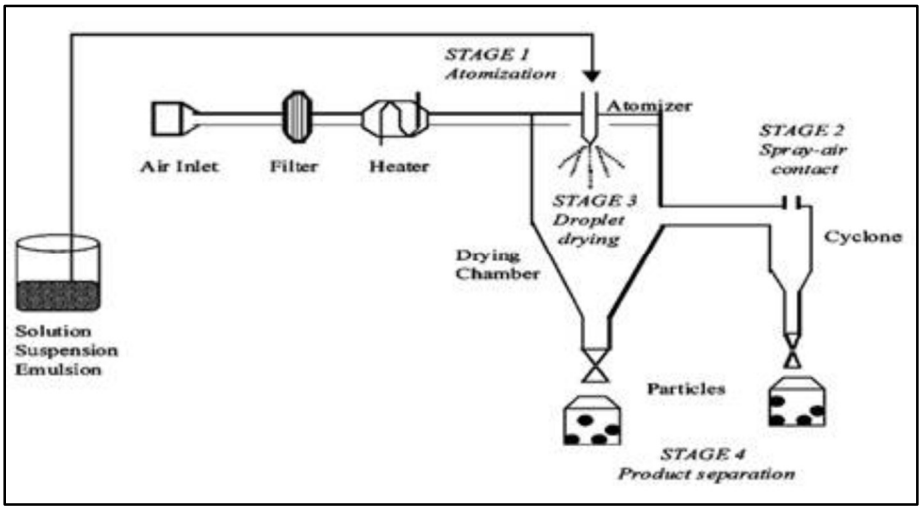

Figure 1: Spray drying technique

Principle:

Three steps involved in spray drying:

a) Atomization: of a liquid feed change into fine droplets.

b) Mixing: it involves the passing of hot gas stream through spray droplets which result in evaporation of liquids and leaving behind dried particles.

c) Dry: Dried powder is separated from the gas stream and collected.

In this technique polymer is first dissolved in a suitable volatile organic solvent such as dichloromethane, acetone, etc. The drug in the solid form is then dispersed in the polymer solution under high-speed homogenization spray congealing. Very rapid solvent evaporation, however leads to the formation of porous micro particles.

Solvent evaporation method:

For the formation of the emulsion between polymer solution and an immiscible continuous phase in aqueous (o/w) as well as nonaqueous phase (w/o). The suspension of microspheres was filtered, washed and dried. Magnesium stearate was also added for preventing agglomeration as a preventing agent. The results showed that average particle size decreased with increasing amount of magnesium stearate used for microsphere preparation. chitosan glutamate and a combination of the two prepared by solvent evaporation with microcapsules of hyaluronic acid and gelatine prepared by complex coacervation.

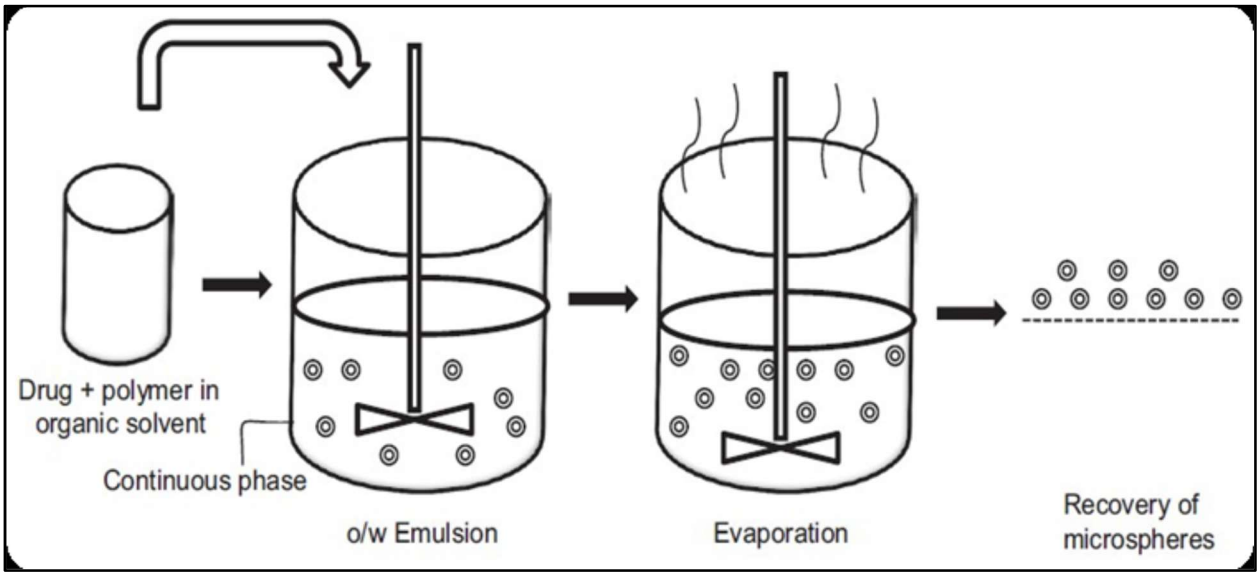

Figure 2: Solvent Evaporation Method

Phase separation coacervation technique:

It is the simple separation of a micro molecular solution into two immiscible liquid phases. In this process, the polymer is solubilized to for a solution. This process is designed for preparing the reservoir type system e.g. encapsulate water soluble drugs i.e. peptides, proteins etc. The principle of coacervation is decreasing the solubility of the polymer in organic phase to affect the formation of polymer rich phase called the coacervates.

Spray drying and spray congealing:

Spray drying technique is also useful for preparing chitosan microsphere used formaldehyde as a cross linking and also reported a novel method in which cimetidine and famotidine were entrapped in microspheres prepared by spray drying of multiple emulsions (o/w/o or w/o/w). They found that the release of the drugs from microspheres by this novel method was significantly sustained as compared to those prepared by conventional spray drying or o/w emulsion method was used spray drying used for the preparation of PCL microspheres.

Solvent extraction:

In this method preparation of micro particles, involves removal of the organic phase by extraction of the organic solvent. Isopropanol can be used as water miscible organic solvents. By extraction with water, Organic phase is removed. Hardening time of microsphere can be decrease by this method. One variation of the process involves direct addition of the drug or protein to polymer organic solution **[6]**.

EVALUATION OF MICROSPHERES

Particle size analyser

Microsphere (50 mg) are suspended in distilled water (5mL) containing 2%w/v of tween 80, to prevent microsphere aggregation, the above suspension is sonicated in water bath and the particle size is expressed as volume mean diameter in micrometer.

Optical microscopy

This method is used to determine particle size by using optical microscope (Meizer OPTIK) The measurement i done under 450x (10x eye piece and 45x objective) and100 particles are calculated.

Scanning electron microscopy (SEM)

Surface morphology is determined by the method SEM. In this microcapsule are mounted directly on the SEM sample slab with the help of double sided sticking tape and coated with

gold film under reduced pressure and analyzed.

Swelling index

This technique is used for characterization of sodium alginate microspheres. Different

solution (100mL) are taken such as [distilled water, buffer solution of pH (1.2, 4.5, 7.4)] and alginate microspheres (100mg) are placed in a wire basket and kept on the above solution and swelling is allowed at 37°C. Thus, changes in weight variation between initial weight of microspheres and weight due to swelling is measured by taking weight periodically and soaking with filter paper.

Entrapment efficiency

Microspheres containing of drug (5mg) are crushed and then dissolved in distilled water with the help of ultrasonic stirrer for 3 hr, filtered then assayed by uv-vis spectroscopy. Entrapment efficiency is equal to ratio of actual drug content to theoretical drug content.

X-ray diffraction

Change in crystalinity of drug can be determined by this technique. Micro particles and its individual components are analysed by the help of XRD Instrument. Scanning range angle between 80°C - 70°C **[7, 8]**.

Thermal analysis

Thermal analysis of microcapsule and its component can be done by using

- Differential scanning calorimetry (DSC)
- Thermo gravimetric analysis (TGA)
- Differential thermometric analysis (DTA)

Accurately the sample is weighed and heated on alumina pan at constant rate of 10oc/min under nitrogen flow of 40 ml/min.

FTTR

The drug polymer interaction and also degradation of drug while processing for microencapsulation can be determined by FTIR.

Stability studies

Stability Studies are done by placing the microspheres in screw capped glass container and storing them at following conditions:

Ambient humid condition

Room temperature (27+/-2 °C)

Oven temperature (40+/-2 °C)

Refrigerator (50+/-8 °C).

It was carried out of for 60 days and the drug content of the microsphere is analysed.

Zeta potential

The polyelectrolyte shell is prepared by incorporating chitosan of different molecular weight into the W2 phase and the resulting particles are determined by zeta potential measurement.

Applications in Drug Delivery System

Ophthalmic Drug Delivery

Polymer exhibits favorable biological behavior such as bioadhesion, permeability-enhancing properties, and interesting physico-chemical characteristics, which make it a unique material for the design of ocular drug

delivery vehicles. Due to their elastic properties, polymer hydro gels offer better acceptability, with respect to solid or semisolid formulation, for ophthalmic delivery, such as suspensions or ointments. Ophthalmic chitosan gels improve adhesion to the mucin, which coats the conjunctiva and the corneal surface of the eye, and increase precorneal drug residence times, showing down drug elimination by the lachrymal flow. In addition, its penetration enhancement has more targeted effect and allows lower doses of the drugs. In contrast, polymer based colloidal system were found to work as transmucosal drug carriers, either facilitating the transport of drugs to the inner eye (chitosan-coated colloidal system containing indomethacin) or their accumulation into the corneal/conjunctival epithelia (chitosan nanoparticulate containing cyclosporine). The micro particulate drugcarrier (microspheres) seems a promising means of topical administration of acyclovir to the eye. The duration of efficacy of the of loxacin was increased by using high MW (1930 kd) chitosan **[9, 10]**.

Gene delivery

Gene delivery systems include viral vectors, cationic liposomes, polycation complexes, and microencapsulated systems. Viral vectors are advantageous for gene delivery because they are highly efficient and have a wide range of cell targets. However, when used in vivo they cause immune responses and oncogenic effects. To overcome the limitations of viral .vectors, non-viral delivery systems are considered for gene therapy. Non-viral delivery system has advantages such as ease of preparation, cell/tissue targeting, low immune response, unrestricted plasmid size, and large-scale reproducible production. Polymer has been used as a carrier of DNA for gene delivery applications. Also, polymer could be a useful oral gene carrier because of its adhesive and transport

properties in the GI tract. Mac Laughlin et al showed that plasmid DNA containing cytomegalo virus promoter sequence and a luciferase reporter gene could be delivered in vivo by chitosan and depolymerized chitosan oligomers to express a luciferase gene in the intestinal tract.

Intratumoral and local drug delivery

Intratumoral and local drug delivery strategies have gained momentum recently as a promising modality in cancer therapy. In order to deliver paclitaxel el at the tumor site in therapeutically

relevant concentration, polymer films were fabricated. Paclitaxel could be loaded at 31% (w/w) in films, which were translucent and flexible. polymer films containing paclitaxel were obtained by casting method with high

loading efficiencies and the chemical integrity of molecule was unaltered during preparation according to study.

Oral drug delivery

The potential of polymer films containing diazepam as an oral drug delivery was investigated in rabbits. The results indicated that a film composed of a 1:0.5 drug-polymer mixture might be an effective dosage form that is equivalent to the commercial tablet dosage forms. The ability of polymer to form films may permit its use in the formulation of film dosage forms, as analternative to pharmaceutical tablets. The pH sensitivity, coupled with the reactivity of the primary amine groups, make polymer a unique polymer for oral drug delivery applications.

Nasal drug delivery

The nasal mucosa presents an ideal site for bioadhesive drug delivery systems. Polymer based drug delivery systems, such as microspheres, liposomes and gels have been demonstrated to have good bioadhesive characteristics and swell easily when in contact with the nasal mucosa increasing the bioavailability and residence time of the drugs to the nasal route. Various polymer salts such as chitosan lactate, chitosan aspartate, and chitosan glutamate and chitosan hydrochloride are good candidates for nasal sustained release of vancomycin hydrochloride. Nasal administration of Diphtheria Toxoid incorporated into chitosan micro particles results in a protective systemic and local immune response against Diphtheria Toxoid with enhanced IgG production. Nasal formulations have induced significant serumIgG responses similar to secretory IgA levels, which are superior to parenteral administration of the vaccine. Nasal absorption of insulin after administration in to polymer powder were found to be the most effective formulation for nasal drug delivery of insulin in sheep compared to chitosan nanoparticles and chitosan solution.

Buccal drug delivery

Buccal tablets based on chitosan microspheres containing chlorhexidine diacetate gives prolonged release of the drug in the buccal cavity improving the antimicrobial activity of the drug. Polymer microparticles with no drug incorporated have antimicrobial activity due to the polymer. The buccal bilayered devices (bilaminated films, palavered tablets) using a mixture of drugs (nifedipine and propranolol hydrochloride) and chitosan, with or without anionic cross linking polymers (polycarbophil, sodium alginate, gellan gum) has promising potential for use in controlled delivery in the oral cavity.

Gastrointestinal drug delivery

Polymer granules having internal cavities prepared by deacidification when added to acidic and neutral media are found buoyant and provided a controlled release of the drug prednisolone. Floating hollow microcapsules of melatonin showed gastroretentive controlled-release delivery system. Release of the drug from these microcapsules is greatly retarded with release lasting for 1.75 to 6.7hours in simulated gastric fluid. Most of the mucoadhesive microcapsules are retained in the stomach for more than 10 hours e.g., Metoclopramide and glipizide loaded chitosan microspheres.

Peroral drug delivery

As polymer and most of its derivatives has a mucoadhesive property, a presystemic metabolism of peptides can lead to a strongly improved bioavailability of many per-orally given peptide drugs, such as insulin, calcitonin, and buserelin. Unmodified chitosan has permeation-enhancing effect for peptide drugs. A protective effect for polymer-embedded peptides towards degradation by intestinal peptidases can be achieved by the immobilization of enzyme inhibitors on the polymer. The mucoadhesive property of polymer gel can be enhanced by threefold to sevenfold by admixing chitosan glyceryl mono-oleate. Drug release from the gel followed a matrix diffusion controlled mechanism. Nifedipine embedded in a chitosan matrix in the form of beads have prolonged

release of drug compared to granules.

Vaginal drug delivery

Polymer, modified by the introduction of thioglycolic acid to the primary amino groups of the polymer, embeds clotrimazole, animidazole derivative, is widely used for the treatment of mycotic infections of the genitourinary tract. By introducing thiol groups, the mucoadhesive properties of the polymer are strongly improved and this is found to increase the residence time of the vaginal mucosa tissue (26 times longer than the corresponding unmodified polymer),guaranteeing a controller drug release in the treatment of mycotic infections. Vaginal tablets of polymer containing metronidazole and acriflavine have showed adequate release and good adhesion properties.

Transdermal drug delivery

Polymer has good film-forming properties. The drug release from the devices is affected by the membrane thickness and cross-linking of the film. Chitosan-alginate polyelectrolyte complex has been prepared in-situ in bead sand microspheres for potential applications in packaging, controlled release systems and

wound dressings. Polymer gel beads are a promising biocompatible and biodegradable vehicle for treatment of local inflammation for drugs like prednisolone which showed sustained release action improving therapeutic efficacy. The rate of drug release was found to be dependent on the type of membrane used. A combination of chitosan membrane and chitosan hydrogel containing lidocaine-hydrochloride, a local anesthetic, is a good transparent system for controlled drug delivery and release kinetics.

Colonic drug delivery

Polymer has been used for the specific delivery of insulin to the colon. The chitosan capsules were coated with enteric coating (Hydroxy propyl methyl cellulose phthalate) and contained, apart from insulin, various additional absorption enhancer and enzyme inhibitor. It was found that capsules specifically disintegrated in the colonic region. It was suggested that this disintegration was due to either the lower pH in the ascending colon as compared to the terminal ileum or to the presence
bacterial enzyme, which can degrade the polymer.

Multiparticulate delivery system

H. Steckel and F. Mindermann-Nogly have prepared chitosan pellets using the extrusion/ spheronization technology. Microcrystalline cellulose was used as additive in concentrations range from 0-70 %.The powder mixture was extruded using water and dilute acetic acid in different powder to liquid ratios. The study showed that chitosan pellets with a maximum of 50 %(m/m) could be produced with demineralized water as granulating fluid. The mass fraction of chitosan within in the pallets could be increased to 100% by using dilute acetic acid for the granulation step **[11]**.

RECENT ADVANCEMENT IN MICROSPHERE

1. Important utilizations of chitosan polymer Cholesterol-lowering effects

Chitosan and cellulose were used as examples of fibers with high, intermediate and low bile acid-binding capacities, respectively. The serum cholesterol levels in a control group of mice fed a high fat/high cholesterol diet for 3 weeks increased about 2-fold to 4·3mM and inclusion of any of these fibers at 7·5% of the diet prevented this increase from occurring. In addition, the amount of cholesterol accumulated in hepatic stores due to the HFHC diet was reduced by treatment with these fibers. The three kinds of fibers showed similar hypocholesterolaemic activity; however, cholesterol depletion of liver tissue was greatest with cholestyramine. The

mechanisms underlying the cholesterol lowering effect of cholestyramine were,

1) Decreased cholesterol (food) intake,

2) Decreased cholesterol absorption efficiency, and

3) Increased faecal bile acid and cholesterol excretion.

The latter effects can be attributed to the high bile acid binding capacity of cholestyramine.

In contrast, incorporation of chitosan or cellulose in the diet reduced cholesterol (food) intake, but did not affect either intestinal cholesterol absorption or faecal sterol output. The present study provides strong evidence that above all satiation and satiety effects underlie the cholesterol lowering**.**

2. Increase Stability of Drug

Chitosan polymer is used to increase the stability of the drug in which the drug is complexed with chitosan and make slurry and kneading for 45 minutes until dough mass. This dough mass is pass through sieve no.16 and make a granules is completely stable at different condition.

3. Orthopaedic Patients

Chitosan is a biopolymer that exhibits osteo conductive, enhanced wound healing and antimicrobial properties which make it attractive for use as a bioactive coating to improve Osseo integration of orthopedic and craniofacial implant devices. It has been proven to be useful in promoting tissue growth in tissue repair and accelerating wound-healing and bone regeneration.

4. Cosmetics industry

Cosmetic compositions are disclosed for the treatment of hair or skin, characterized by a content of new quaternary chitosan derivatives of the formula. The chitosan derivatives have a good substantial, particularly to hair keratin, and prove to have hair strengthening and hair conditioning characteristics. e.g.; Hair setting lotion, Oxidation Hair-coloring Composition, Hair toning

Composition, Skin Cream, Hair treatment Composition, Gel-form.

5. Enhanced Bone Formation by transforming growth factor (TGF-pl)

Chitosan composite microgranules were fabricated as bone substitutes for the purpose of obtaining high bone-forming efficacy. The chitosan microgranules were fabricated by dropping a mixed solution into a NaOH/ethanol solution. TGF-pl was loaded into the chitosan microgranules by soaking the microgranules in a TGF-pl solution **[12, 13]**.

FUTURE CHALLENGES

Future challenges of microspheres look bright particularly in the area of medicinal field because of its wide spectrum of application in molecular biology, eg: microsphere based

genotyping platform is used to detect six single nucleotide polymorphism, yittrium-90 microspheres is used to prevent tumours after liver transplantation and it's advanced way in delivery of vaccines and proteins.

CONCLUSION

The present review article that is microspheres are better of drug delivery system than other type of drug delivery system. In upcoming days this microsphere novel drug delivery system which shows more effective in cancer therapy or in any other disease treatment like a pulmonary related, cardiac related, nervous system related this microsphere formulation shows more potency this having more effective in in-vivo delivery system.

REFERENCE:

[1] Freitas S, Merkle HP, Gander B. Microencapsulation by solvent Extraction/Evaporation: reviewing the state of the art of microsphere preparation process technology. J Controlled Release 2004;102:313–32.

[2] Sahil K, Akanksha M, Premjeet S, Bilandi A, Kapoor B, Microsphere: a review. Int J Res Pharm Chem 2011;1:2231-781.

[3] Rajput S, Agrawal P, Pathak A, Shrivasatava N, Baghe SS, Baghe RS. A review on microspheres: methods of preparation and evaluation. World J Pharm Pharm Sci 2012;1:422-38.

[4] Agusundaram M, Madhu S C et al. Microsphere As A Novel Drug Delivery System A Review. International Journal of Chem Tech Research. 2009; 01(3): 526-534.

[5] Amsden B G, Goosen M. An examination of the factors affecting the size, distribution, and release characteristics of polymer microbeads made using electrostatics. J. Control. Rel. 1997; 43:183–196.

[6] Bodmeier R, Wang J, Bhagwaywar H. Microencaps Pharm Sci. 1992; 09: 89-98.

[7] Cellulose acetate butyrate and polycaprolactone for ketoproton spray-dried microsphere preparation. J Microencapsul. 2005; 381-393.

[8] Dandagi P.M., Mastiholimath VS., Patil M.B., Gupta M.K., Biodegradable microparticulate system of captopril. International Journal of Pharmaceutics. 307, 2006, 83-88.

[9] Chinna Gangadhar B, Shyam Sunder R., Vimal Kumar Varma. M., Sleeva Raju M., Sai Kiran M, Formulation and Evaluation of Indomethacin Microspheres using natural and

synthetic polymers as Controlled Release Dosage Forms. International Journal of Drug Discovery, 2(1), 2010,8-16.

[10] Venkatesan K, Manavalan R, Valliapan K. 2009. Microencapsulation: a vital technique in novel drug delivery system. J Pharm Sci Res. 1(4): 26-35.

[11] Jain NK, Controlled and Novel drug delivery, 04: 236-237

[12] Vyas SP, Khar RK, Targeted and Controlled drug delivery, 07: 418.

[13] Ghulam M, Mahmood A, Naveed A, Fatima R.2009.Comparative study of various microencapsulation techniques. Effect of polymer viscosity on microcapsule characteristics, Pak. J. Sci. 22 (3): 291-300.