



FORMULATION AND EVALUATION OF NOVEL DRUG DELIVERY SYSTEM IN SUSTAINED RELEASE USING SYNTHETIC POLYMERS (EUDRAGIT) – AN UPDATED REVIEW

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ABSTRACT

This Collection of updated review articles provides a comprehensive overview of the latest advancements in Eudrajit polymers, a widely used material in drug delivery systems. The review covers various aspects of Eudrajit polymers, including their properties, applications, and recent developments in formulation technologies. The collection includes discussions on: *Novel applications of Eudrajit polymers in drug delivery systems *Recent advancements in Eudrajit-based nanoparticles, microspheres, and films *Eudrajit polymers in combination with other materials for hybrid drug delivery systems *Updated information on the physiochemical properties and characterization of Eudrajit polymers. Eudrajit polymer S-100, L-100, RLPO and RS, have revolutionized drug delivery systems with their unique properties and versatility. This collection of updated review articles provides a comprehensive overview of the latest developments in Eudrajit-based drug delivery system. The reviews cover the properties and characterization of Eudrajit S-100 and L-100, including their solubility, permeability, and stability. Applications in oral drug delivery, such as Tablets, capsules, and Powders, are discussed, along with their use in topical and transdermal drug delivery systems. Injectable formulations and implantable device using Eudrajit polymers are also explored. Recent advancements in formulation technologies, including nanoparticles and microparticles, are highlighted, as well as the comparison of Eudrajit S-100 and L-100 with other Eudrajit grades. The collection also discusses future directions and emerging trends in Eudrajit-based drug delivery systems. This comprehensive collection serves as a valuable resource for researchers, scientist, and professionals in the pharmaceutical industry, providing insights into the latest developments and application of Eudrajit S-100 and L-100. By exploring the potential of these polymers, this collection aims to advance the field of drug delivery and improve patient outcomes.

Keywords: Drug Delivery Systems, Sustained release, Polymer properties, nanoparticles, microparticles.

INTRODUCTION

Proteins and peptides are polymeric microspheres and microcapsules that have attracted much attention for the controlled delivery of therapeutically useful proteins. Microparticle systems can be prepared by a variety of methods, including physicochemical processes (solvent evaporation, phase separation) and mechanical processes (e.g., spray drying). Solvent evaporation is widely used for microsphere preparation

due to its simplicity, reproducibility, and rapid throughput with minimal control of process variables, making it easy to implement at the industrial level.^{3,4} However, it is often used for water-insoluble drugs. Due to the entrapment efficiency of water-soluble drugs, the loss of drug is low because it is lost from the organic emulsion polymer phase before the polymer solidifies into microspheres.^{5,6} Therefore, process optimization can help to efficiently entrap water-insoluble drugs such

as therapeutic enzymes. Moreover, a suitable emulsifier is often required to stabilize the emulsion during the microemulsion process. Generally, polyvinyl alcohol (PVA) is one of the most used polymeric surfactants, but it is well known that it remains on the particle surface and is difficult to completely remove. PVA is also potentially carcinogenic¹⁰. Therefore, we tried alternative nonionic surfactants Tween 20, 40, and 80 as possible stabilizers for better protein encapsulation. In this study, Serratio peptidase and Eudragit S100 were used as a water-soluble acid-labile enzyme model and a water-insoluble polymer, respectively, to prepare microspheres for oral delivery of acid-labile enzymes.

Synthetic Biodegradable Polymers Used in Drug Delivery Systems

The Polymers used in drug delivery systems can be classified based on their origin as natural, artificial (chemically modified natural polymers), and synthetic. Additionally, synthetic polymers can be classified based on their biostability as biodegradable and non-biodegradable. Synthetic polymers offer a wide range of compositions with controlled properties. These materials open up the possibility of developing new DDSs with specific properties (chemical, interfacial, mechanical and biological) for a given application simply by changing the building blocks or the preparation technique. The most used synthetic biodegradable polymer families are polyesters, polycaprolactones, polyanhydrides and polyorthoesters.

Sustained Release Drug Delivery System

The Novel drug delivery systems provide a means to enhance the therapeutic efficacy of combined drugs by providing sustained, controlled delivery and/or targeting of the drug to the desired site.

Controlled-Release

This is a type of drug or other biologically active product whose delivery system is planned and predictable over a long period of time and releases the drug more slowly than normal.

Extended Release

A pharmaceutical formulation that releases the drug more slowly than usual at a predetermined rate, inevitably reducing the frequency of administration by half.

Delayed Release

Delayed-release systems are systems that provide repeated, intermittent administration of a drug from one or more immediate-release units combined into a single dosage form.

Factors Affecting the Formulation of Oral SR DDS:

The release rate of DDS is influenced by two main factors. These are:

1. Physicochemical factors
2. Biological factors.

Classification of SR DDS:

- A. Diffusion sustained system.
 - i. Reservoir type
 - ii. Matrix type
- B. Dissolution sustained system.
 - i. Reservoir type
 - ii. Matrix type
- C. Methods using Ion-exchange.
- D. Methods using osmotic pressure.
- E. pH-independent formulation
- F. Altered density formulation. :

Methods to Achieve Oral Sustained Drug Delivery:

There are various methods employed for the fabrication of oral sustained release delivery systems. Ritschel has given a detailed report of these techniques. These are as follows.

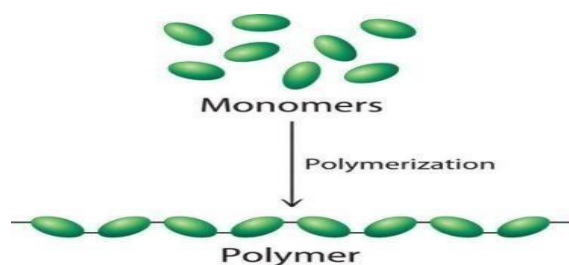
- a. Hydrophilic matrix
- b. Plastic matrix
- c. Barrier resin beads
- d. Fat embedment
- e. Repeat action.

Evaluation of Sustained Release Tablets:

1. In – Vitro Methods	2. In-Vivo Methods
a. Beaker method	a. Clinical response
b. Rotating disc method	b. Blood level data
c. Rotating Bottle method	c. Urinary excretion studies
d. Rotating Basket method	d. Nutritional studies
e. Stationary Basket Method	e. Toxicity studies
f. Oscillating tube method.	f. Radioactive tracer techniques
g. Dialysis method	

3. Stability Studies Polymer

Polymers are the backbone of pharmaceutical drug delivery systems. Polymers have been used as an important tool to control the drug release rate from the formulations and they are also enhanced as stabilizer, taste-masking agent, and protective agent in oral drug delivery. Polymers can bind the particles of a solid dosage form and change the flow properties of a liquid dosage form. Advances in polymers led to development of several novel drug delivery systems due to proper consideration of surface and bulk properties of polymers. Due to this reason, polymers have been widely used in developing new technologies by many researchers.



Definition

The word “polymer” is derived from two Greek words: “**poly**” means **many**, and “**mer**” means **unit** or **part**. Polymers are large molecules of high molecular weight, called macromolecules, formed by joining replicating structural units together on a large scale. The replicating units are made up of simple, reactive molecules known as monomers, which are linked together by covalent bonds. The process of forming a polymer from separate monomers is called polymerization.

Classification

Based on sources

- Natural Polymers:** Polymers that occur in nature are also called natural polymers or biopolymers. Examples of such polymers include karaya gum, guar gum, xanthan gum, starch, cellulose, chitosan, proteins, and polysaccharides.
- Semi synthetic polymer:** They are chemically modified natural polymers such as hydrogenated, cellulose nitrate, methyl cellulose, starch, HPMC, silicones, Sodium carboxymethyl cellulose.
- Synthetic polymer:** Polymers synthesized in a laboratory environment are called synthetic polymers. They are also called artificial polymers.
Eg: Polyvinyl alcohol (PVA), Polyacrylic acid.

Role of Polymers in Drug Delivery

- Immediate release dosage forms Tablets.
- Modified release dosage form.
- Extended-release dosage forms.
- Gastro retentive Dosage Forms.

Types of Polymers in Pharmaceutical Drug Delivery

- Polymers as floating drug delivery system
- Polymers used in mucoadhesive drug delivery system.
- Polymers used as Colon Targeted Drug Delivery.
- Polymers for Sustained Release.
- Polymers in implantable drug delivery.
- Polymeric micelles.
- Polymers in tissue engineering.
- Polymers used in micro and nanoparticles for targeted drug delivery.

Eudrajit Polymer

Eudrajit prepared by the polymerization of acrylic and methacrylic acids or their esters, **e.g.**, butyl ester or dimethyl aminoethyl ester. Eudrajit introduced in USP NF, BP, PhEur, Handbook of pharmaceutical excipients.

Types of Eudrajit Polymers

Soluble Poly (Meth)Acrylates: They dissolve in digestive juices due to salt formation. Examples are L, S, FS and E Polymers. These Polymers with acidic or alkaline groups enable pH dependent release of the active ingredient.

Insoluble Poly (Meth)Acrylates

Insoluble but permeable to digestive fluids. Some examples include Eudrajit RL and RS polymers with alkaline groups and Eudrajit NE polymers with neutral groups, which provide controlled release time of active ingredients through pH-independent swelling.

Formulation Methods for Timecontrolled Drug Release

Matrix formulation: Eudrajit serves as a matrix within which the active ingredient is embedded. The matrix structure is obtained by direct compression, granulation, or melt extrusion. Eudrajit NM 30 D is particularly suitable for the granulation process in the manufacture of matrix.

Microparticulate formulation: Eudrajit is generally used as a coating material to coat granules or particles that are filled into capsules or compressed into tablets. These granules or particles act as diffusion cells in the digestive tract and release a constant amount of drug per unit time (multicomponent dosage form).

Applications of Eudrajit Polymers

- Ophthalmic Drug Delivery
- Buccal and Sublingual Drug Delivery
- Gastrointestinal Drug Delivery
- Intestinal Drug Delivery
- Colon Drug Delivery

Commercial Form

EUDRAJIT® L 100

Solid substance. The product contains 0.3% Sodium Laurylsulfate ph. Eur./NF on solid substance. EUDRAJIT® L 100 is described as Copolymer (1:1), Type A or Copolymer L in the monographs quoted above.

EUDRAJIT® S 100

Solid substance. The product contains 0.3% Sodium Laurylsulfate ph. Eur./NF on solid substance. EUDRAJIT® S 100 is described as Copolymer (1:2), Type B or Copolymer S in the monographs quoted above.

Chemical Structure

EUDRAJIT® L 100 and EUDRAJIT® S 100 are anionic copolymers based on methacrylic acid and methyl methacrylate. The ratio of the free carboxyl groups to the ester group is approx. 1:1 in EUDRAJIT® L 100 and approx. 1:2 in EUDRAJIT® S 100.

Characters

A. Description

White powder with a faint characteristic odour.

B. Solubility

1g of EUDRAJIT® L 100 or EUDRAJIT® S 100 dissolves in 7g Methanol, ethanol, in aqueous isopropyl alcohol and acetone (containing approx.3% water), as well as in 1N sodium hydroxide to give clear to cloudy solutions.

EUDRAJIT® L 100 and EUDRAJIT® S 100 are practically insoluble in ethyl acetate, methylene chloride, petroleum ether and water.

Tests

A. Test Solution

A 12.5% solution of the dry substance is used for the test solution: a quantity of EUDRAJIT® L 100 or EUDRAJIT® S

100 corresponding to 12.5g dry substance is dissolve in a mixture of 84.9g isopropyl alcohol and 2.6g water.

B. Particle Size

At least 95% less than 0.25mm. The particle size is determined according to ph.Eur.2.1.4 or USP<811>.

C. Film Formation

When the Test solution is poured onto a glass plate, a clear film forms upon evaporation of the solvent.

D. Dry Substance / Residue on Evaporation

At least 95.0%. The least is performed according to ph. Eur. 2.2.32 method d.1 g powder is dried in an oven for 6 hrs at 110° C.

E. Loss on Drying

Max. 5.0% according to “dry substance / residue on evaporation”.

F. Assay

EUDRAJIT® L 100: 46.0-50.6 % Methacrylic Acid units on dry substance (DS) Acid Value:300330 mg KOH per g DS.

EUDRAJIT® S 100:27.6-30.7% Methacrylic Acid units on dry substance (DS) Acid Value :180-200 mg KOH per g DS.

The assay is performed according to ph. Eur. 2.2.20 “potentiometric titration” or USP <541>. Approx.

0.5g EUDRAJIT® L 100 or EUDRAJIT® S 100 are dissolved in 60ml isopropyl alcohol and 40ml water with stirring at approx. 50°C within 30-60 mins. Sodium hydroxide (NaOH) 0.5N used as the titrant. Under the same condition a blank value is determined.

1 ml 0.5 N NaOH corresponds to 43.045 mg methacrylic acid units.

$$\text{MethacrylicAcidUnits} = \frac{\text{ml 0.5 N NaOH} \cdot 430.45}{\text{sampleweight(g)} \cdot \text{DS}}$$

G. VISCOSITY/APPARENT VISCOSITY

EUDRAJIT® L 100:60 -120 mPa.s

EUDRAJIT® S 100:50 -200 mPa.s

The test is performed according to Ph.Eur.2.2.10 or USP <911>.

H. Viscosity/Kinematic Viscosity

JPE: EUDRAJIT® L 100:10-24 mm²/s. EUDRAJIT® S 100:22-52 mm²/s. The test is performed according to the JPE monograph.

I. Refractive Index

n_D^{20} :1.390-1.395. The Refractive index of the test solution is determined according to Ph.Eur.2.2.6.

J. Relative Density

d_{20}^{20} :0.831-0.852. The relative density of the test solution is determined according to Ph.Eur.2.2.5.

Purity

A. Sulphated Ash

Max.0.1%. The Test is performed according to Ph.Eur.2.4.14 or USP <281>. 1g substance is used for the test.

B. Heavy Metals

Max.20 ppm. The Test is performed according to Ph.Eur.2.4.8 method C or USP <231> method II.1g substance is used for the test.

C. Arsenic

JPE:Max.2 ppm. The test is performed according to JP method 3. 1g substance is used for the test.

D. Monomers

Max.500 ppm. The test is performed according to the Ph. Eur. or USP/NF monographs.

E. Residual Solvents

No Organic Solvents are used in the manufacture, packing and storage of this product. Small amounts of Methanol may be detectable in the product within the minimum stability period. The Concentration remains below 0.1%. The Test is performed according to Ph.Eur.2.2.24 sample preparation 2 or USP <467>for water-insoluble substances.

F. Microbial Count

Total aerobic microbial count (TAMC):max.10³ CFU/g.

Total combined yeasts and mould counts (TYMC):max.10² CFU/g.

(Acceptance criteria according to Ph.Eur.5.1.4/USP <1111>).The Test is performed according to Ph.Eur.2.6.12 or USP <61>.

6. Identity Testing

A. First Identification

The Material must comply the with the tests for “Assay” and “Viscosity/Apparent Viscosity”.

B. Second Identification

IR Spectroscopy on a dry film approx.15µm thick. Add about 60mg of the dry substance to a mixture of 60% (w/w) isopropyl alcohol and 40%(w/w) acetone and dilute to about 1g. Use a magnetic stirrer and stir until the substance is completely dissolved. To obtain the film, a few drops of the sample solution are placed on a crystal disc (KBr, NaCl) and dried in vacuo for about 2 hours at 70 ° C.

Microspheres

Microspheres can be used as drug delivery systems and provide controlled & sustained released drug release over time.

Solid Dosage Form

Solid dosage forms Drugs are often administered via the oral route. The physicochemical properties of the drug, as well as the excipients added to the formulation, help ensure the desired therapeutic activity.

Tablets

It is apharmaceutical oral dosage form (OSD) or solid unit dosage form. Tablets may be defined as the solid unit dosage form of medication with suitableexcipients.It comprises a mixture of active substances and excipients, usually in powderform, that are pressed or compacted into a solid dose. The main advantages of tablets are that they ensure a consistent dose of medicine that is easy to consume.

Orally Disintegrating Tablets (ODT)

Anorally disintegrating tablet or orally dispersible tablet (ODT), is a drugdosageformavailable for a limited range of over-the-counter (OTC) andprescriptionmedications.

Capsule

A capsule is a type of dosage form consisting of a small, airtight container made of a thin, flexible material, usually gelatin or hydroxypropyl methylcellulose (HPMC). Capsules are designed to hold

a precise amount of medication, which may be in powder, liquid, or semi-solid form.

Bilayer sustained release tablets

Bilayer tablets are produced by compressing two disparate formulations into a single solid oral tablet while maintaining a physical barrier between each formulation by layering one on top of the other. This enables the controlled delivery of either a single or multiple APIs within an individual tablet. **PILLS:** A pill was a small, round, solid oral dosage form. The etymology of the word reflects the historical concept of grinding ingredients using a pestle and mortar, rolling the resulting paste or paste into a lump.

Defects/Imperfections Arising During Tablet Manufacturing.

- **Formulation related:** sticking, picking, binding.
- **Processing:** capping, lamination, cracking, chipping
- **Machine:** double impression.

Liquid Dosage Form

Liquid formulations are intended to provide maximum therapeutic response and/or achieve rapid therapeutic effect in target populations who have difficulty swallowing tablets and capsules. The main ingredient in most liquid formulations is water.

Injectable Dosage Form

An injectable is a type of pharmaceutical product that is administered directly into the body through a needle injection, rather than being taken orally or applied topically. Injectables can be used to deliver a wide range of medications, including:

Vaccines, Insulin and other hormones, Antibiotics

Injectables can be Formulated in Various Ways, Including

- **Solutions:** liquid preparations
- **Suspensions:** liquid preparations containing solid particles
- **Emulsions:** mixtures of oil and water
- **Powders for reconstitution:** freeze-dried or lyophilized powders that are mixed with a liquid before injection.

Suspension

A liquid preparation consisting of solid particles dispersed in a liquid phase in which the extended-release suspension particles are insoluble. The suspension is formulated to provide at least a reduction in the frequency of administration compared to a drug delivered in a conventional dosage form (e.g., a solution or a conventional immediate-release solid dosage form).

Emulsion: A dosage form consisting of a two - phase system comprised of at least two immiscible liquids, one of which is dispersed as droplets (internal or dispersed phase) within the other liquid (external or continuous phase), generally stabilized with one or more emulsifying agents. (Note: Emulsion is used as a dosage form term unless a more specific term is applicable, e.g., cream, lotion, ointment).

Types

1.Emulsion Solvent Diffusion Method:

Emulsion formed from a mixture of a partially miscible solvent in water (previously saturated with water) that is contain a polymer, with a water-soluble phase(previously saturated with solvent).

2.Emulsion Solvent Evaporation Technique:

In this process involves emulsification polymer in aqueous phase and dispersion in a volatile solvent like, chloroform, ethyl acetate. Then the solvent is evaporated using high temperature, vacuum, or continuous stirring.

Particle Size in Emulsions:

When a solid drug is suspended in an emulsion, the liquid dosage form is known as a coarse dispersion. In addition, a colloidal dispersion has solid particles as small as 10 nm–5micro meter and is considered a liquid between a true solution and a coarse dispersion.

Notes:

1. A liquid is a liquid substance. It flows and takes the shape of its container at room temperature. It exhibits Newtonian or pseudoplastic flow behaviour.
2. Previously the definition of a lotion was “The term lotion has been used to categorize many topical suspensions, solutions, and emulsions intended for application to the skin.” The current definition of a lotion is limited to emulsion.

3. A semisolid is not pourable; it does not flow or conform to its container at room temperature. It does not flow at low shear stress and generally exhibits plastic flow behaviour.

Semi-solid dosage form:

A semi-solid dosage form is a type of pharmaceutical product that has a consistency between a solid and a liquid. It is a non-liquid, non-solid preparation that exhibits some degree of plasticity and can be molded or shaped.

Topical dosage form:

A topical dosage form is a type of pharmaceutical product that is applied directly to the skin or mucous membranes, rather than being ingested or injected. Topical dosage forms are designed to provide localized relief or treatment for a specific area of the body, such as the skin, eyes, ears, nose, or mouth.

To overcome such adverse effects of antifungal drugs, use of novel drug delivery systems has been proposed for the treatment of skin fungal infections. liposomes, niosomes, microemulsion.

GELS:

Gels are semisolid jelly-like substances, usually composed of a mixture of water and a gelling agent such as a polymer or colloid. Gels are characterized by their ability to maintain their shape and structure after removal from their container.

Advance Tenchique:

Pro-biotics:

Probiotics are live, beneficial microorganisms (bacteria or yeast) that, when administered in sufficient amounts, provide health benefits to the host. They are often called “good” or “friendly” bacteria.

Table 1: Taste Masking Drug Delivery System

S. NO	DRUG/ ACTIVE AGENT	TECHNIQUE	POLYMER
1.	IBUPROFEN	Air – suspension Coating	Methacrylic acid copolymer (Eudrajit)
2	ACETAMINOPHEN	Coating	Cellulose acetate, Cellulose acetate butyrate, HPC/cellulose acetate, Eudrajit E 100, PVP
3	MORPHINE HCL	Coating	Cellulose, Eudrajit NE 30 D
4	ROXITHROMYCIN	Granulation and coating	PEG, Eudrajit L 100-55
5	NIZATIDINE	Spray drying	Eudrajit E 100
6	CETRAXATE HCL	Melt granulation and coating	Corn starch, Macrogol-6000, Eudarjit S-100
7	CIPROFLOXACIN	Microencapsulation	Eudarjit NE 30D, HPC
8	IBUPROFEN	Spray coating	Eudrajit L 300, Propylene glycol, Mannitol, and flavour.
9	BIFEMELANE HCL	Coating and spraying	Glycerinmonostearate, Eudrajit L30-D-55,

			PEG, sucrose.
10	CEFUROXIME AXETIL	Emulsion- solvent evaporation	Eudrajit L 55and RL
11	PIRENZEPINE AND OXYBUTYNIN	Dispersion	Eudrajit E 100, MCC, HPC
12	LEVOFLOXACIN	Coating	Eudrajit E 100, Cellulose acetate

Specification and Test Method

Ph. Eur	Methacrylic Acid-Methyl Methacrylate Copolymer (1:1) Methacrylic Acid-Methyl Methacrylate Copolymer (1:2)
USP/NF	Methacrylic Acid Copolymer, Type A-NF * Methacrylic Acid and Methyl Methacrylate Copolymer (1:1)-NF** Methacrylic Acid Copolymer, Type B-NF * Methacrylic Acid and Methyl Methacrylate Copolymer (1:2)-NF ** * Current Monograph name valid until Dec.1,2015 ** New Monograph names valid as of Dec.1,2010, Mandatory as of Dec.1,2015
JPE	Methacrylic Acid Copolymer L Methacrylic Acid Copolymer S

Table 2: Microspheres can be used as drug delivery systems and provide controlled & sustained released drug release over time.

S. NO	JOURNALS	AUTHOUR NAME	DRUG	METHODS	PARTICLE SIZE	USES
1.	Asian Journals of Pharmaceutics	Ramachandra Jat, Sumanjain S.K. Singh, Rishikesh Gupta	QUERCETIN	Emulsion solvent diffusion method.	48.25 ±2.01 – 100.40±3.01µm	Antioxidant.
2.	International Journal of Pharmaceutical Sciences Reviewand Research	Panpaliya, Dinesh	LEVETIRACETAM	Solvent evaporation method	42.8µm- 55.64µm	2°generation Anti-epileptic agent.
3.	International Journal of Trends in Pharmacy and Life Sciences	K.SuriaPrabha, p. Muthu Prasanna	ACECLOFENAC	Emulsion cross linking method, Solvent evaporation technique	–	Anti-inflammatory, Analgesic, To treat Rheumatoid Arthritis.
4.	International Journal of Pharmaceutical and Chemical Science	Manish Dubey, Prashant Kesharwani	METFORMIN	Solvent evaporation technique	608-864µm	Anti-diabetic agent.
5.	An International Journal of Advance in Pharmaceutical Sciences	Kumar Darapu B.N,	RANITIDINE HCL	Solvent evaporation method	60.46±0.38 - 101.4 ±1.26 µm	Duodenal ulcer
6.	International journal of Pharmaceutics	B.Dortunc, S.Haznedar	ACETAZOLAMIDE	Solvent evaporation method	250µm	Glaucoma, Also treat Epilepsy
7.	AAPS Pharmaceutical Science and	Govind P. Agarwal	5 - FLUOROURACIL	Oil-in- oil solvent evaporation	–	To treat Colon cancer

	Technology					
8.	International Journal of Chemtech Research	Mahajan H.S.	KETOPROFEN	Quasi- emulsion solvent diffusion method.	104 - 108µm	Anti – Inflammatory
9.	International Journal of Trends in Pharmacy and Life Sciences	D.Thulasi Ram, V. Hema Faith	VALACYCLOVIR	Solvent diffusion method	95.03– 152.48 µm	Anti – viral agent
10.	Journals of Micro Encapsulation	Wasfy M. Obeidat	PIROXICAM AND THEOPHYLLINE	Solvent evaporation method	125 - 500µm	Anti- Inflammatory Anti- asthmatic agent
11.	Tropical Journals of Pharmaceutical Research	Kapil Kumar	CURCUMIN	Solvent diffusion method	251 - 387µm	Anti - Inflammatory agent
12.	Scholars Research library	B.Senthil Kumar	CELECOXIB	Emulsion polymerisation method	2.3µm	To treat rheumatoid arthritis

Table 3:

S. NO	JOURNALS	AUTHOR	DRUG	METHOD	PARTICLE SIZE	USES
1.	Iranian Journal OF Pharmaceutical Research	Hosseinali Tabandeh	ASPIRIN	Direct compression method	12mm	To relief Aches and pains. Also, lower risk of heart attack
2.	Global Pharmaceutical Sciences	Rashid Javed	TRAMADOL HCL & ACETAMINOPHEN	Wet granulation Technique	5.5mm – 6.2mm	To relieve pain, Anti - pyretic agent
3.	AAPS Pharmaceutical Science AND TECHNOLOGY	Sateesh Kumar Vemula	FLURBIPROFEN	Dip coating method	9mm	Anti– inflammatory agent
4.	DER Pharmacia Lettre	Pruthviraj S Pawar	BUDESONIDE	Dip coating method	2.11± 0.08mm	Ulcerative colitis, Diarrhoea, Colon cancer.
5.	Journal of drug delivery and Therapeutics	Sharma Madhu	MESALAZINE	Enteric coating	±5%	Ulcerative colitis
6.	American Journal of Advanced drug delivery	Lana Alsharkas	VANCOMYCIN	Enteric coating	±5%	To treat Clostridium difficile colitis
7.	World journal Of Pharmaceutical research	Nampelly Karnakar	BALSALAZIDE	Enteric coating	-	Anti– inflammatory agent

Table 4:

S. NO	JOURNALS	AUTHOR	DRUG	METHOD	PARTICLE SIZE	USES
1.	Nternational journals	Juntayin,		Solvent diffusion	0.1	Anticancer

	of Pharmaceutics	Cuiyuxiang, Xiaoyong song.	PSORALIDIN	and high-pressure homogenization process		drug(new)
2.	International Journal of drug Delivery science and technology	Rahitasdeshmak ,Ranjit, Rishikesh Shukla.	SULFASALAZINE PECTIN	Ionic gelation technique	0.02	bowel disease. Anti inflammatory
3.	Material Science And Engineering	Kiran Jyoti, Shiva Sharma, Richa Sinha.	PROTAMINE	The pro liposomes of recombinant human insulin encased in eudragit s-100 coated technique	0.1	Treat the diabetes mellitus
4.	national library of Medicine	Ehsan Ahmadi, Ko mail sadrjavadi, Ghobadmohamadi.	5- FLUOROURACIL	Microemulsion method	0.43	Treat the colon infection
5.	ACTA Scientiarum Health Science	Lucinaarantes, Soares, Eduardo crema	-	The spouted bed coating process	0.21	-

Table 5:

S.NO	JOURNAL (AUTHOR)	DRUG	SYNTHETIC POLYMER	MATERIALS	METHOD	ARTICLE SIZE	USES
1.	International Journal of Drug Developmentand Research (HodaVarasteghan)	DILTIAZEM HCL	Eudragit s- 100	Eudragit S 100, Ethyl Cellulose, Glyceryl Monostearate	Direct compression technology	1.08	To control the angina
2.	ACTA PHARMA-27 (ChinamNiranjanPatra)	OPRANOLOL HCL	Eudragit RLPO	Ethyl cellulose, Eudragit (RLPO), Methyl Methacrylate.	Non-fickian diffusion- controlled method	180	To Treat Hypertensio n
3.	International journal of Pharmacy and Pharmaceutical Science (Yeha)	AMOXICILLIN ESOMEPRAZOLE	Eudragit-RS	Hydroxy propyl cellulose K100M, Carbopol,	Direct compression technology.	45.1	To treat Peptic ulcer
4.	Future journal of Pharmaceutical Science (A.s.Ashok sigh)	FEXOFENADINE & MONTELUKAST	Eudragit s- 100	Polyvinyl pyrrolidine, micro crystalline cellulose, Starch,	Direct compression method.	0.23	To Treat the Asthma
5.	J.pharmaceutical Science& Technology (NaazneenSurti)	AMLODIPINE & LOSARTAN	Eudragit E100	Sodium alginas, Chitosan, Eudragit E-100	Ionotropic gelation method.	0.009	To Treat Hyper tension

Table 6:

S. NO	JOURNAL (AUTHOR)	DRUG	SYNTHETIC POLYMER	MATERIAL	METHOD	PARTICLE SIZE	USES
1.	Journals of Pharmaceutical Native resuts (Rawat)	ESOMEPRAZOLE	Eudragit S100	Polyvinyl pyrrolidine, microcrystalline cellulose,Starch, HPMC phosphate buffer, saline.	Direct compression method	0.1	Gastro intestinal reflux disease.

2.	Materials today Processings (R.B. Sharma)	CARMELLOSE SODIUM	Eudragit S100	Hydroxy propyl cellulose K100M, Carbopol.	Direct compression Method	0.22	Treat colon cancer
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Table 7:

S.NO	JOURNAL	AUTHOR NAME	METHODS	PARTICLE SIZE	USES
1.	International Journal of pharma tech research	*S.C.Dhawale, *A. S. Bankar, M.*N. Patro	A simple oil /water emulsification process	0.1	The treatment of colon cancer
2.	INTERNATIONAL JOURNAL OF NANOMEDICINE	*Enas El Maghawry *Mina I Tadros *Seham A Elkheshen Ahmed Abdelbary	Nano-spray drying technique.	0.2	potent anti inflammatory
3.	COLLOIDS AND SURFACES ' B: BIOINTERFACES	*S. Josea, *M.T. Premaa, *A.J. Chackoa, *A. CinuThomasa, *E.B. Soutob.	emulsion crosslinking technique	6.32_m	chronotherapy of chronic stable angina

Table 8:

S. NO	JOURNAL (AUTHOR)	DRUG	SYNTHETIC POLYMER	MATERIALS	METHODS
1.	International Current Pharddmaceutical Journal (Seemabadhana)	MESALAMINE	Eudragit s100	Chitosan, cochin, Eudragit s-100	Ionic-gelation emulsion method
2.	Aaps pharmaceutical Science and Technology (Manjurawat)	-	Eudragit s100	Tween20,40,80. Serratio peptidase, methanol.	Emulsion solvent diffusion technique
3.	Drug delivery Informa Healthcare USA (M.ghorab)	CAPROLACTONE	Eudragit s100	Sorbitanmonooleate, tween-80, acetonitrile	Double coat celecoxib loaded technique
4.	Asian journals of Pharmaceuticals (s.k.signh)	QUERCETIN	Eudragit s100	Hydroxypropyl cellulose K100M, Carbopol, Lactose.	Emulsion solvent diffusion method

Table 9:

S. NO	JOURNAL	AUTHOR NAME	METHOD OF PREPARATION (USING EMULSION BASE)	APPLICATION
1.	Asian Journals of Pharmaceuticals	s.k.signh	Emulsion solvent diffusion method	Sonication & homogenization
2.	Journal Of Pharmaceutics and Drug Research	Esmat E Zein	emulsion solvent evaporation technique	Encapsulation of drug Within water insoluble polymer

3.	International journal of Pharmaceutical and Chemical sciences	Manish Dubey	Non-aqueous solvent evaporation method	To prepare polymeric nanoparticles.
4.	World journal of Pharmaceutical research	Ritu Verma	Emulsion solvent evaporation technique	A flexible method of particles.
5.	Asian Journal of Pharmaceutics	Ramchandra Jat	Emulsion solvent diffusion method	Used as a spray drying

Table 10:

S. NO	JOURNALS	AUTHOR NAME	DRUG	METHOD	PARTICLE SIZE	USES
1.	International Journal Of applied Pharmaceutics	vishalyadav, prakashjadhav, shailajadombe. anjalibodhe, pranalisalunkhe	OXICONAZOLE	Quasi emulsion solvent diffusion method	0.1	Antifungal agent
2.	Indian journal of Pharmaceutical Sciences	s. y. rai and padminiravikumar	CLOTRIMAZOLE	Emulsion solvent evaporation technique.	1.0	Antifungal agent

Table 11:

S. NO	JOURNAL	AUTHOR	DRUG	METHOD	PARTICLE SIZE	USES
1.	International Journal of Applied Pharmaceutics	Vishal Yadav, Prakash Jadhav	OXICONAZOLE	Quasi emulsion solvent diffusion method	0.01	Anti- fungal agent

Table 12:

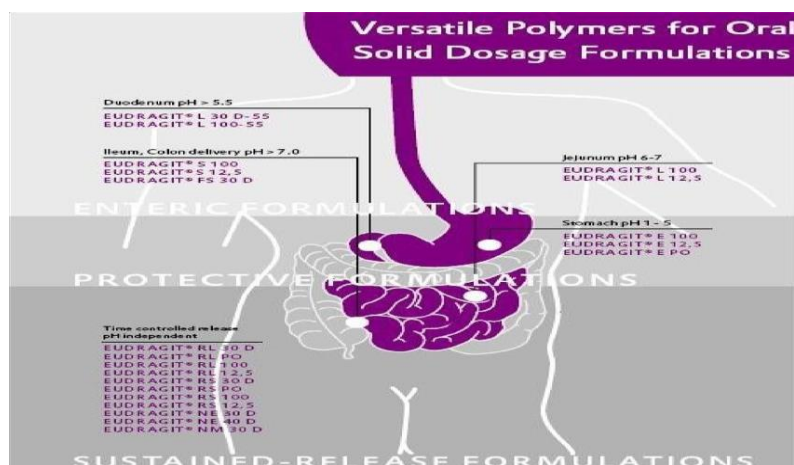
S. NO	JOURNAL	AUTHOR	BACTERIA	METHOD	ISO ELECTRIC POINT(PH)	USES
1.	APPLIED NANOSCIENCE	Farzad Rahmati	Lactobacillus acidophilus and Lactobacillus plantarum	coating of strains, the double coating technique	4.5	Gastrointestinal regulator
2.	ANSARI ET AL. AMB EXPERIMENTS	Fereshte h Ansari, Hadi Pourjafar, VahidJodat, Javad Sahebi.	Lactobacillus acidophilus, Lactobacillus rhamnosus	microencapsulated probiotic bacteria	7.5	The improving viability of probiotic bacteria

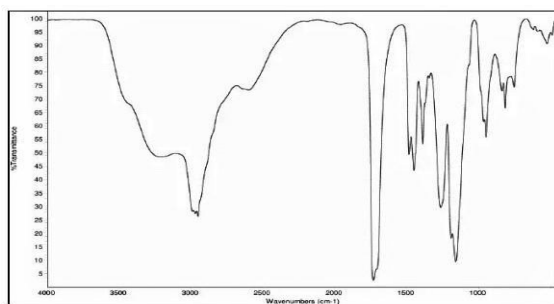
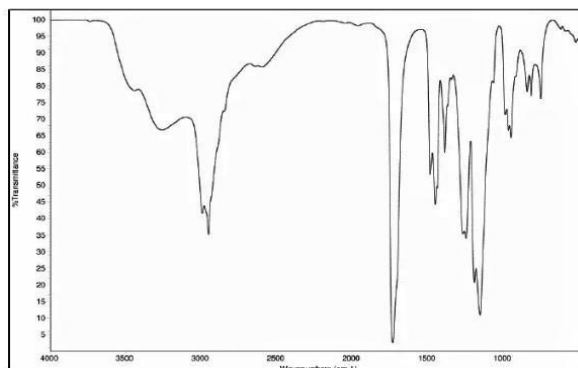
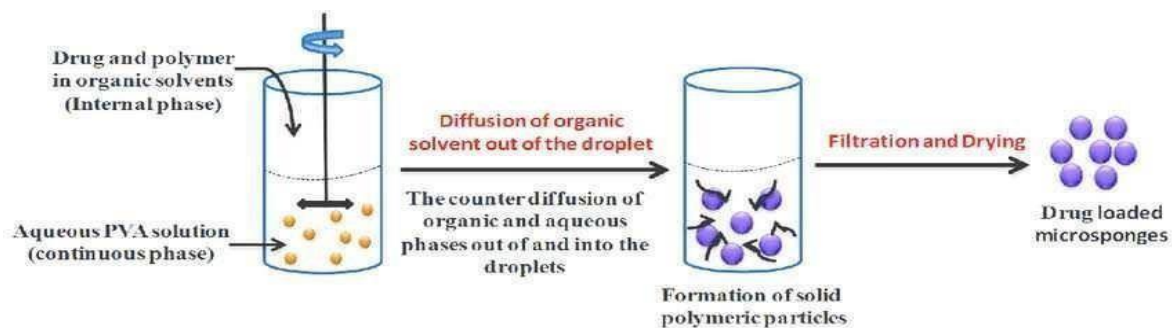
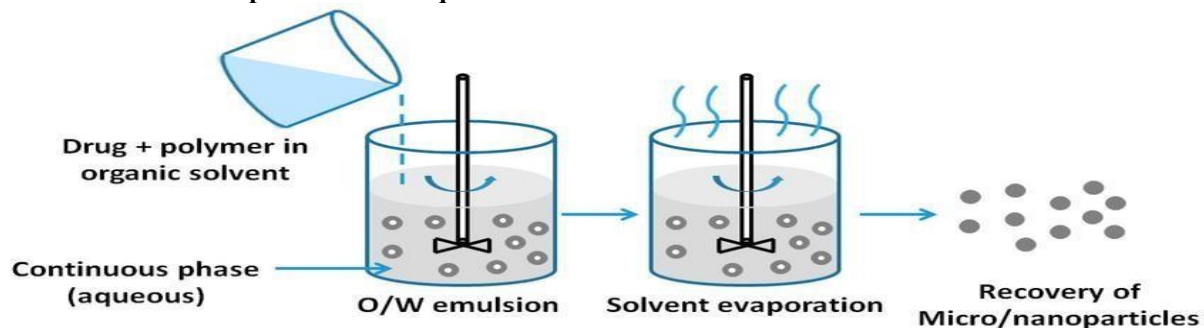
Specific Site of Action

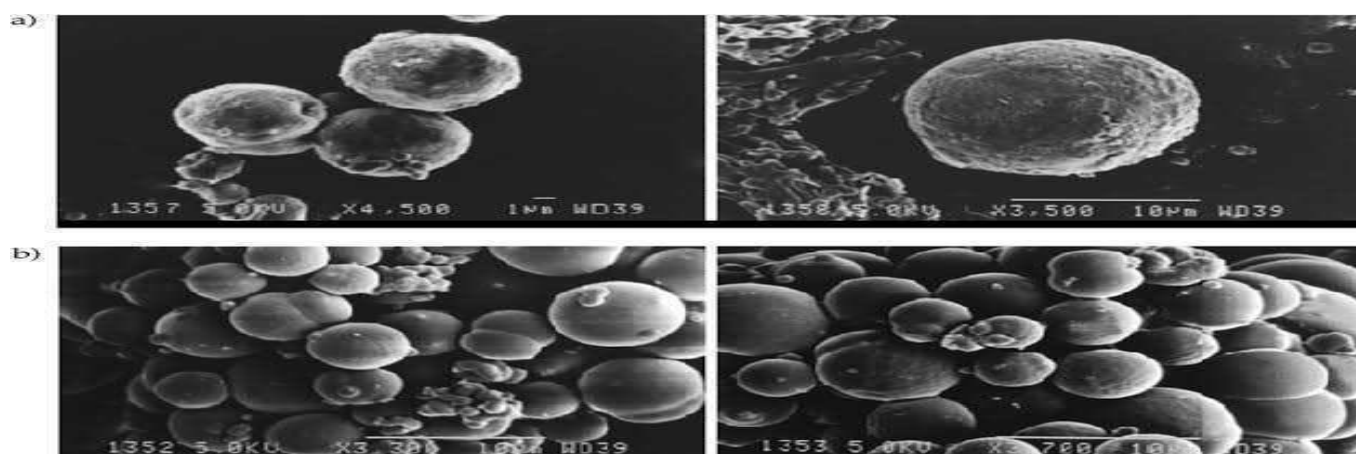
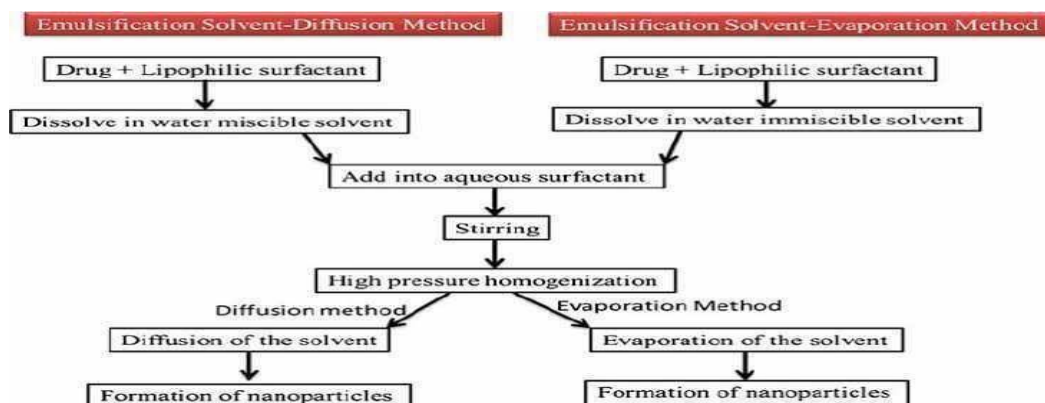
S. NO	SITE OF ACTION	SYNTHETIC POLYMER	MATERIALS	METHOD OF PREPARATION	PARTICLE SIZE RANGE
1.	Colon delivery (Colon)	chitosan microspheres coated with eudragit S100.	*Cochin*Hydrochloric acid, *Disodium hydrogen phosphate, *Potassium dihydrogen phosphate,	Emulsion method using glutaraldehyde across linking agent	The size range 61 and 110µm

			Methanol Dichloromethane		
2.	Enzyme-entrapped insulin (Pancreas)	Eudragit S100 Microspheres	*Serratiopeptidase (molecular weight 52 ka). *Eudragit S100. *Tween 20, 40, and 80	Emulsion solvent diffusion technique	Dry microspheres (10mL)
3.	Antioxidant and anticarcinogenic activity (Quercetin)	Eudragit S100	*Quercetin dihydrate, DRDE, *Eudragit S100	Eudragit microspheres Entrapment Method.	Size Range (48.2 to 2.01)
4.	Anti-asthmatic drug (theophylline)	Eudragit-S100 microspheres	*Methacrylic acid copolymer (Eudragit S 100, Rohm), *Piroxicam, *theophylline, *Magnesium stearate, *Heptane, *mineral oil	The emulsion solvent evaporation method	Standard sieves from 106–600mm
5.	Non-steroidal antiinflammatory drugs (Piroxicam)	Eudragit L 100-55 and Eudragit Rs100	*Ethyl cellulose, *Eudragit Rs100, *Eudragit L100- 55, *Ethanol, *Methanol, *Dichloromethane, SLS	Emulsion solvent evaporation technique	0.5nm
6.	Anti-diabetic agent (Metformin Hydrochloride)	Eudragit S100	*EC, *Cellulose acetate, HPMC, * HCl *Acetone, Span 80, * Petroleum ether *CaCl ₂ , *Eudragit S100, *Liquid paraffin	Emulsion solvent evaporation technique.	50 microspheres
7.	Antiviral agent (Ritonavir)	Eudragit S100	*Dichloromethane, Sodium lauryl sulphate	microspheres differential scanning calorimetry was done on microspheres.	100 nm
8.	Colon targeting of 5-Fluorouracil (5-FU)	Eudragit S100	Eudragit S100, Pectin (P9135, pectin from citrus peel, galacturonic acid, pepsin (bovine) and dialysis method	Citrus pectin nanoparticles (CPNs)	0.05

Figure 2:



EUDRAJIT L 100.**EUDRAJIT S 100****Orally Disintegrating Tablets (ODT):****Emulsion Solvent Diffusion Method.****Emulsion Solvent Evaporation Technique.**



DISCUSSION

In this review article we have investigated the formulation evaluation development of different dosage form. Microsphere contains a synthetic polymer eudragit various grade like eudragit S 100, Eudragit L 100 and Eudragit RLPO etc..... Some technique used in the determination of different pharmaceutical dosage form. Also discussed about the Eudragit advancement and polymer profile and the polymer formulation methods of

determination in different pharmaceutical dosage forms like solid, liquid, semi-solid, probiotics.

CONCLUSION

The main objective of this review is to compile the recent literatures on the different formulations of microsphere contain a Eudragit synthetic polymer in different pharmaceutical dosage forms.

REFERENCES

1. Jain, N. K. Controlled and novel drug delivery. *CBS Publishers*, 2004, 236–237, 21.
2. Venkatesan, P., Manavalan, R., & Valliappan, K. Microencapsulation: A vital technique in novel drug delivery system. *Journal of Pharmaceutical Sciences and Research*, 1(4), 2009, 26–35.
3. Ramteke, K. H., Jadhav, V. B., & Dhole, S. N. Microspheres: As carriers used for novel drug delivery system. *IOSR Journal of Pharmacy*, 2(4), 2012, 44–48.
4. Sachan, A. K., Gupta, A., & Arora, M. Formulation & characterization of nanostructured lipid carrier (NLC) based gel for topical delivery of etoricoxib. *Journal of Drug Delivery and Therapeutics*, 6(2), 2016, 4–13.
5. Verma, N. K., Alam, G., Vishwakarma, D. K., Mishra, J. N., Khan, W. U., Singh, A. P., Roshan, A. Recent advances in microspheres technology for drug delivery. *International Journal of Pharmaceutical Sciences and Nanotechnology*, 8(2), 2015, 2799–2813.
6. Khar, R. K., & Vyas, S. P. Targeted and sustained drug delivery - Novel carrier systems. *CBS Publications and Distributors*, 1st edition, New Delhi, 2002, 417–418.
7. Kreuter, J., Nefzger, M., Liehl, E., Czok, R., & Voges, R. Microspheres – A novel approach in drug delivery system. *Journal of Pharmaceutical Sciences*, 72, 1983, 1146.

8. Singh, C., Purohit, S., Singh, M., & Pandey, B. L. Design and evaluation of microspheres: A review. *Journal of Drug Delivery Research*, 2(2), 2013, 18–27.
9. Midha, K., Nagpal, M., & Arora, S. Microspheres: A recent update. *International Journal of Recent Scientific Research*, 2015, 5859–5867.
10. Sharma, S., Pawar, S., & Jain, U. K. Development and evaluation of topical gel of curcumin from different combination of polymers formulation and evaluation of herbal gel. *Int J Pharm PharmSci*, 4, 2012, 452–456.
11. DrugBank. (2017). [Last accessed on 10/2017]. Available at: <https://www.drugbank.ca/drugs/DB00239>
12. O'Neil, M. J. The Merck Index, An encyclopedia of chemicals, drugs, and biologicals. 14th Edition, 2006, 6937.
13. Makwana, R., Patel, H., & Patel, V. Photostability enhancement of miconazole nitrate by micro sponge formulation. *Int J Curr Trends Pharm Res*, 2, 2014, 437–458.
14. Durgapal, S., Mukhopadhyay, S., & Goswami, L. Preparation, characterization, and evaluation of floating microparticles of ciprofloxacin. *Int J Appl Pharm*, 9, 2017, 1–8.
15. Jadhav, N., Patel, V., Mungekar, S., Bhamare, G., Karpe, M., & Kadams, V. Micro sponge delivery system: An updated review, current status, and future prospects. *J Sci Ind Res*, 2, 2013, 1097–1110.
16. Ali, M. O., Osmani, R., Aloorkar, N. H., Ingale, D. J., Kulkarni, P. K., Umme, H., Bhosale, R. R., et al. Micro sponge based novel drug delivery system for augmented arthritis therapy. *Saudi Pharm J*, 23, 2015, 562–572.
17. Yadav, P., & Nanda, S. Development and evaluation of some micro sponge-loaded medicated topical formulations of acyclovir. *Int J Pharm Sci Res*, 5, 2014, 1395–1410.
18. Abdelmalak, N. S., & El-Menshawe, S. F. A new topical fluconazole micro sponge-loaded hydrogel: Preparation and characterization. *Int J Pharm PharmSci*, 4, 2012, 460–469.
19. Katkade, M., Kalkotwar, R., Jain, N., Patil, P., Gadakh, R., & Naikwade, J. Ethyl cellulose-based micro sponge delivery system for antifungal vaginal gels of tioconazole. *J Drug Delivery Ther*, 3, 2013, 14–20.
20. Ravi, R., Senthil Kumar, S., & Parthiban, S. Formulation and evaluation of the micro sponge gel for an anti-acne agent for the treatment of acne. *Int J Pharm Sci Res*, 3, 2013, 328.
21. More, H. N., & Hajare, A. A. Practical Physical Pharmacy. *Career Publications*, 2nd edition, 2015, 153–155.
22. Costa, P., & Lobo, J. M. S. Modeling and comparison of dissolution profiles. *Eur J Pharm Sci*, 13, 2001, 123–133.
23. Lamprecht, A., Schäfer, U., & Lehr, C. M. Size-dependent bio adhesion of micro- and nanoparticulate carriers to the inflamed colonic mucosa. *Pharm Res*, 18(6), 2001, 788–793.
24. Chaudhury, A., & Das, S. Recent advancement of chitosan-based nanoparticles for oral controlled delivery of insulin and other therapeutic agents. *AAPS Pharm Sci Tech*, 12(1), 2011, 10–20.
25. Sharma, S., Parmar, A., Kori, S., & Sandhir, R. PLGA-based nanoparticles: A new paradigm in biomedical applications. *TrAC Trends Anal Chem*, 80, 2016, 30–40.
26. Stevanović, M., Savić, J., Jordović, B., & Uskoković, D. Fabrication, in vitro degradation, and release behaviors of poly(DL-lactide-co-glycolide) nanospheres containing ascorbic acid. *Colloids Surf B Biointerfaces*, 59(2), 2007, 215–223.
27. Taylor, D., Thomas, R., & Penfold, J. Polymer/surfactant interactions at the air/water interface. *Adv Colloid Interface Sci*, 132(2), 2007, 69–110.
28. Budhian, A., Siegel, S. J., & Winey, K. I. Controlling the in vitro release profiles for a system of haloperidol-loaded PLGA nanoparticles. *Int J Pharm*, 346(1), 2008, 151–159.
29. Fambri, L., Migliaresi, C., Kesenci, K., & Piskin, E. Biodegradable polymers. *Ronaldo Barbucci (Ed.) Integrated Biomaterials Science*, Springer, 2002, 119–187.
30. Dunne, M., Corrigan, O., & Ramtooil, Z. Influence of particle size and dissolution conditions on the degradation properties of polylactide-co-glycolide particles. *Biomaterials*, 21(16), 2000, 1659–1668.
31. Raghuvanshi, R. S., Singh, M., & Talwar, G. Biodegradable delivery system for single-step immunization with tetanus toxoid. *Int J Pharm*, 93(1–3), 1993, R1–R5.
32. Stevanović, M., Jordović, B., & Uskoković, D. Stereological analysis of DLPLG nanoparticles containing ascorbic acid during in vitro degradation process. 2007.
33. Zweers, M. L., Grijpma, D. W., Engbers, G. H., & Feijen, J. The preparation of monodisperse biodegradable polyester nanoparticles with a controlled size. *J Biomed Mater Res B Appl Biomater*, 66(2), 2003, 559–566.
34. Kaihara, S., Matsumura, S., Mikos, A. G., & Fisher, J. P. Synthesis of poly(L-lactide) and polyglycolide by ring-opening polymerization. *Nat Protoc*, 2(11), 2007, 2767–2771.
35. Makadia, H. K., & Siegel, S. J. Poly lactic-co-glycolic acid (PLGA) as biodegradable controlled drug delivery carrier. *Polymers*, 3(3), 2011, 1377–1397.
36. Jovanović, I., Stevanović, M., Nedeljković, B., & Ignjatović, N. The effect of processing parameters on characteristics of poly-L-lactide microspheres. *Paper presented at: Materials Science Forum*, 2007.
37. Allison, S. D. Effect of structural relaxation on the preparation and drug release behavior of poly(lactic-co-glycolic) acid microparticle drug delivery systems. *J Pharm Sci*, 97(6), 2008, 2022–2035.

38. Mohamed, F., & van der Walle, C. F. Engineering biodegradable polyester particles with specific drug targeting and drug release properties. *J Pharm Sci*, 97(1), 2008, 71–87.
39. Babu, R. C., Babu, V. R., Rangaswamy, V., Patel, P., & Aminabhavi, T. M. Nano/micro technologies for delivering macromolecular therapeutics using poly(D, L-lactide-co-glycoside) and its derivatives. *J Controlled Release*, 125(3), 2008, 193–209.
40. Li, X., Anton, N., Arpagaus, C., Belleiteix, F., & Vandamme, T. F. Nanoparticles by spray drying using innovative new technology: the Büchi nano spray dryer B-90. *J Controlled Release*, 147(2), 2010, 304–310.
41. Gautier, S., Arpagaus, C., Schafroth, N., Meuri, M., Deschamps, A., & Maquet, V. Very fine chitosan microparticles with narrow & controlled size distribution using spray-drying technologies. *Drug Delivery Technol*, 10(8), 2010, 30–37.
42. Triefenbach, F. Design of experiments: The D-optimal approach and its implementation as a computer algorithm. *Bachelor's Thesis in Information and Communication Technology*, 2008.
43. Arai, H., Suzuki, T., Kaseda, C., & Takayama, K. Effect of an experimental design for evaluating the nonlinear optimal formulation of theophylline tablets using a bootstrap resampling technique. *Chem Pharm Bull*, 57(6), 2009, 572–579.
44. Dixit, R., & Nagarsenker, M. Self-nanoemulsifying granules of ezetimibe: Design, optimization, and evaluation. *Eur J Pharm Sci*, 35(3), 2008, 183–192.
45. Elnaggar, Y. S., El-Massik, M. A., & Abdallah, O. Y. Self-nanoemulsifying drug delivery systems of tamoxifen citrate: Design and optimization. *Int J Pharm*, 380(1–2), 2009, 133–141.
46. Nahata, T., & Saini, T. R. D-optimal designing and optimization of long-acting microsphere-based injectable formulation of aripiprazole. *Drug Dev Ind Pharm*, 34(7), 2008, 668–675.
47. Czitrom, V. One-factor-at-a-time versus designed experiments. *Am Stat*, 53(2), 1999, 126–131.
48. Abdel-Hafez, S. M., Hathout, R. M., & Sammour, O. A. Towards better modeling of chitosan nanoparticles production: Screening different factors and comparing two experimental designs. *Int J Biol Macromol*, 64, 2014, 334–340.
49. Garud, N., & Garud, A. Preparation and in-vitro evaluation of metformin microspheres using non-aqueous solvent evaporation technique. *Trop J Pharm Res*, 11(4), 2012, 577–583.
50. Singh, S., Mishra, A., Verma, A., Ghosh, A. K., & Mishra, A. K. A simple ultraviolet spectrophotometric method for the determination of etoricoxib in dosage formulations. *J Adv Pharm Technol Res*, 3(4), 2012, 237.
51. Fang, Z., & Bhandari, B. Comparing the efficiency of protein and maltodextrin on spray drying of bayberry juice. *Food Res Int*, 48(2), 2012, 478–483.
52. Ratner, B. D., Hoffman, A. S., Schoen, F. J., & Lemons, J. E. *Biomaterials Science: An Introduction to Materials in Medicine*. Elsevier, 2004.
53. Kaundal, A., Bhatia, R., Sharma, A., & Sukrial, P. A review on micro sponge's drug delivery system. *Int J Adv Pharm*, 4, 2014, 177–181.