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ROLE OF CHITOSAN AND EUDRAGIT IN POLYMER - BASED EXTENDED RELEASE MATRIX TABLETS - A REVIEW

Amaresh Prusty[*1] and Bijon Kumar Gupta [2]

Department of Pharmaceutics [1], College of Pharmaceutical Sciences, Puri - 752002, Odisha, India.
Department of Pharmaceutical Technology [2], Jadavpur University of Technology, Kolkata - 700032, West Bengal, India.

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Correspondence to Author:
Mr. Amaresh Prusty

Assisstant Professor,
Department of Pharmaceutics,
College of Pharmaceutical Sciences,
Puri - 752002, Odisha, India.

E-mail: amareshprusty@gmail.com

ABSTRACT: The present article describes the recent role of polymers as carriers for delivery of drug at target site to extending its release. These polymers are widely used in delivery due to their inherent characteristics such as biocompatibility, biodegradability. Chitosan and Eudragit are choice of drug in extended release matrix tablets. Chitosan is an amino polysaccharide polymer which is biodegradable, biocompatibility and nontoxic nature. Due to its cationic nature, Chitosan form complex with anions like Eudragit giving rise to polyelectrolyte complexes. Chitosan enhances the dissolution of poor soluble drugs. Similarly Eudragit polymers are also copolymers derived from esters of acrylic and methacrylic acid and have large number of applications in extending drug delivery. This article reviewed the role of Chitosan and Eudragit in controlled release drug formulations. Also, the article included role, property and uses of Chitosan and Eudragit and their use in different drug delivery system for various therapeutic applications.

INTRODUCTION: The aim of drug therapy is to achieve a steady-state at blood or tissue level which is therapeutically effective and side by side it must be non toxic during release period of time. This is usually accomplished by maximizing drug availability, *i.e.* by attempting to attain a maximum rate and extent of drug action through formulation. Controlled drug delivery system is delivery system which delivers the drugs at a predetermined rate, locally or systematically, for a specified period of time.

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Though now days various novel drug delivery systems are available but scientist still discovering various new techniques along with new polymeric materials for modulating and extending drug release.

Hydrophilic gel polymer matrix systems are used in oral controlled drug delivery to obtain a desirable drug release profile, for cost effectiveness, and broad regulatory acceptance [1, 3]. The advantage of Polymer-based monolithic matrix tablets is due to their economic benefits, relative simplicity of process development and scale-up procedures [4, 5]. Polymeric materials which are used in extended-release matrix systems can be classified into as (a) hydrophilic system; (b) erodible system; and (c) insoluble system [6, 7]. Even also to achieve desirable release profiles, polymers should be optimized

based on their physicochemical properties associated with release mechanisms. Polymers are macromolecules composed of repeating structural units of monomers connected by covalent chemical bonds and this process is known as polymerization. As per their origin, they are may be natural or from synthetic source.

Natural polymers such as proteins (collagen, silk and keratin), carbohydrates (starch, glycogen) are widely used materials for conventional and novel dosage forms in comparison to synthetic source. These materials are chemically inert, nontoxic, less expensive, biodegradable, eco-friendly and widely available [8, 9].

Chitosan: It is a biodegradable polymeric material which can be recycled or it can be decomposed by microorganisms or sunlight providing carbon dioxide and water. The large use of chitosan include from fertilizers to pharmaceuticals due to its economical and easily availability property. Chitosan is no longer just a waste by-product from the seafood processing industry.

Sources and Extraction of Chitosan from Raw Materials: Chitin, the main source of chitosan is widely distributed both in the animal and the plant kingdom. Henry Braconnot was the first isolated chitin from mushrooms. The possible sources of chitin are Fungi, Algae, Echiruda, Annelida (Segmented worms), Mollusca, Cnidaria (jellyfish), Aschelminthes (roundworm), Entoprocta, Bryozoa (Moss or lace animals, Phoronida (Horse shoe worms), Brachiopoda (Lamp shells), Arthropoda and Ponogophora. They are also found in arthropods tendons, exoskeletons and the linings of their digestive, excretory and respiratory systems as well as in some fungi and in the iridophores (reflective material) of both eyes and epidermis of cephalopods and arthropods of phylum Mollusca and the epidermal cuticle of the vertebrates.

During extraction process first crab or shrimp shells are washed and grinded in to powdered form and then it is deproteinized by treatment with an aqueous 3-5% solution of sodium hydroxide. After that it is neutralized and demineralised at a room temperature by treating it with aqueous 3-5% of hydrochloric solution to form a white or slightly pink precipitate of chitin. The collected product then deacetylated by treatment with an aqueous 40-45% of sodium hydroxide solution and the precipitate is then washed with water. The insoluble part is removed by dissolving in an aqueous 2% acetic acids solution and the supernatant solution is then neutralized with an aqueous sodium hydroxide solution to obtain a purified Chitosan.

Chitosan is a linear randomly distributed, hetero polysaccharide consisting of (1-4) linked 2-acetamido-2-deoxy-D-glucopyranose and 2-amino-2-deoxy-Dglycopyranose units (**Fig. 1**). It is prepared by deacetylation of chitin, a linear polymer of (1-4) linked N-acetyl-D-glucosamine units composed of mucopolysaccharides and amino sugars.

Chemical Methodology for the Preparation of Chitosan: Preparation of chitosan involves four steps: deproteinization, demineralization, decoloration and deacetylation. Deproteinization is carried out by alkaline treatment using 3-5% NaOH (w/v) aqueous solution at room temperature overnight. Other inorganic constituents remaining are removed by treatment with 3-5% aqueous HCl (w/v) solution at room temperature for 5 hr. The product is again reacted with 40-45% NaOH solution at 120 °C for 4-5 hr. This treatment gives the crude sample of chitosan. The crude sample is purified by precipitating the chitosan from its aqueous acetic acid solution of NaOH and washing with distilled water [10].

Properties of Chitosan: Chitosan has attracted increasing attention in the past decade due to its unique properties including nontoxicity, biocompatibility, and biodegradation including many others discussed in the pending text. One; among the notable and much exploited is; its antimicrobial commotion inhibiting the growth of a wide variety of fungi, yeasts and bacteria making it beneficial for use in the field of biomedicine. It can also bind toxic metal ions, beneficial for use in air cleaning and water purification applications. These properties arise as a result of protonation of NH_2 groups on the chitosan. Structurally, chitosan is a linear-chain copolymer composed of D-glucosamine and N-acetyl-D-glucosamine being obtained by the partial deacetylation of chitin. The structure of chitosan is very much similar to that of

cellulose and is the second most abundant natural polymer after cellulose [11]. The solubility, bio-degradability and reactivity of chitosan and adsorption of substrates depend on the extent of protonated amino groups in the chain of polymer. Chitosan is incapable of being dissolved in water, organic solvents and aqueous bases however get dissolved after stirring in acetic, nitric, hydrochloric, perchloric and phosphoric acids [12].

The amino group of chitosan is not protonated in alkaline or neutral medium and therefore it is insoluble in water; while in acidic pH it gets the resultant soluble protonated polysaccharide. Chitosan forms water-soluble salts with inorganic and organic acids including glyoxylate, pyruvate, tartarate, malate, malonate, citrate, acetate, lactate, glycolate, and ascorbate [13]. Inherent chitosan becomes soluble in organic acids when the pH of the solution is less than 6.5. The water-soluble salts of chitosan may well be formed by neutralization with acids such as lactic acid, hydrochloric acid, acetic acid, or formic acid.

There are various other factors which may affect the physicochemical properties of chitosan enabling the researchers to formulate different grades of chitosan which differ primarily in molecular weight, crystallinity and degree of deacetylation. During its processing from raw material, different conditions such as type and concentration of reagents, time and temperature employed can affect the physical characteristics of chitosan product. Its molecular weight also depends on solubility, viscosity, elasticity and tears strength.

Physicochemical and Biological Properties of Chitosan: Chitosan is a semi crystalline polymer which exhibits polymorphism. It is a colourless, odourless flake and is readily soluble in aqueous acidic solution. The solubilisation occurs through protonation of amino groups on the C-2 position of D-glucosamine residues, whereby polysaccharide is converted into polycataion in acidic media. Chitosan has a low solubility at physiological pH of 7.4 as it is a weak base (pKa 6.2-7).

Chitosan has different DD (Degree of Deacetylation) and MW (Molecular weight) [14]. DD is defined as of the percentage of primary amino groups in the polymer backbone. The DD and Mw property can be changed by changing the reaction conditions during the manufacture of chitosan from chitin. Generally a typical commercial chitosan has a DD of 66-95%. Higher Mw chitosan of approximately 1,400 kDa shows a stronger level of mucoadhesion due to higher level of viscosity than low Mw chitosan of 500-800 kDa. The viscosity of chitosan solution increases with an increase in chitosan concentration and DD but with a decrease in solution temperature and pH.

The degree of deacetylation of molecular chain of chitin can also be increased by increasing the temperature or strength of the alkaline solution. The degree of deacetylation can also be determined by its ratio of 2- acetamido- 2- deoxy- D glucopyranose to 2- amino- 2- deoxy- D-glucopyranose structural units. When the number of 2-amino-2-deoxy-D glucopyranose units is more than 50 percent, the biopolymer is said to be Chitosan and when the number of 2-acetamido-2-deoxy-Dglucopyranose units is higher, the polymer is said to be chitin. Adjusting solution pH to approximately 7.5 induces flocculation due to deprotonation and insolubility of the polymer [15]. Chitosan possess a good complexing capacity and form complex with an oppositely charged polymer such as poly (acrylic acid), sodium salt of poly (acrylic acid), carboxymethyl cellulose, xanthan, carrageenan, Eudragit, alginate, pectin etc.

Chitosan shows pseudo plastic material property and an excellent viscosity-enhancing agent in acidic environments and the viscosity increases with an increase in Chitosan concentration and decreases with increase in temperature. Sometimes the viscosity of Chitosan influences the biological properties such as wound-healing properties as well as biodegradation by lysozyme. The solubility of Chitosan can be decreased by cross-linking it with covalent bonds using glutaraldehyde. Swelling property of the Chitosan decreases with the increase in concentration of cross-linking agent.

Limitations of Chitosan: Though CS offers good advantage as a polymer in drug delivery, but it has some limitations like

- Chitosan suffers from low solubility at a physiological pH of 7.4, limiting its use as

absorption enhancer in, for example, nasal or per oral delivery systems [16].

- Another limitation of chitosan for the preparation of sustained release systems arises from its rapidly adsorbing water and higher swelling degree in aqueous environments, leading to fast drug release. In order to overcome these problems, a number of chemically modified chitosan derivatives have been synthesized [17.]

Some times to avoid these limitations different grades of Chitosan which differ primarily in molecular weight and degree of deacetylation can be used. The molecular weight depends on viscosity, solubility, elasticity. In alkaline or neutral medium Chitosan is insoluble in water as free amino group of chitosan is not protonated, but in acidic pH, due to protonation of free amino groups it gets solubilized. Chitosan forms water-soluble salts with inorganic and organic acids includes glyoxylate, pyruvate, tartarate, malate, malonate, citrate, acetate, lactate, glycolate, ascorbate. The pka, solubility of CS can be modified by changing the DD or by modifying the pH and ionic strength of the formulation. In neutral pH, CS molecules losses their charge and get precipitated from the solution. Chemical modification of various reactive (amino, hydroxyl) groups present on the molecule provides a powerful means to promote new biological activities and to modify its mechanical properties. The characteristic features of Chitosan such as being cationic, insoluble at high pH can be completely reversed by a sulfation process which makes the molecule anionic and water-soluble and also introduce anticoagulant properties.

Chitosan Role in Drug Delivery: For drugs whose actions correlate with their serum drug concentration, the sharp fluctuations often cause unacceptable side-effects at the peaks, followed by inadequate therapy at the troughs [18]. Drugs covalently attached to biodegradable polymers or dispersed in a polymeric matrix of such macromolecules may be released by erosion or degradation of the polymer. Therapeutic molecules, complexes by polymers, may also be released from gels by diffusion. Chitosan is non-toxic and easily bio absorbable [19] with gel-forming ability at low pH. Chitosan matrix formulations appear to float and gradually swell in an acid medium. All these interesting properties of chitosan make this natural polymer an ideal candidate for controlled drug release formulations [20-23].

Chitosan Tablets for Controlled Release Anionic–Cationic Interpolymer Complex: Chitosan has a unique property as a release-controlling agent in drug delivery, but it disintegrates easily when used alone neutral pH due to its strong ability to absorb water. So chitosan is used along with anionic polymers as a carrier for oral controlled-release preparations. It has been observed that chitosan contained in tablets at levels below 70% acts as a disintegration agent [24-26] investigated the sustained-release characteristics of ethyl cellulose tablets containing theophylline as the model drug. The drug release mechanism of CS reveal that, at high drug loading drug was released by a diffusion mechanism with a constant rate that increased with an increase in aqueous solubility. At low drug loading, polymer relaxation also becomes a component of the release mechanism. However, its contribution to drug release was less pronounced as drug solubility decreased, becoming negligible in the case of theophylline. Mi *et al.* [27] have explained the swelling and erosion rates of chitosan tablets in acidic media. In order to examine the swelling / diffusion mechanism of various tablets containing drug along with chitosan and the drug release mechanism of various tablets have been carried out using Peppas's model and during study nuclear magnetic resonance imaging microscopy was used to analysis [28].

Modification of Chitosan: Most chemical modifications of chitosan are performed at the free amino groups of the glucosamine units by which Chitosan has improved property like mucoadhesion and permeation enhancement and this improved changes in property may be a reason why chitosan has advantages use now a days over other polysaccharides. Sometimes modifications can also taking place in chitosan hydroxyl group [29]. During specific modifications without too many difficulties at C-2 position specific groups can be introduced to design polymers for selected applications. The main reaction easily performed involving the C-2 position is the quarterisation of the amino group or

a reaction in which an aldehydic function reacts with $–NH_2$ by reductive amination [30].

Eudragits: These are synthetic polymers obtained by polymerization of acrylic acid (prop- 2-enoic acid; CH_2=CHCOOH) and methacrylic acids or their esters like butyl ester or dimethylaminoethyl ester and whose physicochemical properties are determined by their functional groups.

History of Eudragit: Before nineteenth century the main disadvantage in drug release was, it was not possible to control the time or the release location of the active substances. So scientists are planning how they will modulate the drug release by using polymer. In this context the discovery of EUDRAGIT by Röhm and Haas plays bigger role for solution to this problem. EUDRAGIT are having varying degrees of solubility. As the time proceeds various grades of EUDRAGIT are discovered and are used in dosages forms as excipients to coat solid drugs such as tablets, capsules or granules. The first discovery in drug release using Eudragit takes place in the year 1950's, when a pill coating that dissolves in stomach acid came onto the market. In the meantime, other variants of EUDRAGIT have become available, which can also control the time for drug released.

TABLE 1: YEAR OF INTRODUCTION EUDRAGIT GRADE

Year of Introduction	Eudragit grade
1954	Eudragit L 12.5
	Eudragit S 12.5
1959	Eudragit E 12.5
1961	Eudragit E 100
1968	Eudragit RL 100
	Eudragit RS 100
1972	Eudragit NE 30 D (formerly Eudragit E 30 D)
	Eudragit L 30 D-55 (formerly Eudragit L 30 D)
	Eudragit RS PO
	Eudragit RL PO
1977	Eudragit L 100
1983	Eudragit NE 40 D
1985	Eudragit L 100-55
1986	Eudragit RL 30 D
	Eudragit RS 30 D
1999	Eudragit E PO
	Eudragit FS 30 D

These are called retard preparations which resistant to stomach pH and but releases drug in Intestinal pH. The study of different grades of Eudragit and their formulation mainly occurs in Chemicals Business Area of Evonik Industries AG and production taking place at Darmstadt, Weiterstadtand Worms' sites [31]. Eudragit is trademark of Rohm GmbH and Co. KG. Eudragit prepared by the polymerization of acrylic and methacrylic acids or their esters, *e.g.*, butyl ester or dimethylaminoethyl ester. Eudragit introduced in USPNF, BP, PhEur, Hand book of pharmaceutical excipients [32]. The different Eudragit grades being introduced in the following chronological order as shown in **Table 1.**

Glass Transition Temperature (Tg): The glass transition temperature is an important factor for describing the physical properties of polymers. On a macroscopic level it describes the solidification of an anisotropic polymer melt. The glass–liquid transition or glass transition for short is the reversible transition in amorphous materials (or in amorphous regions within semi crystalline materials) from a hard and relatively brittle "glassy" state into a viscous or rubbery state as the temperature is increased.

TABLE 2: GLASS TRANSITION TEMPERATURE OF DIFFERENT EUDRAGIT GRADES

Eudragit grade	Tg (°C)
Eudragit RL 100	63 ± 5
Eudragit RL PO	63 ± 5
Eudragit RL 30 D	55
Eudragit RS 100	65
Eudragit RS 30 D	55
Eudragit RL 100	63 ± 5
Eudragit L 100	>130
Eudragit L 12.5	>130
Eudragit S 100	>130
Eudragit S 12.5	>130
Eudragit L 30D-55	96
Eudragit L 100-55	96
Eudragit NE 30 D	9

Properties of Different Eudragit Grades and their Applications: Eudragit polymers can be classified on the basis of use or type of formulation produced. These include Eudragit polymers for:

- Time-controlled drug release by sustained release formulations.
- Gastro-resistance and gastrointestinal (GI) targeting by enteric formulations.
- Moisture protection and odour/taste masking by protective formulations.

TABLE 3: PROPERTIES OF DIFFERENT EUDRAGIT GRADES AND THEIR APPLICATIONS

Trade name	Form and permeability	Physical properties	IUPAC name	Applications
Eudragit RL 100	Granule High permeability	Colorless, clear to cloudy granules, faint amine-like odour	Poly (ethyl acrylate-co-methyl methacrylate-co-trimethyl ammonioethyl methacrylate chloride) 1:2:0.2	Sustained release
Eudragit RL PO	Powder High permeability	White powder with a faint amine like odour		Sustained release
Eudragit RL 30 D	30% aq. dispersion High permeability	Milky-white liquid of low viscosity with a faint odour		Sustained release
Eudragit RS 100	Granule Low permeability	Colorless, clear to cloudy granule, faint amine like odour	Poly (ethyl acrylate-co-methyl meth acrylate-co-trimethylammonioethyl methacrylate chloride) 1:2:0.1	Sustained release
Eudragit RS 30 D	30% aq. dispersion Low permeability	Milky-white liquid of low viscosity with a faint odour		Sustained release
Eudragit RS 12.5	12.5% organic solution Low permeability	Light yellow liquid of low viscosity, clear to slightly cloudy with odor of solvents		Sustained release
Eudragit L 100	Powder	White powder with faint odour	Poly (methacylic acid-co-methyl methacrylate) 1:1	Enteric coatings
Eudragit L 12.5	12.5% organic solution	Colorless to slightly cloudy liquid, odor of isopropyl alcohol		Enteric coatings
Eudragit S 100	Powder	White powder with a faint odour	Poly (methacylic acid-co-methyl methacrylate) 1:2	Enteric coatings
Eudragit S 12.5	12.5% organic solution	Colorless to slightly cloudy liquid, odor of isopropyl alcohol		Enteric coatings
Eudragit L 30D-55	30% Aq. dispersion	Milky-white liquid of low viscosity with faint odour	Poly (methacylic acid-co-ethyl acrylate) 1:1	Enteric coatings
Eudragit L 100-55	Powder	White powder with faint odor		Enteric coatings
Eudragit E 100	Granules	Colorless to yellow tinged granules with a characteristic amine-like odour	Poly (butyl methacrylate-co-(2-dimethylaminoethyl) methacrylate-co-methyl methacrylate) 1:2:1	Film coating
Eudragit E 12.5	12.5% organic solution	Light yellow liquid of low viscosity, clear to slightly cloudy, characteristic odour of the solvents		Film coating
Eudragit E PO	Powder	White powder with characteristic amine-like odour		Film coating

Role of Eudragit in Drug Delivery:

Matrix Formulation: Eudragit serves as a matrix within which the active ingredient is embedded. The matrix structure is obtained by direct compression, granulation, or melt extrusion. Eudragit NM 30D is particularly suitable for granulation processes in the manufacture of matrix tablets. Prusty *et al.* developed an extended release matrix tablet containing drug Tramadol hydrochloride using Eudragit L 100D, which extended drug release up to 20 hours and useful for treating pain and Rheumatoid arthritis patients.

Multiparticulate Formulations: Eudragit is employed as a coating material, usually for the coating of pellets or particles that are filled into capsules or compressed into tablets. These pellets or particles act as diffusion cells in the digestive tract and release a constant drug quantity per unit of time (multi-unit dosage forms). Chandak *et al.* developed a matrix-type transdermal formulation of pentazocine using mixed polymeric grades of eudragit RL/RS. The matrix transdermal films of pentazocine were evaluated for physical parameters and *in-vitro* dissolution characteristic using Cygnus' sandwich patch holder. *In-vitro* dissolution study revealed that, with an increase in the proportion of eudragit RS (slightly permeable) type polymer, dissolution half-life (t_{50}%) increases and dissolution rate constant value decreases [33].

Through Swellable Matrix: Eudragit are attractive matrix forming materials, due to their high chemical stability, good compatibility properties, and large variety of available grades with different physicochemical characteristics. In swellable matrix, drug release is controlled by continuously changing dimension of the diffusive barrier, which serves as a barrier and through it drug transport or permeation takes place. The swellable matrices are examples of typical moving boundary release systems. Formulation of Matrix tablets containing Eudragit can occur by different methods like direct compression [34], wet granulation [35] or melt extrusion [36].

Out of these methods direct compression has been largely used as a method for the preparation of Eudragit-based matrix tablets. Ceballos and co-workers prepared extended-release theophylline matrix tablets by a direct compression of drug and different pH-dependent (Eudragit L 100, S 100 and L 100-55) and time-dependent (Eudragit RL PO and RS PO) polymer combinations. Matrix tablets contains L 100/RL PO and L 100/RS PO Eudragit grade give the best results, showing the highest percentage of theophylline release. This was achieved by the combination of the good erodible properties of L 100 with the swelling properties of RL PO and RS PO polymers [37]. Colo and his co-workers studied compressed matrix tablets taking a pH-sensitive poly (ethylene oxide) and Eudragit L 100 compounds and found a complete release of the active substance takes place during the transit from stomach to jejunum which is unaffected by gastric pH variations.

Release in the gastric fluid was controlled by matrix swelling and / or drug dissolution, whereas matrix dissolution controlled release in simulated jejunum fluid. Similarly matrix tablets of carteolol hydrochloride is prepared taking Eudragit RS as a supporting material along with other excipients like mannitol, polyethylene glycol 6000 and Eudragit L 12.5 as a wetting liquid. The two-phase release profile has been accounted for as the release of a drug on the surface of a tablet and the particles of the drug which are not completely surrounded by the Eudragit, during the first phase and the release of drug contained in the inert matrix during the second phase [38]. Melt extrusion as a method for producing the sustained release pellets of poly (meth) acrylates is practicable since Eudragits are thermoplastic polymers, their physiochemical properties such as melt viscosity, glass transition temperature, and temperature stability are ideal for use in melt extrusion [39-42].

Sustained - Release Formulations or Time-Controlled Drug Release: The high frequency of administration and severe adverse effects of active drug molecule by the oral route can be overcome by sustained release formulation. Eudragit polymers can be used in the sustained release tablet formulation due to its property of formation of a matrix system. Eudragit polymers can help to achieve desired release profile. When Eudragit polymers mixed with vancomycin (VCM) by w/o/w double emulsion solvent evaporation method using Eudragit RS as a retardant material and its *in-vitro* release studied it was found the drug release extended up to 24 hrs. Which conform its oral sustained administrations [43].

Some Other Role of Eudragit Polymers in Drug Delivery System:

Ophthalmic Drug Delivery: Due to their nontoxicity and controlled release profiles behaviour, they are used in ophthalmic application. Pignatello *et al.,* prepared Ibuprofen nano-suspension of ophthalmic drug delivery using Eudragit RS100 [44]. Verma *et al.,* prepared acetazolamide-loaded eudragit RL 100 nanoparticle suspension by nano-precipitation method to

increase topical ocular bioavailability and to sustain the release of drug for a longer time [45].

Gene Delivery: Various hereditary diseases could be treated by the genetic therapy. Basakar *et al.*, formulated nanoparticles by blending PLGA with methacrylate copolymer (Eudragit E100) which can safely deliver plasmid DNA for the prevention of autoimmune diabetes [46] Gargouri *et al.*, developed a tool for DNA delivery composed of methacrylic polymeric (Eudragit RS and RL) nanoparticles by nanoprecipitation and double emulsion technique. It was found that Eudragit RS and RL nanoparticles could introduce transgene into different types of cells [47].

Buccal Drug Delivery: Bio-adhesive polymers have extensively used in buccal drug delivery systems which can adhere to either hard or soft tissue in buccal cavity. Moreover buccal film must also possess good mucoadhesive strength so that it is retained in mouth for the desired duration. Diarra *et al.*, developed a fluoride controlled release delivering system for intra-buccal use by formulating tablets that have a granular matrix composed of pure hydroxyapatite, eudragit (R) and ethyl cellulose. The matrix permits to reach high enough local concentrations for desirable therapeutic effect with minimal side effects [48].

Enteric Delivery: Hao *et al.*, prepared enteric eudragit L100-55 nanoparticles of omeprazole by ultrasonic dispersion and diffusion solidification. The prepared nanoparticles were in spherical shape and showed a strong pH-sensitive release *in-vitro*. These results indicated that the enteric eudragit L 100-55 nanoparticle could be synthesized successfully *via* ultrasonic solidification method [49].

Vaccine Delivery: Lee *et al.*, carried *in-vivo* studied of a vaccine delivery system based on thiolated eudragit microsphere for its ability to elicit mucosal immunity against enterotoxigenic *Escherichia coli*. The results suggested that thiolated eudragit microsphere may be a promising candidate for an oral vaccine delivery system to elicit systemic and mucosal immunity [50]. Dea-Ayuela *et al.*, formulated microcapsules by spray drying method using eudragit L100 for oral delivery of vaccines against enteral/parenteral nematode parasite *Trichinella spiralis*. The results indicated that microcapsules formulated with eudragit L100 may be useful for oral vaccination against nematode infections [51].

CONCLUSION: Due to their unique properties, Chitosan and Eudragit polymers have made significant contributions to many types of formulations. This review suggests their role as a novel and versatile polymer in future discovery of drug delivery.

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