



COMPREHENSIVE REVIEW ON EUDRAGIT POLYMERS

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ABSTRACT

For ideal Pulsatile drug delivery system, dosage form should possess three main properties: (a) It will be a single dose for the whole duration of treatment. (b) It will deliver the active drug directly at the site of action. (c) It will possess possible fewer side effects. Above approaches are achieved with the help of suitable choice of polymer. Release rate of drug from the formulation and duration depend on selection of polymer. One would always like to have an ideal polymer for controlled release of drug from particular dosage form that must possess the following two properties. 1) Polymer stability in acidic environment with desired buoyancy. 2) It should dissolve slowly enough to serve predictable release rate. This review focuses on recent literature regarding use of Eudragit polymer in different drug delivery systems with special attention to used in its fabrication along with their physicochemical properties. Collected data of polymers will provide a deep and current knowledge for further researchers to conduct study regarding Pulsatile drug delivery system.

Keywords: Pulsatile drug delivery system, Polymers, Controlled release, Eudragit, Physicochemical properties.

INTRODUCTION

If you need to protect your active from the gastric fluid and would like to improve drug effectiveness – EUDRAGIT® L and S polymers are your preferred choice of coating polymers. They enable targeting specific areas of the intestine. Pharma Polymers offers a broad product portfolio of anionic EUDRAGIT® grades which dissolve at rising pH values. In addition, the different grades can be combined with each other, making it possible to adjust the dissolution pH, and thus to achieve the required GI targeting for the drug. Targeted drug release in the colon is required for local treatment of intestinal disorders such as Crohn's disease, ulcerative colitis or intestinal cancer. It is also required for drugs that are poorly soluble in the upper gastrointestinal tract. Moreover, the gastroresistance of the coating ensures that the oral dosage form is patient compliant. The preferred coating is EUDRAGIT® FS 30 D, which combines release in the colon with the following technical advantages:

- Aqueous processing

- Highly flexible coatings
- Suitable for multiparticulate tablet preparation.^{1,2,3}

Eudragit RL 100³

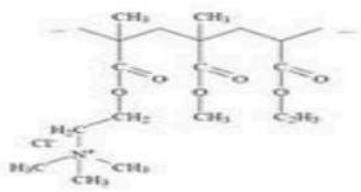
It is a copolymer of Ethyl acrylate, methyl methacrylate and a low content of methacrylic acid ester with quaternary ammonium groups. The ammonium groups are present as salts and make the polymers permeable.

Product Form- Granules

Targeted Drug Release Area- Time controlled release, pH independent

Characteristics-

- Insoluble
- High permeability
- pH independent swelling
- Customized release profile by combination of RL and RS grades in different ratios.
- Suitable for matrix structures

Structure	
Nonproprietary Names	Ammonio Methacrylate Copolymer Ph.Eur.
Category	Bio adhesive material; controlled-release agent; emulsifying agent; emulsion stabilizer; rheology modifier; stabilizing agent; suspending agent; tablet binder, film former.
Description	Colorless, clear to cloudy granules with a faint amine-like odour
Solubility	1 g of the substances dissolves in 7 g aqueous methanol, ethanol and isopropyl alcohol (containing approx. 3 % water), as well as in acetone, ethyl acetate and methylene chloride to give clear to cloudy solutions. The substances are practically insoluble in petroleum ether, 1 N sodium hydroxide and water.
Film formation	When the Test solution is poured onto a glass plate a clear film forms upon evaporation of the solvents.
Dry substance / Residue on evaporation	Not less than 97.0 %. 1 g of the substances is dried in an oven for 5 hrs in vacuum at 80 °C.
Loss on drying	Max. 3.0 % according to "Dry substance / Residue on evaporation."
Storage	Protect from warm temperatures. Protect from moisture. It tends to form lumps at warm temperatures. This has no influence on the quality. The lumps are easily broken up again.
Stability	Stable at room temperature.
Incompatibilities	Some NSAIDS showed incompatibilities with Eudragits specifically Eudragit RL100 and RS100.

Eudragit RS 100³

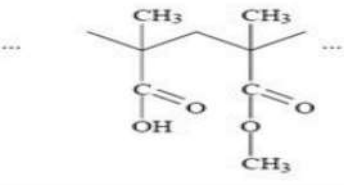
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Structure	
Nonproprietary Names	Ethacrylic acid copolymer USP
Category	Bio adhesive material; controlled-release agent; emulsifying agent; emulsion stabilizer; rheology modifier; stabilizing agent; suspending agent; tablet binder, film former.
Description	White powder with characteristic faint odour
Solubility	1 g of EUDRAGIT® L 100 or EUDRAGIT® S 100 dissolves in 7 g methanol, ethanol, in aqueous isopropyl alcohol and acetone (containing approx. 3 % water), as well as in 1 N sodium hydroxide to give clear to slightly cloudy solutions. EUDRAGIT® L 100 and EUDRAGIT® S 100 are practically insoluble in ethyl acetate, methylene chloride, petroleum ether and water.
Film formation	When the Test solution is poured onto a glass plate, a clear film forms upon evaporation of the solvent.
Dry substance / Residue on evaporation	At least 95.0 %. 1 g powder is dried in an oven for 6 hrs at 110 ° C, according to Ph. Eur. 2.2.32 method.
Loss on drying	Max. 5.0 % according to "Dry substance / Residue on evaporation."
Storage	Protect from warm temperatures. Protect against moisture
Stability	Stable at room temperature.
Incompatibilities	The use of acidic film former like Eudragit L100 in instability of the acid labile proton pumps inhibitors.

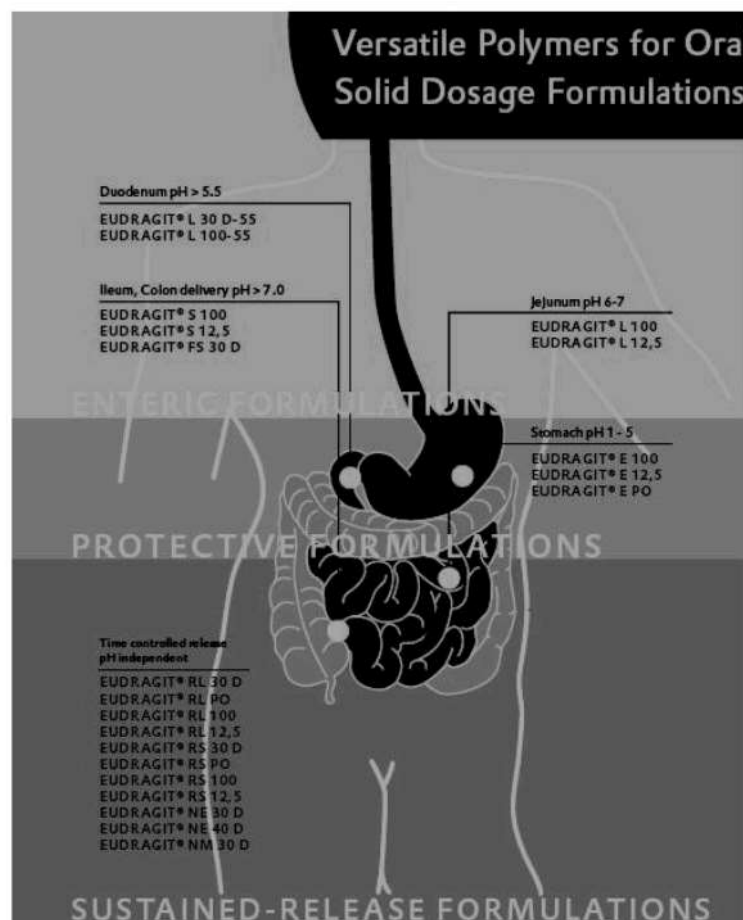


Figure: Versatile Polymers for Oral Solid Dosage Formulations

Applications of Eudragit RL and Eudragit RS

Ophthalmic Drug Delivery

A major problem being faced in ocular therapeutics is the attainment of an optimal concentration at the site of action. Poor bioavailability of drugs from ocular dosage forms is mainly due to the tear production, non-productive absorption, transient residence time, and impermeability of corneal epithelium. Eudragit exhibits favorable behavior, such as no toxicity, positive charge and controlled release profile this make them suitable for ophthalmic application.^{2,4,5,6,7,8,9}

Buccal and Sublingual Drug Delivery

The oral mucosae in general are somewhat leaky epithelia intermediate between that of the epidermis and intestinal mucosa. It is estimated that the permeability of the buccal mucosa is 4-4000 times greater than that of the skin. In general, the permeabilities of the oral mucosae decrease in the order of sublingual greater than buccal, and buccal greater than palatal. At physiological pH the mucus network carries a negative charge (due to the sialic acid and sulfate residues) which may play a role in mucoadhesion. At this pH mucus can form a strongly cohesive gel structure that will bind to the epithelial cell surface as a gelatinous layer. Major limitation of the buccal route of administration is the lack of dosage form retention at the site of absorption. Consequently, bioadhesive polymers have extensively been employed in buccal drug delivery systems. Polymers which can adhere to either hard or soft tissue have been used for many years in surgery and dentistry. Diverse classes of polymers have been investigated for their potential use as mucoadhesives. These include synthetic polymers such as monomeric a cyanoacrylate, polyacrylic acid and poly methacrylate derivatives. An ideal buccal film should be flexible, elastic, and soft yet strong enough to withstand breakage due to stress from activities in the mouth. Moreover, it must also possess good mucoadhesive strength so that it is retained in the mouth for the desired duration. To prevent discomfort, swelling of the film should not be too extensive. The mechanical, bioadhesive, and swelling properties of buccal films are critical and must be evaluated. Various mucoadhesive devices, including tablets, films, patches, disks, strips, ointments, and gels, have recently been developed. Eudragit providing good drug release barrier with good adhesive strength.

Gastrointestinal Drug Delivery

The need for gastroretentive dosage forms has led to extensive efforts in both academia and industry towards the development of such drug delivery systems. These efforts resulted in gastroretentive dosage forms that were designed, in large part, based on the following approaches, Low density form of the dosage form that causes buoyancy in gastric fluid, Highdensity dosage form that is retained in the bottom of the stomach, Bioadhesion to stomach mucosa, Slowed motility of the gastrointestinal tract by concomitant administration of drugs emptying of the dosage form through the pyloric sphincter. All these techniques we can achieved with different grades of eudragit.

Intestinal Drug Delivery

Sustained intestine delivery of drugs was developed that could bypass the stomach and release the loaded drug for long periods into the intestine by coating of eudragit polymer. Eudragit L and Eudragit S are two forms of commercially available enteric acrylic resins. Both of them produce films

resistant to gastric fluid. Eudragit L and S are soluble in intestinal fluid at pH 6 and 7 respectively. Eudragit L is available as an organic solution (Isopropanol), solid or aqueous dispersion. Eudragit S is available only as an organic solution (Isopropanol) and solid. Sodium para aminosalicylate Pellets were coated with Eudragit L 30 D-55 using fluidized bed processor and evaluated for *in vitro* dissolution behavior in 0.1 N HCl for two hours and then media was changed to phosphate buffer pH 6.8. A 60% w/w coating level of Eudragit L30 D 55 has produced the most acceptable results against the gastric attack.

Colon Drug Delivery

Colonic drug delivery is a relatively recent approach for the treatment of diseases like ulcerative colitis, Crohn's disease, and irritable bowel syndrome. pH-sensitive polymers that dissolve, or above pH 7 used for colonic drug delivery. Tegaserod maleate was used as a drug for irritable bowel syndrome, whereas Eudragit L 100 and S100 mixture (1:1, 1:2, and 1:3) were used.

Transdermal Drug Delivery

The mechanical properties of casted Eudragit E-100 films were tested for the combined effect of two cohesion promoters (succinic or citric acid) and triacetin as a plasticizer. The prepared films were elastic, self-adhesive, transparent and pale yellow in colour. Eudragit E100 polymer was found to result in wrinkle-free transparent films with good adhesion to skin. Release kinetics from transdermal therapeutic system was observed due to erosion of hydrophilic Eudragit E100 polymer, and 100% release was observed within 20 minutes.

Vaginal Drug Delivery

Eudragit RS100 vaginal suppositories containing sildenafil, and other excipients give adequate release. Intravaginal tablet were prepared with 1:1 ratio of lactic acid to Eudragit E-100, tablets disintegrating into a gelform at physiological range of 3.8-4.4 pH. These gels possess an acid reserve that might be able to neutralise the excess of alkali present in severe vaginal infections.

Gene Delivery

The course of many hereditary diseases could be reversed by gene delivery. In addition, many acquired diseases such as multigenetic disorders and those diseases caused by viral genes could be treated by genetic therapy. Nanoparticles prepared by blending PLGA with methacrylate copolymer (Eudragit(R) E100) can efficiently and safely deliver plasmid DNA encoding mouse interleukin-10 leading to prevention of autoimmune diabetes. New Anionic nanoparticles were prepared by Eudragit L100/55 provide a versatile platform for protein surface adsorption and a promising delivery system particularly when the maintenance of the biologically active conformation is required for vaccine efficacy. Antisense oligodeoxynucleotides were successfully delivered by nanoparticles prepared by Eudragit RL100, RS100.

Vaccine Delivery

Anionic surfactant-free polymeric core-shell nanospheres and microspheres were prepared by Eudragit L100/55. Vaccines were administered by different routes, including intramuscular, subcutaneous or intranasal and the results were compared to immunization with Tat alone or with Tat delivered with the alum adjuvant. The data demonstrate that

the nano and microspheres/Tat formulations are safe and induce robust and long-lasting cellular and humoral responses in mice after systemic and/or mucosal immunization. Weight ratio of Noveon and Eudragit S-100 had a significant effect on adhesion time of bilayer films. Postloaded plasmid DNA and beta-gal remained stable after being released from bilayer films (release of -60-80% in 2 h for both). Buccal

immunization using novel bilayer films (109 +/- 6-microm thickness) containing plasmid DNA led to comparable antigen-specific IgG titer to that of subcutaneous protein injection. All rabbits immunized with plasmid DNA via the buccal route but none by the subcutaneous route with protein antigen demonstrated splenocyte proliferative immune responses.

Eudragit Tests with their limits^{3,10}

Test	Limit
Description	Colorless, clear to cloudy crystals with faint amine like odour.
Solubility	1 gm substance + 7 gm aq. Methanol + Ethanol + IPA + Acetone + Dichloromethane to give clear cloudy solution.
Residue On Evaporation	NLT 97% (1 gm of substance is dried in an oven for 5hrs at 80°C.
Loss On Drying	NMT 3%
Assay	Eudragit RL 100-8.85%-11.96% (on DS); Eudragit RS 100-4.48%-6.77% (on DS)
Refractive Index	1.380-1.385
Relative Density	0.816-0.836
Sulphated Ash	NMT 0.1%
Heavy Metals	Maximum 20 ppm
Arsenic	Maximum 2 ppm
Residual Solvent	Contains small amount of Methanol Eudragit RL-NMT 1.5%; Eudragit RS-NMT 1%
Microbial Count	NMT 10 CFU / g
Identification	By IR Spectroscopy
Storage	In between 8° to 25°C

CONCLUSION

From the above review process it can be concluded that Eudragit polymers have vast role in the Formulation and Development of suitable dosage form in treatment of various diseases.

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