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Review Article

ROLE OF EUDRAGIT IN TARGETED DRUG DELIVERY

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ABSTRACT

An ideal drug delivery system will 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. When it comes to targeted drug release profiles, Eudragit is the pharmaceutical industry's preferred choice of product. The range of Eudragit Poly(meth)acrylate-based products provides full flexibility for solid oral dosage forms. Eudragit offers a strong protection of sensitive contents and improved patient compliance even Eudragit has the formulations which allow customer- tailored release profiles and releases over a specific period of time. This review gives an overview on Eudragit and its pharmaceutical properties.

Keywords: Eudragit, Targeting, Protective coating, Sustained delivery

INTRODUCTION

Eudragit is trademark of Rohm GmbH & Co. KG. Darmstadt in Germany, first marketed in 1950s. Eudragit prepared by the polymerization of acrylic and methacrylic acids or their esters, e.g., butyl ester or dimethylaminoethyl ester (1).

Eudragit polymers are copolymers derived from esters of acrylic and methacrylic acid, whose physicochemical properties are determined by functional groups (R). Eudragit polymers are available in a wide range of different physical forms (aqueous dispersion, organic solution granules and powders). Classification of Eudragit polymers are shown in Fig 1.

TYPES OF EUDRAGIT POLYMERS

1. Soluble Poly(meth)acrylates

They are soluble in digestive fluids by salt formation. Examples are- Eudragit L, S, FS and E polymers. These polymers with acidic or alkaline groups enable pH-dependent release of the active ingredient.

Applications: from simple taste masking through gastric resistance to controlled drug release in all sections of the intestine.

2. Insoluble Poly(meth)acrylates

These are insoluble but permeable in digestive fluids. Some of the examples are- Eudragit RL and RS polymers with alkaline and Eudragit NE polymers with neutral groups enable controlled time release of the active ingredient by pH-independent swelling.

Applications: delayed and sustained drug release.

EUDRAGIT POLYMERS – PHARMACEUTICAL PROPERTIES

Poly(meth)acrylates are known worldwide in the industry under the trade name Eudragit. These polymers allow the active in solid dosage form to perform during the passage of the human body. The flexibility to combine the different polymers enables to achieve the desired drug release profile by releasing the drug at the right place and at the right time and, if necessary, over a desired period of time. Other important functions are protection from external influences

(moisture) or taste/odor masking to increase patient compliance. The range of product portfolio provides full flexibility for targeted drug release profiles by offering best performance for enteric, protective or sustained-release properties (Fig 5).

- **Enteric formulations**

Gastroresistance and GI Targeting

To protect the active ingredient from the gastric fluid and to improve drug effectiveness– Eudragit L and S polymers are 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 (Table 1, Fig 2). 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

- **Protective formulations**

Moisture Protection and Odor/Taste Masking

The active ingredient needs to protect from moisture or light to increase patient compliance. Eudragit E polymers help to seal sensitive actives and increase patient compliance by masking tastes and odors. Even thin layers of Eudragit provide the desired effect, making it an extremely economical application. Pharma Polymers offer various cationic Eudragit E grades for protective coatings as shown in Table 2 (2).

- **Sustained-release formulations**

Time-controlled drug release

When drug release is needed over a specific period of time or one would like to benefit from the advantages of multiparticulate or matrix formulations – Eudragit polymers can help to achieve desired release profile. Drug delivery can be controlled throughout the entire gastrointestinal tract to increase therapeutic effect and patient compliance. Different polymer combinations of Eudragit RL and RS grades as shown in Table 3 allow custom tailored release profiles to achieve the desired drug delivery performance. Eudragit NE and NM grades are neutral ester dispersions which do not require addition of plasticizer.

Formulation methods for time controlled drug release

1. 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 30 D is particularly suitable for granulation processes in the manufacture of matrix tablets (Fig 3).

2. 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) (Fig 4).

ADVANTAGES OF EUDRAGIT POLYMERS

Eudragit offers valuable advantages for enteric coatings

- PH-dependent drug release
- Protection of actives sensitive
- to gastric fluid
- Protection of gastric mucosa
- from aggressive actives
- Increase in drug effectiveness
- Good storage stability
- GI and colon targeting

Advantage of protective Eudragit coatings

- pH-dependent drug release
- Protection of sensitive actives
- Taste and odor masking
- Moisture protection
- Economical application
- Improved passage of the dosage form
- Smooth and glossy surfaces, good color coating

Benefit from Eudragit coatings with sustained release

- Time-controlled release of active ingredients
- Therapeutically customized release profiles
- Higher patient compliance due to reduced number of doses to be taken
- Cost-effective processing

ROLE OF EUDRAGIT IN TARGETED DRUG DELIVERY

Targeting the proximal colon

Eudragit and other enteric coatings are widely used to produce acid resistant formulations, and with appropriate control of dissolution time may be reasonably effective in achieving release of drug in the ascending colon. For colonic delivery, Eudragits L and S, which are anionic copolymers of methacrylic acid and methyl methacrylate, have been widely used. These polymers are insoluble at low pH but form salts and dissolve above pH 6 and 7, respectively. Eudragit L100–55, a copolymer of methacrylic acid and ethyl acrylate, is water soluble which avoids the need for organic solvents in the coating process. The first study which employed Eudragit S for colon-targeting used sulphapyridine as a marker for drug release. Hard gelatin capsules containing the drug, and barium sulphate to aid radiological visualisation, were coated with the polymer and administered to 6 subjects who each swallowed 6 capsules. Twelve hours after administration, 4 capsules had broken in the distal ileum, 23 in the colon and 9 remained intact. The same approach was used with 5-aminosalicylic acid (5-ASA) but the thickness of the polymer coating was reduced from 120 to 80 μm. This formed the basis of the commercial formulation of 5- ASA tablet. There has been at least one report of patients taking 5-ASA and reporting the transit of intact tablets in their stools. This is probably a result of the high pH at which the Eudragit S-based coatings dissolve.

The study of Eudragit S coated tablets (10 mm diameter) in 7 volunteer subjects using gamma scintigraphy yielded some interesting results. In some subjects, stasis at the ileocaecal junction was noted. Other subjects had rapid transit through the colon, leading the authors to speculate whether the variability in transit meant that a pH-based coating was an unreliable means of delivery to the colon (3).

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 & Eudragit S are two forms of commercially available enteric acrylic resins. Both of them produce films resistant to gastric fluid. Eudragit L & S are soluble in intestinal fluid at pH 6 & 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. Rahman et. al. prepared sodium para aminosalicylate pellets 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 (4).

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 opthalmic application (5).

Vaginal Drug Delivery

Eudragit RS100 vaginal suppositories containing sildenafil, and other excipients give adequate release (6). 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 ableto neutralise the excess of alkali present in severe vaginal infections (7).

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 (8).

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 (9). 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 (10). 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 (11). Antisense oligodeoxynucleotides were successfully delivered by nanoparticles prepared by Eudragit RL100, RS100 (12).

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 (13). 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 (14),(15).

Table 1: Different grades of Eudragit polymers to achieve GI targeting

EUDRAGIT® Polymer	Availability	Dissolution Properties
L 30 D-55	30 % Aqueous Dispersion	Dissolution above pH 5.5
L 100-55	Powder	
L 100	Powder	Dissolution above pH 6.0
L 12,5	12.5 % Organic Solution	
S 100	Powder	Dissolution above pH 7.0
S 12,5	12.5 % Organic Solution	
FS 30 D	30% aqueous dispersion	

Table 2: Eudragit E grades for protective coatings

EUDRAGIT® Polymer	Availability	Dissolution Properties
E 100	Granules	Soluble in gastric fluid up to pH 5.0.Swellable and permeable above pH 5.0.
E 12,5	12.5 % Organic Solution	
EPO	Powder	

Table 3: Different polymer combinations of Eudragit RL and RS grades to allow tailored release

Eudragit Polymer	Availability	Dissolution Properties
RL 100	Granules	Insoluble
RL PO	Powder	**High permeability**
RL 30 D	30 % Aqueous Dispersion	pH-independent swelling
RL 12,5	12.5 % Organic Solution	
RS 100	Granules	Insoluble
RS PO	Powder	**Low permeability**
RS 30 D	30 % Aqueous Dispersion	pH-independent swelling
RS 12,5	12.5 % Organic Solution	
NE 30 D 30 %	Aqueous Dispersion	Insoluble, low permeability,
NE 40 D	40 % Aqueous Dispersion	pH-independent swelling
NM 30 D	30 % Aqueous Dispersion	**No plasticizer required** Highly flexible

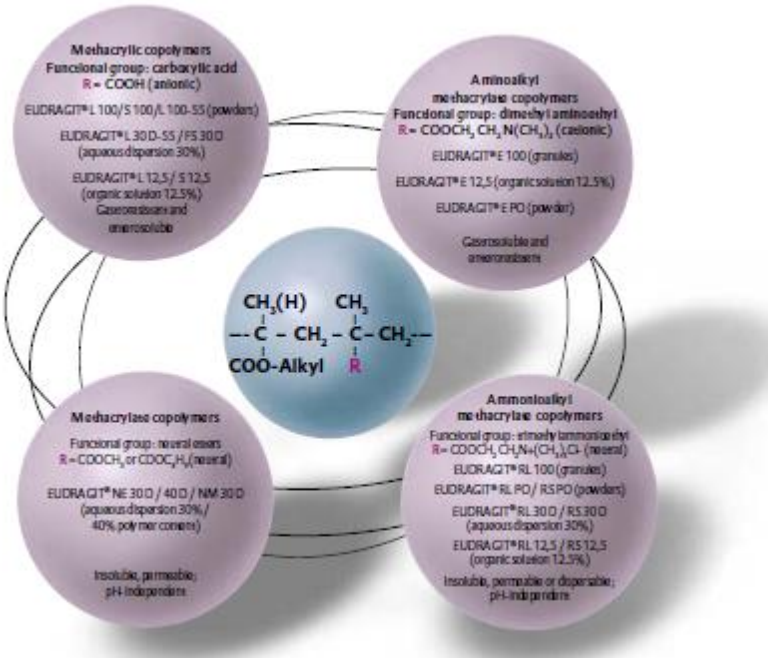

Fig. 1: Classification of Eudragit polymers

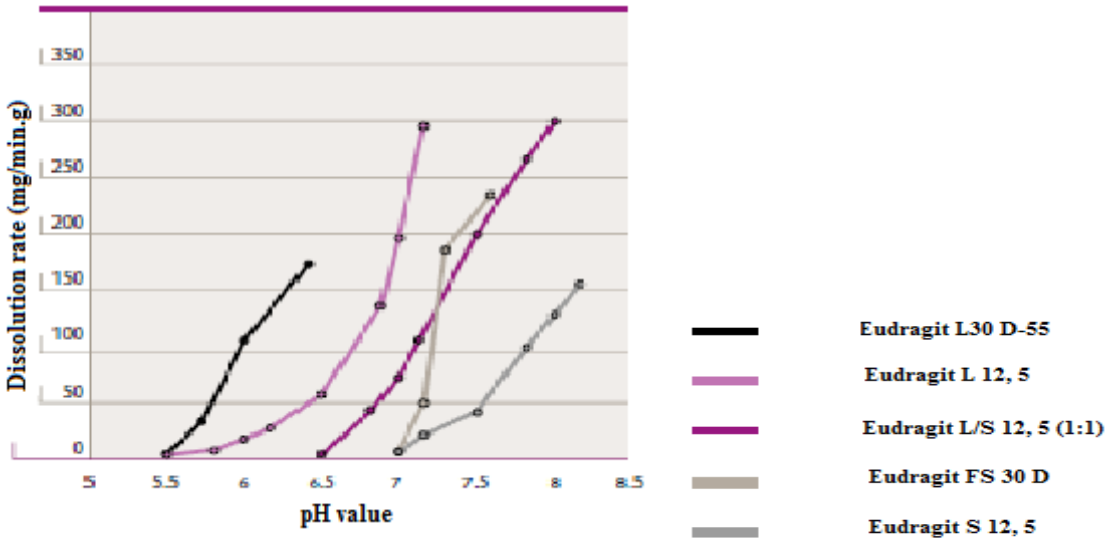

Fig. 2: Dissolution rate of Eudragit polymers at different pH for GI targeting

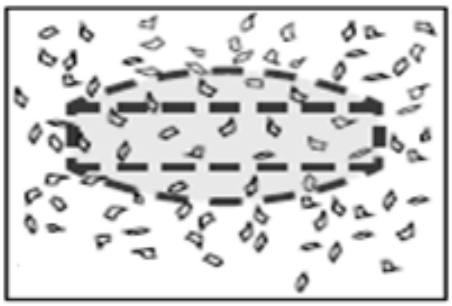

Fig. 3: Structure of Matrix tablet

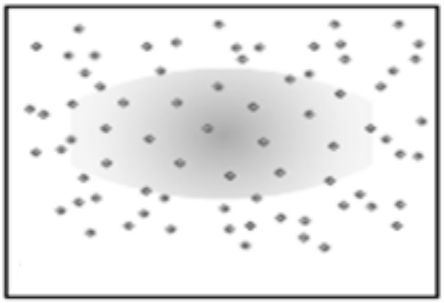

Fig. 4: Structure of Multiparticular tablets

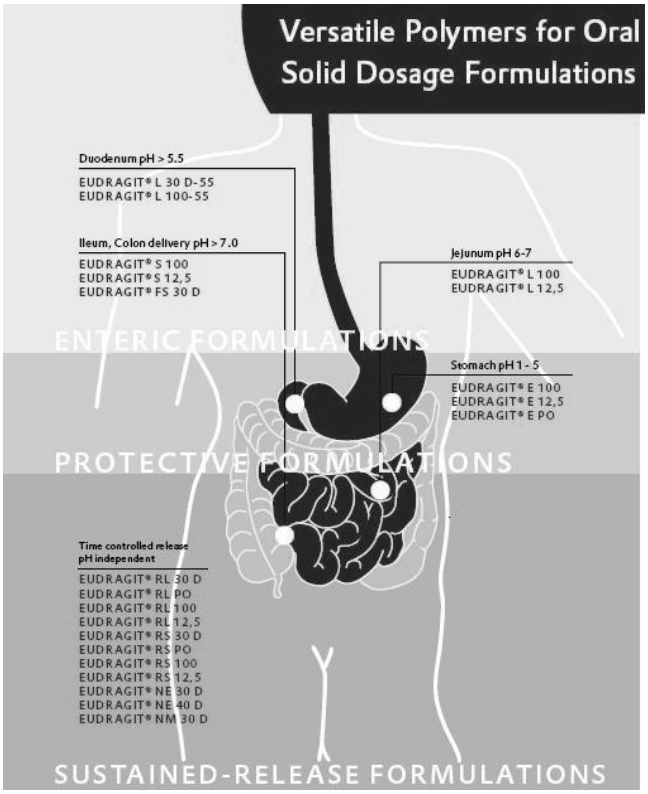

Fig. 5: Eudragit in oral solid dosage formulations

CONCLUSION

Due to their unique properties, Eudragit polymers have made significant contributions to many types of formulations. This review suggests the role of Eudragit as a novel and versatile polymer which can become more significant in future.

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