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Review Article

AN OVERVIEW OF MULTIFACETED SIGNIFICANCE OF EUDRAGIT POLYMERS IN DRUG DELIVERY SYSTEMS

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ABSTRACT

Polymers constitute the major part of pharmaceutical formulations functionality and significance. Development of novel drug delivery system (NDDS) has been made possible by eudragit polymers to modify the release pattern of drug. The basic objective of sustained drug release is to achieve more effective therapies by eliminating potential for both under and overdosing. Other advantages include maintenance of drug concentration with in desired range, fewer administration, optimal drug use and patient compliance. This review article gives outline of classification, nomenclature, physiological, and pharmaceutical properties of eudragit polymers. Eudragit polymers can be classified on the basis of use or type of formulation produced and includes time-controlled drug release by sustained release formulations, gastro-resistance and GI targeting by enteric formulations and moisture protection and odor/taste masking by protective formulations. Eudragit polymers are available in wide range of physical forms *viz.* aqueous dispersion, organic solution, granule and powder with varying degrees of solubility. Eudragit polymers have numerous drug release mechanism and wide applications in different drug delivery systems i.e. ophthalmic, buccal, sublingual, enteric, oral, colon, vaccine, gene, vaginal and transdermal drug delivery. It has been concluded that eudragit polymers have multifaceted applications in pharmacy and drug delivery system.

Keywords: Eudragit, Time-controlled, Sublingual.

INTRODUCTION

Pharmaceutical excipients are non-active ingredients that are mixed with therapeutically active compound to form medicines. Excipients affect the behavior and effectiveness of drug product. Polymers constitute major part of pharmaceutical formulations functionality and significance. Polymer that may be natural or synthetic tends to release the drug in a pre-designed manner [1]. The choice of polymer always suffers from problems of non-biocompatible, non-biodegradable and expensive. Eudragit polymers acts as versatile keystroke tool for fabrication of sustained release formulation and development of novel drug delivery system (NDDS) [2]. The basic objective of sustained drug release is to achieve more effective therapies by eliminating the potential for both under and overdosing. Other advantages include maintenance of drug concentration with in a desired range, fewer administration, optimal drug use and patient compliance [3].

Eudragit polymers are versatile polyacrylate polymers having varying degree of solubility which make it suitable for sustained release formulation [4]. Its production took place at Darmstadt, Weiterstadtand and was first marketed in the 1950s by Evonik Industries [5]. It is a trademark of Rohm Gmbh and Co. KG. Darmstadt in Germany. It was manufactured by polymerization of acrylic and methacrylic acids or their esters whose physicochemical properties are governed by functional group R. Eudragit has been introduced in USPNF, BP, PhEur and Handbook of Pharmaceutical excipients [6].

CLASSIFICATION OF EUDRAGIT POLYMERS

Eudragit polymers can be classified on the basis of use or type of formulation produced. These include eudragit polymers for [6,7]:

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

EUDRAGIT FOR TIME-CONTROLLED DRUG RELEASE

Eudragit polymers can be used to produce formulations which allow custom-tailored release profiles and releases over a specific period of time. Drug delivery can be controlled throughout the entire GI tract (GIT) to increase the therapeutic effect and patient compliance. Different polymer combinations of eudragitRL and RS grades allow custom-tailored release profiles to achieve the desired drug delivery performance [7]. Various characteristics of eudragit RL (eudragit RL 100, eudragit RL PO, eudragit RL 30 D, and eudragit RL 12.5) and eudragit RS (eudragit RS 100, eudragit RS PO, eudragit RS 30 D, and eudragit RS 12.5) has been given in Fig. 1. EudragitNE an NM grades are neutral ester dispersions, which do not require additional plasticizers. Various characteristics of eudragit NE 30 D, eudragit NE 40 D and eudragit NM 30 D has been given in Fig. 2.

The distinguishing characteristics of various grades of eudragit RL, eudragit RS, eudragit NE and eudragit NM has been given in Table 1. Benefit from eudragit coatings with sustained release include time-

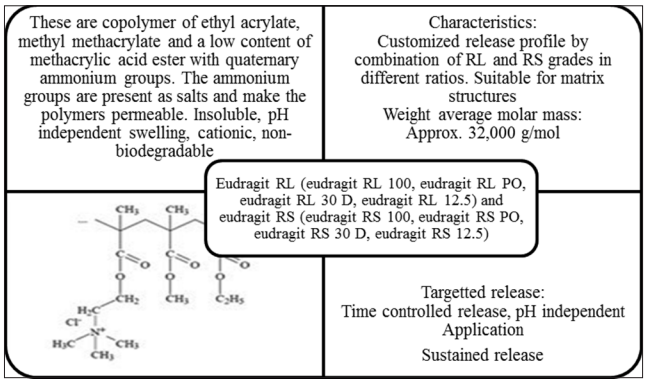

Fig. 1: Characteristics of various grades of eudragit RL and eudragit RS

Table 1: Distinguishing characteristics of various grades of eudragit RL, eudragit RS, eudragit NE and eudragit NM

Trade name	MFT (°C)	Tg (°C)	Form and permeability	Physical properties	IUPAC name
Eudragit RL 100	-	63±5	Granule High permeability	Colorless, clear to cloudy granules, faint amine-like odor	Poly (ethyl acrylate-co-methyl methacrylate-co-trimethyl ammonioethyl methacrylate chloride) 1:2:0.2
Eudragit RL PO	-	63±5	Powder High permeability	White powder with a faint amine like odor	
Eudragit RL 30 D	~ 40	55	30% aq. dispersion High permeability	Milky-white liquid of low viscosity with a faint odor	
Eudragit RL 12.5	-	-	12.5% organic solution High permeability	Light yellow liquid of low viscosity, clear to slightly cloudy with odor of solvents	
Eudragit RS 100	-	65	Granule Low permeability	Colorless, clear to cloudy granule, faint amine like odor	Poly (ethyl acrylate-co-methyl meth acrylate-co-trimethylammonioethyl methacrylate chloride) 1:2:0.1
Eudragit RS PO	-	65	Powder Low permeability	White powder with a faint amine like odor	
Eudragit RS 30 D	-	55	30% aq. dispersion Low permeability	Milky-white liquid of low viscosity with a faint odor	
Eudragit RS 12.5	-	-	12.5% organic solution Low permeability	Light yellow liquid of low viscosity, clear to slightly cloudy with odor of solvents	
Eudragit NE 30 D	5	−8	30% aq. dispersion Low permeability	Milky-white liquid of low viscosity with a faint odor	
Eudragit NE 40 D	5	−8	40% aq. dispersion Low permeability	Milky-white liquid of low viscosity with a faint odor	
Eudragit NM 30D	5	11	30% aq. dispersion Low permeability	Milky-white liquid of low viscosity with a faint odor	

controlled release of active ingredients, therapeutically customized release profiles, higher patient compliance due to reduced number of doses to be taken, cost-effective processing.

EUDRAGIT FOR GASTRO-RESISTANCE AND GI TARGETING

It protects the active ingredient from gastric fluid and will improve drug effectiveness. EudragitL and S polymers are the preferred choices of coating polymers. They enable targeting specific areas of the intestine. These anionic eudragit grades dissolve at rising PH values. In addition, different grades can be combined with each other, making it possible to adjust the dissolution pH and thus to achieve required GI targeting for drug [7]. Eudragitoffers valuable advantages for enteric coatings include pH-dependent drug release, increase in drug effectiveness, good storage stability, colon targeting and protection of actives sensitive to gastric fluid.

EudragitL and S polymers are copolymer based on methacrylic acid and ethyl acrylates. These are anionic, white free flowing powder with a weight average molar mass of approximately 125,000 g/mol. The various characteristics of eudragit L and eudragit S include effective and stable enteric coatings with a fast dissolution in the upper bowel, granulation of drug substances in powder form for controlled release, site-specific drug delivery in intestine by combination with eudragit S grades, variable release profiles.

Chemical structure of eudragit L (Eudragit L 100, Eudragit L 12.5), eudragit S (Eudragit S 100 and Eudragit S 12.5), eudragit L 30D-55 and eudragit L 100-55 has been depicted in Fig. 3.

The distinguishing characteristics of various grades of eudragit L (Eudragit L 100, Eudragit L 12.5, Eudragit L 30D-55 and Eudragit L 100-55) and eudragit S (Eudragit S 100 and Eudragit S 12.5) has been given in Table 2.

EUDRAGIT FOR MOISTURE PROTECTION AND TASTE MASKING

Eudragit offers a strong protection of sensitive contents and improved patient compliance. These polymers protect active ingredients from moisture or light and increase patient compliance. Eudragit E polymers help seal sensitive actives and increase patient compliance by taste and odor masking. Even thin layers of eudragit E provide the desired effect, making it an extremely economical application. Various cationic

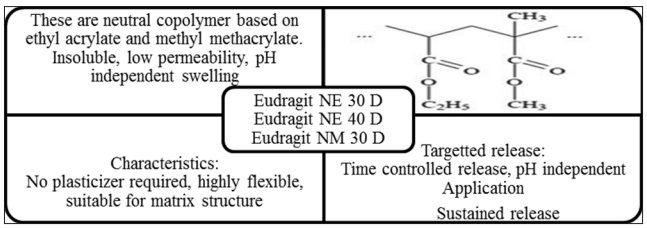

Fig. 2: Characteristics of eudragit NE 30 D, eudragit NE 40 D and eudragit NM 30 D

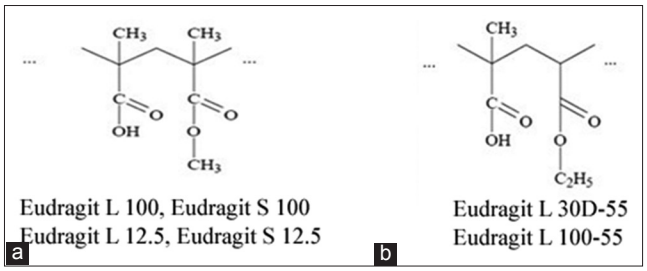

Fig. 3: Chemical structure of (a) eudragit L 100, eudragit S 100, eudragit L 12.5 and eudragit S 12.5 (b) eudragit L 30D-55 and Eudragit L 100-55

eudragit E grades with dimethyl-amino ethyl methacrylate as functional group provide protective coatings [6,7]. Various characteristics of eudragit E (Eudragit E 12.5, Eudragit E 100 and Eudragit E PO) has been given in Fig. 4. The distinguishing characteristics of various grades of eudragit E has been given in Table 3.

Advantage of protective eudragit coatings include pH-dependent drug release, taste and odor, masking, protection of sensitive actives against moisture, economical application, improved, transit of the dosage form, excellent color coating and smooth glossy surfaces.

DRUG RELEASE MECHANISM FROM EUDRAGIT POLYMERS

Drug release from oral sustained preparation of eudragit polymers is governed by following principles [4]:

Table 2: Distinguishing characteristics of various grades of eudragit L and eudragit S

Trade name	Form	Tg (°C)	Target drug release area	Physical properties	IUPAC name
Eudragit L 100	Powder	>130	Jejunum Dissolution above pH 6.0	White powder with faint odor	Poly (methacylic acid-co-methyl methacrylate) 1:1
Eudragit L 12.5	12.5% organic solution	>130	Jejunum Dissolution above pH 6.0	Colorless to slightly cloudy liquid, odor of isopropyl alcohol	
Eudragit S 100	Powder	>130	Colon Dissolution above pH 7	White powder with a faint odor	Poly (methacylic acid-co-methyl methacrylate) 1:2
Eudragit S 12.5	12.5% organic solution	>130	Colon Dissolution above pH 7	Colorless to slightly cloudy liquid, odor of isopropyl alcohol	
Eudragit L 30D-55	30% Aq. dispersion	96	Duodenum Dissolution above pH 5.5	Milky-white liquid of low viscosity with faint odor	Poly (methacylic acid-co-ethyl acrylate) 1:1
Eudragit L 100-55	Powder	96	Duodenum Dissolution above pH 5.5	White powder with faint odor	

Table 3: Distinguishing characteristics of various grades of eudragit E

Trade name	Form	Physical properties	IUPAC name
Eudragit E 100	Granules	Colorless to yellow tinged granules with a characteristic amine-like odor	Poly (butyl methacrylate-co-(2-dimethylaminoethyl) methacrylate-co-methyl methacrylate) 1:2:1
Eudragit E 12.5	12.5% organic solution	Light yellow liquid of low viscosity, clear to slightly cloudy, characteristic odor of the solvents	
Eudragit E PO	Powder	White powder with characteristic amine-like odor	

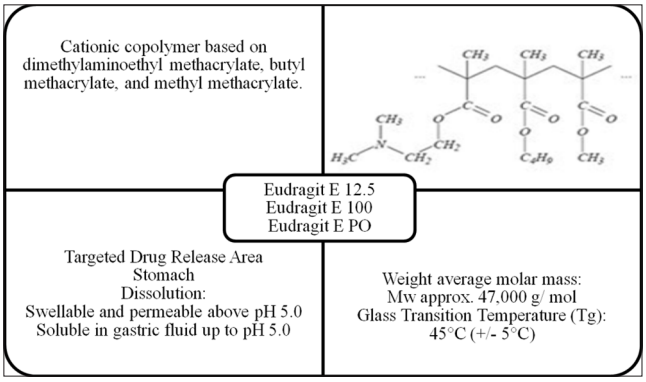

Fig. 4: Characteristics of various grades of eudragit E

- Dissolution
- Diffusion
- Osmotic pressure
- Ion-exchange.

DISSOLUTION

The rate-limiting step to absorption of drugs from the GIT is often dissolution from dosage form. Dissolution is the process by which a solid substance solubilizes in a given solvent i.e., mass transfer from the solid surface to the liquid phase. Dissolution controlled dosage forms can be divided into reservoir and matrix system. Eudragit S coated 5-ASA has dissolution to be the responsible mechanism of controlling drug release [8]. Dissolution release pattern is shown in Fig. 5 (a).

Diffusion

Diffusion is the movement of a substance down to concentration gradient i.e. drug molecules diffuse from high concentration to lower concentration in gastro intestinal fluids. Several factors that affect the rate of diffusion include temperature, density of the diffusing substance, medium of diffusion and concentration gradient. The release of propranolol HCL from monolithic matrix of eudragit NE 30 D was by a combination of diffusion through polymer and pores [9]. A desirable release profile of diphenhydramine was achieved by incorporating eudragit L in a carnauba wax matrix. The drug release from polymer-wax matrices is described by a combination diffusion/erosion mechanism [10]. Eudragit

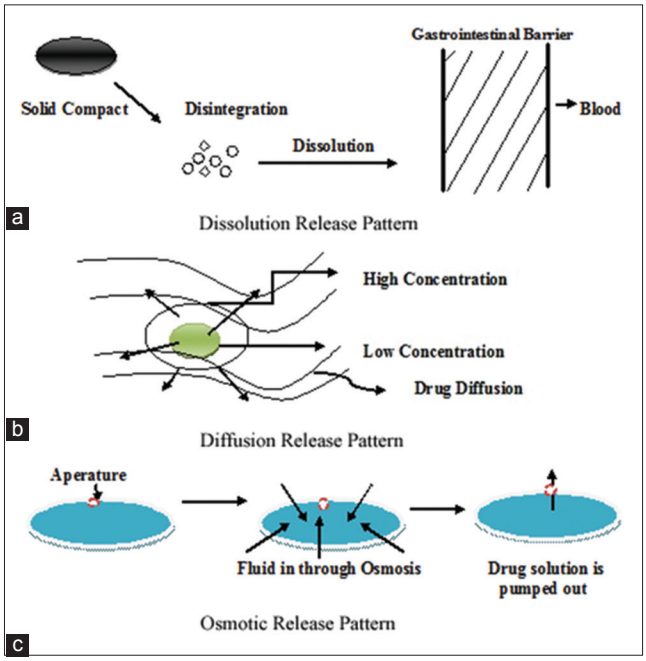

Fig. 5: Drug release mechanisms from polyacrylate polymers (a) dissolution release pattern (b) diffusion release pattern (c) osmotic release pattern

RS PO releases carbamazepine drug by complex mixture of diffusion and erosion mechanism [11]. Diffusion release pattern is shown in Fig. 5 (b).

Osmosis

Osmosis refers to the process of movement of solvent molecules from a lower concentration to higher concentration across semi-permeable membrane. The osmotic pressure created due to imbibitions of fluid from the external environment into dosage form regulates delivery of the drug from the osmotic device [12]. The release rate of drugs from osmotic dispensing devices is dependent on solubility and molecular weight and activity coefficient of solute. The osmotic release pattern is shown in Fig. 5 (c).

Ion-exchange

The use of ion exchange resins into drug delivery systems have been encouraged because of their physicochemical stability, inert nature, uniform size, spherical shape assisting coating and equilibrium driven reproducible drug release in the ionic environment. Ion exchange resins are cross-linked; water insoluble, polymer-carrying, ionizable functional groups. The drug is released from drug-resin complex by exchanging with ions in the GI fluid, followed by drug diffusion. Eudragit RS 30 D-coated theophylline beads proved ion exchange to be a responsible mechanism of controlling polymer permeability as a function of anionic species and concentration [13].

EUDRAGIT POLYMERS IN DRUG DELIVERY SYSTEM

Ophthalmic drug delivery

A major problem usually faced in ocular therapeutics is attainment of an optimal concentration at the site of action. Poor bioavailability of drugs from ocular dosage forms is mainly due to 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. Ana Rita *et al.* prepared ophthalmic drug delivery systems of acetazolamide using eudragit RS 100 and RL 100 by compressed anti-solvent technology. The prepared micro particles exhibited a slower release than the single drug. Drug release rate was controlled by a diffusion mechanism, however; polymer swelling also contributes to the overall transport mechanism [14].

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 [15]. Zhang *et al.* (2014) studied the ocular performance of a cationic eudragit (EDU) RS 100-coated genistein encapsulated NLC (GEN-NLC) produced by melt-emulsification technique followed by surface absorption of EDU RS 100. The obtained EDU RS 100-GEN-NLC showed extended precorneal clearance and significantly increased corneal penetration. The results indicate that NLC surface modified by EDU RS 100 significantly improves NLC properties and exhibits many advantages for ocular use [16].

BUCCAL AND SUBLINGUAL DRUG DELIVERY

It is estimated that permeability of buccal mucosa is 4-4000 times greater than that of skin. Sublingual delivery gives rapid absorption and good bioavailability for some small molecules, although this site is not well suited to sustained-delivery systems. The buccal mucosa, by comparison, is considerably less permeable, but is probably better suited to the development of sustained-delivery systems. For these reasons, the buccal mucosa may have potential for delivering some of the growing number of peptide drugs, particularly those of low molecular weight, high potency and long biological half-life [17]. In general, permeabilities of oral mucosae decrease in order of sublingual greater than buccal and buccal greater than palatal [18]. 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 [19].

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. 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 mouth for the desired duration. To prevent discomfort, swelling of film should not be too extensive. The mechanical, bio adhesive, and swelling properties of buccal films are critical [20]. For systemic drug therapy, buccal and sublingual routes are commonly used due to their trans mucosal permeability [21].

Sublingual mucosa is more permeable, thinner with a richer blood supply compared to buccal mucosa, producing a rapid onset of action which makes it appropriate for drugs with a short delivery period [22,23]. However the buccal mucosa is less permeable than the sublingual mucosa and it does not yield a rapid onset of action as seen with sublingual delivery. The mucosa of the buccal area has a large, smooth and relatively immobile surface, which is suitable for the placement of a retentive system and it offers sustained and controlled drug delivery [24,25]. 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 [26].

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 [27].

ORAL DRUG DELIVERY

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. Badir *et al*. prepared and evaluated eudragit vancomycin (VCM) nanoparticles by w/o/w double emulsion solvent evaporation method using eudragit RS as a retardant material. *In-vitro* release study showed biphasic release pattern; an initial burst for 0.5 hrs followed by a very slow release pattern during a period of 24 hrs. It was concluded that VCM nanoparticle preparations can be successfully utilized for oral sustained administrations [28].

Jingling *et al.* improved the oral bioavailability of genistein by preparing nanoparticles of genistein by nanoprecipitation technique using eudragit E100 as carriers. The release of drug from genistein nanoparticles was two times greater than that from the conventional capsules [29]. Momoh *et al.* formulated and evaluated eudragit RS100/RL100 microspheres by a solvent-evaporation technique for improved delivery of diclofenac sodium. Effective clinical utilization of non-steroidal anti-inflammatory drugs such as diclofenac sodium is significantly limited by ulcerogenic potential and poor bioavailability after oral administration. It was found that microsphere formulations based on eudragit® polymers would likely offer a reliable and alternative means of delivering DS orally [30].

Meltem *et al.* formulated and characterized eudragit L100 and eudragit L100-poly (lactic-co-glycolic acid) (PLGA) nanoparticles containing diclofenac sodium. Diclofenac generates severe adverse effects with risks of toxicity. It was demonstrated that efficacy of eudragit nanoparticles were efficacious in sustaining diclofenac sodium release profile [31].

COLON DRUG DELIVERY

The pH-sensitive polymers that dissolve, or above pH 7 are used for colonic drug delivery. Daniela *et al.* designed and evaluated colonic drug delivery system containing mesalamine (M). To facilitate this, a tablet core was coated with two thin layers. The first compounded by chitosan, which was responsible for core protection in the small intestine until it reached the colon. Once at the colon, microbiological enzymatic activity of the caecal content would degrade the Ch layer, thus triggering drug release. The second layer, outer one, was compounded with Eudragit L100 (EL), with its function being to avoid the dissolution of Ch-covered core along the GIT [32].

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 [33]. 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 [34].

Voltan *et al.* aimed to develop novel core-shell poly (methyl methacrylate) (PMMA) nanoparticles as a delivery system for protein vaccine candidates. Anionic nanoparticles consisting of a core of PMMA and a shell deriving from eudragit L100/55 were prepared by an innovative synthetic method based on emulsion polymerization. These nanoparticles can provide a versatile platform for protein surface adsorption and promising delivery system for vaccine delivery [35].

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 the genetic therapy. Basakar *et al.* prepared nanoparticles by blending PLGA with methacrylate copolymer (eudragit E100) which can efficiently and safely deliver plasmid DNA encoding mouse interleukin-10 leading for the prevention of autoimmune diabetes [36].

Wang *et al*. 2003 investigated the possibility of polymethacrylate nanoparticles for antisense oligodeoxynucleotides delivery system. The nanoparticles were prepared by evaporating ethanol solution containing eudragit RL100 or RS100 mixture with oligonucleotides. The polymethacrylate nanoparticles appeared to be a promising vehicle for gene delivery [37].

Gargouri *et al.* developed a new tool for DNA delivery composed of methacrylic polymeric (eudragit RS and RL) nanoparticles. These nanoparticles were prepared by nanoprecipitation and double emulsion technique. It was found that eudragit RS and RL nanoparticles could introduce transgene into different types of cells [38].

VAGINAL DRUG DELIVERY

Drug delivery via vaginal epithelium has suffered from lack of stability due to acidic and enzymatic environments. Yoo *et al.* developed biocompatible pH-sensitive nanoparticles containing sodium fluorescein or nile red using eudragit S-100 (ES) by modified quasi-emulsion solvent diffusion method. Prepared nanoparticles protected loaded compounds from being degraded under rigorous vaginal conditions and achieved their therapeutically effective concentrations in mucosal epithelium. It was concluded that pH-sensitive eudragit nanoparticles would be promising carrier for vaginal-specific delivery of various therapeutic drugs including microbicides and peptides/proteins [39]. Değim *et al.* prepared sildenafil-containing suppositories prepared using eudragit RS100 and witepsol H15. Among various formulations, the most suitable sildenafil release was found to be with sildenafil-containing suppositories prepared using eudragit RS100 and witepsol H15 [40].

TRANSDERMAL DRUG DELIVERY

Verma and Iyer developed a matrix-dispersion-type transdermal drug delivery system of propranolol using different ratios of mixed polymeric grades of Eudragit [41]. Baviskar *et al.* designed a matrix-type transdermal drug delivery system of lornoxicam was prepared with ethyl cellulose: Polyvinylpyrrolidone and eudragit RL 100: Eudragit RS 100 in different ratios with propylene glycol as plasticizer (5%) and Tween 80 as permeation enhancer using the solvent evaporation technique. Evaluation of these formulations was performed through mechanical characterization and *in-vitro* permeation studies. It was found that ethyl cellulose: Polyvinylpyrrolidone and Eudragit RL 100: Eudragit RS 100 can be successfully utilized for formulating transdermal patches of lornoxicam to sustain its release characteristics and to avoid disadvantages of oral routes [42].

Lade *et al.* prepared polymeric films containing budesonide using eudragit RL 100: eudragit RS: drug (7:3:1, 7:2:1) and ethyl cellulose: PVP: Drug (7:3:1, 7:2:1) by mercury substrate method employing polyethylene glycol-400 as plasticizer. Budesonide is highly potent synthetic, a non-halogenated corticosteroid. It was found that polyvinyl alcohol and eudragit RL 100 patches provides best resistance to water vapor and may provide more occlusion to water vapor loss from skin thus making atmosphere beneath the skin more humid that aid in drug permeation [43].

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 [44].

CONCLUSION

Eudragit polymers can produce sustained release formulations for time-controlled drug release, enteric formulations for GI targeting and protective formulations for moisture protection and odor/taste masking. These multifaceted applications of eudragit polymers in NDDS have made significant contributions to NDDS. It has been concluded that eudragit polymers can be significantly utilized as novel and versatile keystroke tool for fabrication of pharmaceutical formulation in future.

REFERENCES

1. Sintze MB, Bernatchez SF, Tabatabay C, Gurny R. Biomaterials in ophthalmic drug delivery. Eur J Pharm Biopharm 1996;42:358-74.
2. Nagai T, Machida Y. Mucosal adhesive dosage forms. Pharm Int 1985;6:196-200.
3. Le Bourlais CA, Treupel-Acar L, Rhodes CT, Sado PT, Leverge R. New ophthalmic drug delivery systems. Drug Dev Ind Pharm 1995;21:19-59.
4. Nikam VK, Kotade KB, Gaware VM. Dolas RT. Eudragit a versatile polymer: A review. Pharmacol Online 2011;1:152-64.
5. Raymond CR, Paul JS, Marian EQ. Handbook of Pharmaceutical Excipients. 6th ed. Washington, London: APHA Publications, Pharmaceutical Press; 2003. p. 525-33.
6. Available from: http://www.scribd.com/doc/5682786/Kollicoat-MAE-grades.
7. Available from: http://www.evonik.com.
8. Bodmeier R, Paeratakul O. Evaluation of drug-containing polymer films prepared from aqueous latexes. Pharm Res 1989;6(8):725-30.
9. Apurba SA, Atiqul HP, Dilasha S, Golam K, Reza-ul J. Investigation of *in-vitro* release kinetics of carbamazepine from Eudragit® RS PO and RL PO matrix tablets. Trop J Pharm Res 2009;8(2):145-52.
10. Wagner K, McGinity J. Influence of chloride ion exchange on the permeability and drug release of Eudragit RS 30 D films. J Control Release 2002;82(2-3):385-97.
11. Pignatello R, Bucolo C, Ferrara P, Maltese A, Puleo A, Puglisi G. Eudragit RS100 nanosuspensions for the ophthalmic controlled delivery of ibuprofen. Eur J Pharm Sci 2002;16(1-2):53-61.
12. Ghebre-Sellassie I, Gordon RH, Nesbitt RU, Fawzi MB. Evaluation of acrylic-based modified-release film coatings. Int J Pharm 1987;37:211-8.
13. Pignatello R, Bucolo C, Puglisi G. Ocular tolerability of Eudragit RS100 and RL100 nanosuspensions as carriers for ophthalmic controlled drug delivery. J Pharm Sci 2002;91(12):2636-41.
14. Duarte AR, Roy C, Vega-González A, Duarte CM, Subra-Paternault P. Preparation of acetazolamide composite microparticles by supercritical anti-solvent techniques. Int J Pharm 2007;332(1-2):132-9.

15. Verma P, Gupta RN, Jha AK, Pandey R. Development, *in vitro* and *in vivo* characterization of Eudragit RL 100 nanoparticles for improved ocular bioavailability of acetazolamide. Drug Deliv 2013;20(7):269-76.
16. Zhang W, Li X, Ye T, Chen F, Yu S, Chen J, *et al.* Nanostructured lipid carrier surface modified with Eudragit RS 100 and its potential ophthalmic functions. Int J Nanomedicine 2014;9:4305-15.
17. Harris D, Robinson JR. Drug delivery via the mucous membranes of the oral cavity. J Pharm Sci 1992;81(1):1-10.
18. Ch'ng HS, Park H, Kelly P, Robinson JR. Bioadhesive polymers as platforms for oral controlled drug delivery II: Synthesis and evaluation of some swelling, water-insoluble bioadhesive polymers. J Pharm Sci 1985;74(4):399-405.
19. Ali J, Khar RK, Ahuja A. Formulation and characterisation of a buccoadhesive erodible tablet for the treatment of oral lesions. Pharmazie 1998;53(5):329-34.
20. Nair MK, Chien YW. Development of anticandidal delivery systems, II: Mucoadhesive devices for prolonged drug delivery in the oral cavity. Drug Dev Ind Pharm 1996;22:243-53.
21. Hoogstraate AJ, Verhoef JC, Tuk B, Pijpers A, Van Leengoed LA, Verheijden JH, *et al*. Buccal delivery of fluorescein isothiocyanate-dextran 4400 and the peptide drug buserelin with glycodeoxycholate as an absorption enhancer in pigs. J Control Release 1996;41(1-2):77-84.
22. Squier CA, Wertz PW. Structure and function of the oral mucosa and implications for drug delivery. In: Rathbone MJ, editors. Oral Mucosal Drug Delivery. New York: Marcel Dekker Inc.; 1996. p. 1-26.
23. Giri TK, Badwaik H, Alexander A, Tripathi DK. Solubility enhancement of ibuprofen in the presence of hydrophilic polymer and surfactant. Int J Appl Bio Pharm Tech 2010;1:793-800.
24. Madhav NV, Shakya AK, Shakya P, Singh K. Orotransmucosal drug delivery systems: A review. J Control Release 2009;140(1):2-11.
25. Shakya P, Madhav NV, Shakya AK, Singh K. Palatal mucosa as a route for systemic drug delivery: A review. J Control Release 2011;151(1):2-9.
26. Diarra M, Pourroy G, Boymond C, Muster D. Fluoride controlled release tablets for intrabuccal use. Biomaterials 2003;24(7):1293-300.
27. Hao S, Wang B, Wang Y, Zhu L, Wang B, Guo T. Preparation of Eudragit L 100-55 enteric nanoparticles by a novel emulsion diffusion method. Colloids Surf B Biointerfaces 2013;108:127-33.
28. Delf Loveymi B, Jelvehgari M, Zakeri-Milani P, Valizadeh H. Statistical optimization of oral vancomycin-eudragit RS nanoparticles using response surface methodology. Iran J Pharm Res 2012;11(4):1001-12.
29. Tang J, Xu N, Ji H, Liu H, Wang Z, Wu L. Eudragit nanoparticles containing genistein: Formulation, development, and bioavailability assessment. Int J Nanomedicine 2011;6:2429-35.
30. Momoh MA, Kenechukwu FC, Adedokun MO, Odo CE, Attama AA. Pharmacodynamics of diclofenac from novel Eudragit entrapped microspheres. Drug Deliv 2014;21(3):193-203.
31. Cetin M, Atila A, Kadioglu Y. Formulation and *in vitro* characterization of Eudragit® L100 and Eudragit® L100-PLGA nanoparticles containing diclofenac sodium. AAPS PharmSciTech 2010;11(3):1250-6.
32. Quinteros DA, Manzo RH, Allemandi DA. Design of a colonic delivery system based on cationic polymethacrylate (Eudragit E100)-mesalamine complexes. Drug Deliv 2010;17(4):208-13.
33. Lee WJ, Cha S, Shin M, Jung M, Islam MA, Cho CS, *et al.* Efficacy of thiolated eudragit microspheres as an oral vaccine delivery system to induce mucosal immunity against enterotoxigenic Escherichia coli in mice. Eur J Pharm Biopharm 2012;81(1):43-8.
34. Dea-Ayuela MA, Rama-Iñiguez S, Torrado-Santiago S, Bolas-Fernandez F. Microcapsules formulated in the enteric coating copolymer Eudragit L100 as delivery systems for oral vaccination against infections by gastrointestinal nematode parasites. J Drug Target 2006;14(8):567-75.
35. Voltan R, Castaldello A, Brocca-Cofano E, Altavilla G, Caputo A, Laus M, *et al.* Preparation and characterization of innovative protein-coated poly(methylmethacrylate) core-shell nanoparticles for vaccine purposes. Pharm Res 2007;24(10):1870-82.
36. Basarkar A, Singh J. Poly (lactide-co-glycolide)-polymethacrylate nanoparticles for intramuscular delivery of plasmid encoding interleukin-10 to prevent autoimmune diabetes in mice. Pharm Res 2009;26(1):72-81.
37. Wang WX, Chen HL, Liang WQ. Study on polymethacrylate nanoparticles as delivery system of antisense oligodeoxynucleotides. Acta Pharm Sin 2003;38:298-301.
38. Gargouri M, Sapin A, Bouli S, Becuwe P, Merlin JL, Maincent P. Optimization of a new non-viral vector for transfection: Eudragit nanoparticles for the delivery of a DNA plasmid. Technol Cancer Res Treat 2009;8(6):433-44.
39. Yoo JW, Giri N, Lee CH. pH-sensitive Eudragit nanoparticles for mucosal drug delivery. Int J Pharm 2011;403(1-2):262-7.
40. Degim IT, Tugcu-Demiröz F, Tamer-Ilbasmis S, Acartürk F. Development of controlled release sildenafil formulations for vaginal administration. Drug Deliv 2008;15(4):259-65.
41. Verma PR, Iyer SS. Transdermal delivery of propranolol using mixed grades of Eudragit: Design and *in vitro* and *in vivo* evaluation. Drug Dev Ind Pharm 2000;26(4):471-6.
42. Baviskar DT, Parik VB, Jain DJ. Development of matrix-type transdermal delivery of lornoxicam: *In vitro* evaluation and pharmacodynamic and pharmacokinetic studies in albino rats. PDA J Pharm Sci Technol 2013;67(1):9-22.
43. Lade UB, Amgaonkar YM, Chikhale RV, Biyani DM, Umekar MJ. Design, formulation and evaluation of transdermal drug delivery system of budesonide. Pharmacol Pharm 2011;2:199-211.
44. Chandak AR, Prasad Verma PR. Eudragit-based transdermal delivery system of pentazocine: Physico-chemical, *in vitro* and *in vivo* evaluations. Pharm Dev Technol 2010;15(3):296-304.