POLYMERIC MATERIALS AS PLATFORMS FOR TOPICAL DRUG DELIVERY: A REVIEW

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ABSTRACT

With the emergence of novel and more effective drug therapies, increased importance is being placed upon the drug delivery technology. Topical formulations are attractive alternatives to oral formulations and offer several advantages, such as avoiding first-pass hepatic metabolism and gastric degradation. The major obstacle to drug delivery across the skin (transdermal) is the barrier nature of the skin which limits permeation of molecules. A wide range of polymeric materials is currently available for enhancing drug delivery to and across the skin. The synthetic polymers such as polyesters, polyamides, polyurethanes, poly anhydrides, and poly(orthoesters) display advantages of reproducibility of synthesis, a range of material properties, and biodegradability, while the natural polymers including polysaccharides, proteins, and lipids have been widely exploited because of the range of materials and properties available, particularly biocompatibility. This review summarises the important features of the widely different polymers which have guided their selection and application as drug carriers in topical drug delivery.

Keywords: Topical drug delivery, Polyester, Polyamide, Polyurethane, Polyanhydride, natural polymer, Polysaccharide, Protein, Lipid

INTRODUCTION

The last few decades have witnessed major academic and industrial efforts aimed at the development and application of polymeric materials for controlled drug delivery [1, 2]. Drug delivery systems can be defined as pharmaceutical dosage forms or formulations which are used to introduce drugs (active entities) into or onto the body. The aim of the delivery system is to transport an active entity to its site of action at a rate and concentration that both minimise side effects, and maximise therapeutic outcome. The successful design of a drug delivery system depends on drug properties, drug dose, route of administration, pathologic condition to be treated, desired therapeutic effect, mechanism of drug release, pharmacokinetics, and pharmacodynamics of drug action [3, 4]. In a broad sense, drugs are delivered to the human body by either enteral or parenteral drug administration. Enteral administration results in drug passing through the gastrointestinal tract to be absorbed into the bloodstream, whereas parental administration does not involve passage through the digestive tract. The enteral routes include oral, nasogastric, sublingual, buccal, and rectal routes, whereas the parenteral routes include topical, transdermal, intradermal, intranasal, subcutaneous, intramuscular, intravenous, endotracheal, intracardiac, intraosseous, inhalational, umbilical, and vaginal routes [5, 6]. In this review, we describe the various synthetic and natural polymers used for topical drug delivery applications and recent developments which hold promise for improving drug bioavailability and efficacy by this particular route of administration.

Topical drug delivery systems

Topical drug administration involves localised drug delivery to the body, for example, ophthalmic tissue, the vaginal epithelium, and skin for local or systemic effects. The main route of topical drug administration is the skin due to the fact that it is the largest human organ of the integumentary system [7, 8]. Topical formulations offer several advantages, such as avoiding first-pass hepatic metabolism and gastric degradation, they are non-invasive and are easy to apply and remove if needed [9, 10]. However, the greatest challenge with topical delivery to the skin is the limited number of drug molecules that can be effectively delivered through the skin in therapeutic quantities because of formidable barrier properties [11, 12].
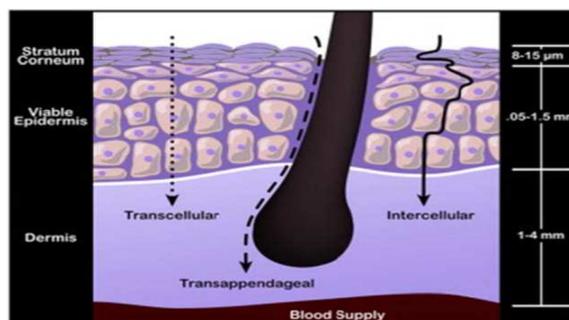

Fig. 1: Drug transport across skin (Source: Topical gel–A review) [12]

Topical drugs permeate into the skin via three pathways, transcellular, intercellular (paracellular), and trans appendageal (fig. 1) [12]. The transcellular route involves sequential partitioning of the drug in the cell and intercellular lipids while it traverses down through the skin layers. The intercellular route involves the movement of drug molecules through the lipid pathways between cells, while the trans-appendageal pathways involve the movement of molecules through skin appendages such as hair follicles and sweat glands.

The skin forms a major barrier which limits the permeation of drug molecules. In order to overcome this obstacle, drug molecules of low molecular weight (<500 Da) and intermediate lipophilicity (log P= 1-3) [13] are generally incorporated in a topical formulation that includes a combination of polymers selected from the class of polyesters, polyamides, and polyurethanes, polysaccharides, proteins, and lipids [14, 15]. In particular, polyesters and lipids are the two most common biomaterials utilised as drug carriers in topical drug delivery applications.

Polyesters

Polyesters can be broadly classified into three types, aliphatic, aromatic, and aliphatic-aromatic polymers. Aliphatic polyesters are generally biodegradable but have poor mechanical and physical

properties. In contrast, aromatic polyesters have excellent mechanical and physical properties but display poor or non-biodegradability when compared with aliphatic polyesters, since the aromatic ring is resistant to hydrolysis and enzymatic or microbial attack. Aliphatic-aromatic polyesters are designed to provide materials with optimum biodegradability materials and physical and mechanical properties [15]. However, their application as drug carriers has been limited, presumably due to long-term toxicological concerns.

To date, the aliphatic polyesters are the most widely studied class of polymeric materials for preparing topical pharmaceutical dosage

forms due to their diversity, versatility, and biodegradability [16]. Aliphatic polyesters can be prepared either by polycondensation of diols and dicarboxylic acids [30, 31] or synthesised from hydroxy acids, HO-R-COOH [17-19]. The common examples of aliphatic polyesters are polyglycolide (PGA), polylactide (PLA), polylactide-co-glycolide copolymers (PLGA), polycaprolactone (PCL), poly (β-hydroxyalcanoate) (PHA) and poly(butylene succinate) (PBS) [19, 20]. The origin and chemical structures of polyesters for pharmaceutical applications are listed in table 1, while their properties are summarised in table 2.

Table 1: Types of polyesters used in pharmaceutical applications

Types	Abbreviation	Origin	Chemical structures
Polyglycolide	PGA	Natural and Mineral	$\left[O-CH_2-\underset{\underset{O}{\|}}{C}\right]_n$
Polylactide	PLA	Natural and Mineral	$\left[O-\underset{\underset{}{\|}}{CH}(CH_3)-\underset{\underset{O}{\|}}{C}\right]_n$
Polylactide-co-glycolide	PLGA	Natural and Mineral	$\left[O-CH_2-\underset{\underset{O}{\|}}{C}\right]_m\left[O-\underset{\underset{CH_3}{\|}}{CH}-\underset{\underset{O}{\|}}{C}\right]_n$
Polycaprolactone	PCL	Mineral	$\left[O-(CH_2)_5-\underset{\underset{O}{\|}}{C}\right]_n$
Polyhydroxyalkanoate	PHA	Natural	$\left[O-\underset{\underset{R}{\|}}{CH}-CH_2-\underset{\underset{O}{\|}}{C}\right]_n$ where R refers to alkyl group
Poly(butylene succinate)	PBS	Mineral	$\left[O-(CH_2)_4-O-\underset{\underset{O}{\|}}{C}-(CH_2)_2-\underset{\underset{O}{\|}}{C}\right]_n$

Table 2: Properties of polyesters [21-30]

Polyester	Glass-transition temperature (°C)	Melting temperature (°C)	Crystallinity	Degradation time (months)
PGA	35-40	220-225	45–55%	6-12
PLLA and PDLA	50-70	170–190	~35%	>24
PDLLA	~60	Amorphous	Amorphous	12-16
PCL	-60	55-60	56-81%	24-36
scl-PHA	-8 to 9	80 to 180	40-80	3-9
mcl-PHA	-60 to 14	30 to 80	20-40	3-9
PBS	-45 to-10	90 to 120	35–40%	>2

Polyglycolide (PGA) is the simplest linear aliphatic polyester and is prepared by ring-opening polymerization of a cyclic lactone, glycolide [31]. High tensile strength PGA (12.5 GPa) has been investigated for bone fixation devices, resorbable sutures, and as tissue engineering scaffolds for cartilage, tendon, tooth, intestine, and spine regeneration. However, the use of PGA in topical drug delivery applications is limited by its low solubility and degradation behaviour which yields acidic products [32]. In order to tailor PGA to specific applications, glycolide has been copolymerized with a number of monomers including lactide [33-36].

Polylactide (PLA) may be prepared using three different methods: (i) direct condensation polymerization, (ii) azeotropic dehydrative condensation, and (iii) ring opening polymerization [37]. PLA is more resistant to hydrolysis than PGA because of the steric shielding effect of the methyl side groups,-CH3 [38]. Lactic acid occurs in two optically active forms, D-lactide (synthetic isomer) and L-lactide (natural isomer). Poly (D-lactide) (PDLA), Poly (L-lactide) (PLLA), and Poly (D, L-lactide) (PDLLA) are formed from D-lactide, L-lactide, and D, L-lactide monomers respectively [39]. PDLA and PLLA are semi-crystalline, PDLLA is amorphous [40]. The rate of degradation of PLA is influenced by the degree of crystallinity and is relatively low when compared to PGA. However, the biodegradability of PLA can be enhanced by either forming copolymers of lactide and glycolide or grafting PLA with other materials (e. g. chitosan) [38]. PLA is well known for its bio-resorbability, biocompatibility, mechanical strength, good processability, and solubility in organic solvents. Therefore it has

been employed to manufacture drug delivery devices, tissue engineering scaffolds and bioabsorbable medical implants. PLA has also been used to produce pellets, microcapsules, microspheres, and nanoparticles for sustained release and targeted delivery of conventional low molecular weight drugs, peptide/protein biopharmaceuticals, and RNA/DNA. For example, Rancan et al. prepared fluorochrome-loaded PLA particles for topical application and tested the delivery system on human skin explants. The results showed that PLA particles provided a constant release of the incorporated fluorochrome for 16 h and were potentially suitable for topical dermato-therapy [41].

Polylactide-co-glycolide (PLGA) is a copolymer composed of GA and LA monomers. PLGA with lactide or glycolide content less than 70% is amorphous in nature and is approved by the US Food and Drug Administration (FDA) for use in humans [42]. Various poly (lactide-co-glycolide) copolymers with different ratios of lactide and glycolide have been commercially developed and are being investigated for biomedical and pharmaceutical applications, such as bioresorbable polymer meshes, sutures, skin replacement materials, and dura mater substitutes. The major popularity of this polymer can be attributed in part to their approval by the FDA for use in humans, good processability which enables fabrication of a variety of structures and forms, controllable degradation rates, good cell adhesion, and proliferation. As such, there has been an extensive investigation of PLGA for drug delivery and tissue engineering applications.

Even though PLGA can undergo surface erosion in some conditions, bulk erosion through hydrolysis of the ester bonds is still the main degradation pathway. The rate of degradation depends on hydrophobicity, crystallinity, glass transition temperature, lactide/glycolide ratio, the molecular weight of the polymer, the shape and structure of the polymer. The composition containing 1:1 of PLA and PGA was shown to be hydrolytically unstable, and the resistance to hydrolysis increases with increasing proportion of either lactide or glycolide. Furthermore, the biodegradability and drug release properties of PLGA can be modified by altering the lactide/glycolide ratio. PLGA with 1:1 lactide: glycolide ratio is commonly used in the preparation of topical nanoparticle formulations [43–45].

PLGA microparticles have been developed for the topical administration of rhodamine [46]. Permeation experiments demonstrated that microparticles effectively entered porcine ear skin through the stratum corneum and reached the epidermis for sustaining drug release. Hrynyk *et al.* prepared insulin-loaded PLGA microspheres for topical applications [47]. Sustained release of insulin from the PLGA microsphere for up to 25 d indicates promise in promoting cutaneous wound healing. Shi *et al.* showed that 5-Aminolevulinic acid-loaded PLGA nanoparticles increased the killing effects of topical 5-aminolevulinic acid photodynamic therapy for skin squamous cell carcinoma [48].

Polycaprolactone (PCL) is a polyester obtained from a low-cost monomeric unit "ε-caprolactone". PCL is approved by the FDA and has been used for the production of sutures, implants, tissue engineering scaffolds and drug delivery systems [49-51]. PCL has been extensively investigated as compatibilizer or 'soft block' in polymer synthesis, particularly polyurethanes. The various biomedical applications of PCL exploit the polymer's high elongation (4700%), good mechanical properties and ease of processing. In drug delivery, PCL's low Tg (−60 °C) results in high permeability to low molecular weight drug species at ambient and body temperature. Furthermore, PCL is soluble in a wide range of solvents, biocompatible, and the degradation products are eliminated through metabolic pathways without producing local acidic environments which could adversely affect drug release and/or drug activity [52-54]. Owing to the high degree of crystallinity and hydrophobicity, PCL is more resistant to hydrolysis than other polyesters and the low biodegradability permits sustained release of drugs over extended time periods of up to one year, for example. Taken together, these properties make PCL a promising candidate for topical drug delivery. Rosado et al., for example, reported that the encapsulation of hydrocortisone in PCL nanoparticles could improve control of atopic dermatitis and minimise side effects [55].

Poly (β-hydroxyalcanoates) (PHA) are natural polyesters produced by bacterial fermentation [56-60] that are thermoplastic, biocompatible and biodegradable and their properties can be tuned by altering the chemical composition (fig. 2). To date, more than 150 different monomer units have been identified as the constituents of PHAs. PHAs can be classified into 3 groups based on the number of carbons in their repeating units; short-chain-length PHA (scl-PHA), medium-chain-length PHA (mcl-PHA), and long-chain-length PHA (lcl-PHA). The scl-PHA, mcl-PHA, and lcl-PHA contain 4-5 carbons, 6-14 carbons, and>14 carbon atoms in their repeating units, respectively (table 3). However, scl-PHA and mcl-PHA demonstrate a broader spectrum of properties that have led to extensive use in various applications.
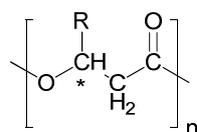

Fig. 2: The chemical structure of polyhydroxyalkanoate (PHA). Asterisk denotes the chiral centre of the PHA-building block. The nomenclature for PHA compounds is determined by the functional alkyl R group

Table 3: The R group, total carbon number in PHA monomer and the nomenclature for PHA (Source: Poly (3-Hydroxyalkanoates): Biodegradable Plastics. Research and Reviews) [57]

R group	Total carbon number in PHA monomer	Nomenclature for PHA
Methyl	C_4	Poly(3-hydroxybutyrate)
Ethyl	C_5	Poly(3-hydroxyvalerate)
Propyl	C_6	Poly(3-hydroxyhexanoate)
Butyl	C_7	Poly(3-hydroxyheptanoate)
Pentyl	C_8	Poly(3-hydroxyoctanoate)
Hexyl	C_9	Poly(3-hydroxynonanoate)
Heptyl	C_{10}	Poly(3-hydroxydecanoate)
Octyl	C_{11}	Poly(3-hydroxyundecanoate)
Nonyl	C_{12}	Poly(3-hydroxydodecanoate)
Decyl	C_{13}	Poly(3-hydroxytridecanoate)
Undecyl	C_{14}	Poly(3-hydroxytetradecanoate)
Dodecyl	C_{15}	Poly(3-hydroxypentadecanoate)
Tridecyl	C_{16}	Poly(3-hydroxyhexadecanoate)

Poly (3-hydroxy butyrate) (PHB) was the first bacterial PHA identified in 1925 by Lemoigne [61]. PHB exhibited high potential for industrial applications due to its high crystallinity (50-70%), excellent gas barrier properties, good elastic modulus (3 GPa), and tensile strength at break of 25 MPa, which are similar to polypropylene. However, PHB found limited application due to high fragility, low impact resistance, and narrow processing temperature range. To overcome these shortcomings, PHB was copolymerized with other monomers especially 3-hydroxyvaleric acid, (HV). The piezoelectric properties associated with these polyesters made them attractive for orthopaedic applications (e. g. bone plates) as they may stimulate bone growth. PHA and their copolymers have found limited application for topical drug delivery, Wang, *et al.* reported that dendrimer-containing PHA matrix enhanced penetration of a model drug (tamsulosin) through shed snake skin [62]. Eke *et al.* demonstrated that PHBV microparticles and nanoparticles offered potential as topical formulations for use on aged or damaged skin or in cases of skin diseases including psoriasis [63].

Poly (butylene succinate) (PBS) is an aliphatic semicrystalline polyester that is produced by condensation of succinic acid and 1,4-butanediol [64-66]. In general, PBS is tough in nature and possess excellent tensile and impact strengths with moderate rigidity. The mechanical properties and biodegradability of PBS depend on the crystal structure and the degree of crystallinity. The low flexibility of PBS limits the applications of 100% PBS-based products. Thus PBS has been blended with other materials to improve the mechanical properties, and the blends have found application in skin tissue engineering and drug delivery. For example, Brunner *et al.* have developed PBS and PBS copolymer microcapsules for controlled delivery of both hydrophilic and hydrophobic drugs [67]. The microcapsules exhibited-sustained delivery of both bovine serum albumin (BSA) and all-trans retinoic acid (atRA). However, the hardness of PBS and their copolymers is expected to limits their use in the preparation of topical formulations.

Polyamides

Polyamides, where the repeating units are held together by amide groups (CO-NH), may be produced by polymerization of amino acids (molecules containing both amino and carboxyl groups), or the interaction of an amine (NH_2) group and a carboxyl (CO_2H) group [68, 69]. In general, polyamides are tough materials with high-performance characteristics such as outstanding mechanical strength, ductility, good thermal resistance and excellent chemical resistance. Polyamides are not generally biodegradable. Therefore recent attention has focused on bio-based polyamides obtained from fully renewable resources and poly (ester-amide) copolymers. As a result of the strong hydrogen bonding ability of amide bonds and the biodegradability imparted by the ester bonds, poly(ester-amide)s have been used in various biomedical applications including bioresorbable suture materials, drug-eluting dressings for burns

treatment, vascular patches, gene delivery vehicles for transfection purpose, coating materials for metallic drug-eluting stents and wound closure biomaterials. Poly (ester-amide)s have also been used in various drug delivery applications, including anticancer drug delivery [70].

Polyurethanes

Polyurethanes (PU, fig. 3) are linear polymers comprising a molecular backbone containing urethane or carbamate groups ($-NHCO_2$). Polyurethane was first studied by the German chemist, Bayer in 1937 [71] and is traditionally formed by reacting a diisocyanate (OCN-R-NCO) with a diol (HO-R-OH). Normally, PU is prepared from three constituents: a diisocyanate, a long chain diol (polyol), and short chain diol (chain extender) [72, 73] forming segmented polymers with alternating hard and soft segments.

The hard segment is obtained from diisocyanates and short chain diols, whereas the soft segment is derived from long chain diols (e. g. polyester polyols and polyether polyols). The soft segment is flexible at room temperature due to the very low density of urethane groups (low polarity), while the hard segment is rigid at ambient temperature due to the high density of urethane groups (high polarity).
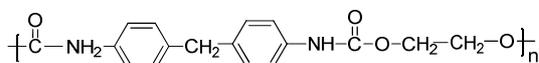

Fig. 3: The chemical structure of polyurethanes

The degradation rate of PUs can be controlled by choice of soft segments. Polyether-based polyurethanes display improved resistance to hydrolysis compared with polyester-based polyurethanes, which are usually biodegradable due to breakage of ester bonds in the soft segments. Development of water-borne PU or poly (urethane-urea) responded to the environmental need to control volatile organic compound emissions and to reduce costs. The resulting polyurethanes have wider application, non-toxicity, and are more environmentally-friendly compared with conventional polyurethanes. PUs have been developed primarily to meet the demands of the adhesives, fibres, elastomers, and coatings industry [74-78]. However, increasing use of biodegradable polyurethanes is predicted in tissue engineering, including, nerve regeneration, and drug delivery.

Polyanhydrides

Polyanhydrides contain two hydrolyzable sites in the repeating unit as shown in the fig. 4. They can be prepared by various methods, such as ring opening polymerization of anhydrides, melt-polycondensation of diacids or diacid esters and interfacial condensation [79, 80]. Aliphatic homo-poly anhydrides have limited applications due to high biodegradability, and thus poly anhydrides are often prepared as copolymers, in which the degradation rate depends on the nature of the monomeric species, particularly the hydrophobic and hydrophilic character.

For example, an increase in the hydrophobicity of the diacid building blocks of the polymer results in slower degradation. In order to enhance the mechanical strength of poly anhydrides, copolymers were developed containing imide groups. Polyanhydrides are unsuitable for thermoplastic processing due to their highly hydrolytic nature. Nevertheless, poly anhydrides are widely used for short-term controlled drug delivery applications where rapid degradation is essential including the preparation of microspheres, *in situ* forming degradable networks for orthopaedic applications, and localised drug delivery systems [81-83].
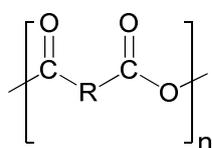

Fig. 4: The chemical structure of poly anhydrides

Poly (orthoesters)

Poly (orthoesters), (POE), are hydrophobic, surface eroding polymers designed specifically for drug delivery applications [84-86]. Although the ortho ester linkages are hydrolytically labile, the polymer is sufficiently hydrophobic such that its rate of erosion in aqueous environments is very low. The rate of degradation, pH sensitivity, and glass transition temperatures of POE may be controlled by using diols with varying levels of chain flexibility. The rate of drug release is predominantly controlled by the rate of polymer hydrolysis through the use of acidic or basic excipients.

POE can be classified into four types, designated as POE 1, POE II, POE III, and POE IV. POE I (fig. 5) is synthesised via transesterification between a diethoxy tetrahydrofuran and diol. The hydrolysis product of POE I, e. g. γ-hydroxybutyric acid has an autocatalytic effect on further degradation of the polymer.
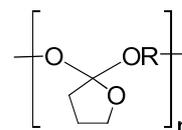

Fig. 5: The chemical structure of POE I

POE II (fig. 6) is produced from the reaction of diols with diketene acetal 3, 9-bis (ethylidene 2, 4, 8, 10-tetraoxaspirol [5,5] undecane). The autocatalytic effect of POE I is absent in POE II and its degradation products are neutral molecules. The degradation rate of the polymer may be modulated by adding acid excipients such as itaconic and adipic acids.
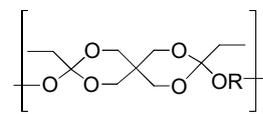

Fig. 6: The chemical structure of POE II

POE III (fig. 7) is prepared by direct polymerization of a triol with an orthoester. POE III is made up of highly flexible polymer chains, thus making it a gel-like material at room temperature. Its viscous nature allows for the incorporation of therapeutic agents into the polymer matrix without the need for solvents.
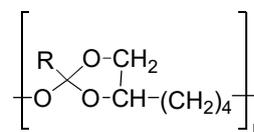

Fig. 7: The chemical structure of POE III

POE IV (fig. 8) is achieved by incorporating short segments based on lactic or glycolic acid into the POE backbone. The rate of degradation can be controlled by changing the amount of the acid segment in the polymer backbone, while solid materials or soft gel-like materials can be obtained by varying the nature of the diol.
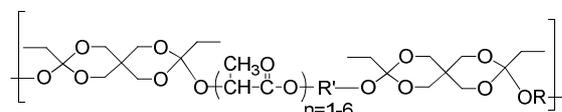

Fig. 8: The chemical structure of POE IV

Among the four different classes of POEs, POE IV is considered to be the biomaterial with greatest potential having not only a scalable procedure for synthesis, but also the ability to provide well-controlled release profiles for a wide range of pharmaceutical agents, including proteins.

Natural polymers

Due to environment concerns, natural polymers obtained from renewable resources have attracted increasing attention in recent years [87-89]. These polymers are formed in nature during the growth cycles of all organisms, and there are three main renewable resources: polysaccharides, proteins, and lipids.

Polysaccharides can be homo-or hetero-polymers [90, 91] and may be obtained from marine and vegetal sources. The common examples from marine sources are chitin and chitosan; while the common examples from vegetal sources are starch, cellulose, and alginic acid (alginate). Polysaccharides, such as hyaluronic acid and chondroitin sulphate, are of human origin.

Proteins are heteropolymers made up of different polar and non-polar α-amino acids [92-94]. Proteins offer a wide range of functional properties and are always used in their natural form due to most proteins being neither soluble nor fusible. The biodegradation of proteins is commonly achieved by amine hydrolysis using enzymes such as proteases. Proteins can be obtained from animal or vegetal sources. The common examples of proteins from animal sources for biomedical applications are silk, gelatin, collagen, elastin, albumin, and fibrin. The common examples of proteins from vegetal sources are wheat gluten, soy protein, peanut, and whey protein.

Lipids could be considered a type of homopolymer is comprising–CH_2 units since there are some arguments for considering lipids as polymers. They constitute a very broad class of organic macromolecules due to the variety of types and sources such as neutral fats, oils, and waxes [95-97]. lipids (e. g. vegetable oils, fatty acids, glycerides, and fatty acid esters) have been shown to be highly advantageous materials for pharmaceutical applications, particularly topical formulations, including liposomes, solid lipid nanoparticles, micro-and nanoemulsions [98-102]. In particular, nanoemulsions prepared from lipids have attracted widespread and increasing interest for oral and topical delivery of anti-inflammatory and anti-cancer compounds (table 4). This is explained by a unique properties spectrum including small droplet size (<100 nm), physical stability, the ability to reduce the cytotoxicity of drugs and the ability to solubilize high quantities of hydrophobic actives. The common lipids that have been extensively researched for emulsions preparation include soybean oil, isopropyl myristate, turmeric oil, clove oil, miglyol 812 liquid oil, isopropyl myristate, cinnamon oil, and virgin coconut oil since the choice of the oil phase in single oil-based emulsions significantly affects the spontaneity of the emulsification process. However, maximising drug solubility, ease of emulsification and drug release kinetics is acknowledged to be problematical in a single oil system, thus making a combination of oil phases necessary to achieve the optimum emulsion formulation with the required range of properties.

Table 4: Nanoemulsions: type of lipid, drug, route of administration and application [98-102]

Type of lipid	Drug/Bioactive compound	Route of administration	Application
Soybean oil	Doxorubicin	Intravenous	Anti-tumor
Soybean oil	Indinavir	Intravenous	In the treatment of HIV infection
Triacetin and anseed oil	Aceclofenac	Oral	Anti-inflammatory analgesic activity
Eucalyptus oil	Clobetasol propionate	Topical	Antipsoriatic activity
Isopropyl myristate	Dapsone	Topical	Leprosy
Tumeric oil	-	Topical	Antipsoriasis
Clove oil	Miconazole nitrate	Topical	Antifungal activity
Miglyol 812 liquid oil	Chalcones	Oral	Targeted cancer chemotherapies
Isopropyl myristate	Baicalin	Oral	Treatment of fever and inflammation
Cinnamon oil	Fluconazole	Oral	Potential anti-fungal applications
Virgin coconut oil	Ketoprofen	Topical	Anti-inflammation applications

Conclusion and outlook

The selection of natural and synthetic polymers for formulating topical drug delivery systems can usually be attributed to their approval by the FDA for use in humans, the required balance of physicochemical properties, biodegradability, biocompatibility and, processability. These polymers are increasingly being formulated as nano-sized drug carriers that are showing great promise for topical application in the treatment of skin diseases [103]. Stimuli-responsive or "smart" polymers, particularly temperature and pH-responsive types, are also becoming established as an important class of materials for topical delivery [104]. Possibilities have long existed to combine antimicrobial compounds with different types of the polymeric carrier in wound dressings, and this area is experiencing a rise in research activity due to the major healthcare and cost burdens placed on society by non-healing wounds. Polymers originating from advanced macromolecular design and synthesised via controlled/living polymerization techniques (ATRP, RAFT, ROP, anionic polymerization) and click chemistry are also being investigated for topical drug delivery applications. Whilst recognizing the potential of new polymers as drug carriers, progressive interdisciplinary research is essential to convert promising topical drug delivery systems into clinically available efficacious preparations which improve drug bioavailability and therapeutic efficacy while minimising side effects.

CONFLICT OF INTERESTS

Authors declare no conflict of interest in the research

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