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The Brief Review on Pharmaceutical Polymer

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Abstract: The current review article focuses on polymers in pharmaceutical drug delivery of therapeutic agents. These dosage forms include tablets, patches, tapes, films, semisolids and powders. Polymers are the backbone of a pharmaceutical drug delivery system as they control the release of the drug from the device. Biodegradable polymers attract the attention of its use as they can be degraded to non-toxic monomers and most important, a constant rate of drug release can be achieved from a biodegradable polymer based controlled release device. Natural polymers can be used as the means of achieving predetermined rates of drug delivery and their physio-chemical characteristics with the ease of availability provide a platform to use it as a polymer for drug delivery systems , We are developing synthetic polymers for pharmaceutical and medical applications. These applications can be broadly grouped on how the polymer will be utilized.

Keywords:Polymer ,Dosage form, Natural polymer, Applications.

I. Introduction:

Over the past decades research at the level of molecular biology has unveiled the molecular basis for many diseases. New important technologies and concepts such as recombinant DNA and gene therapy have provided tools for the creation of pharmaceuticals and methods designed to specifically address such diseases. However progress towards the application of these medicines outside of the laboratory has been considerably slow principally due to the lack of effective drug delivery systems that is mechanisms that allow the release of the drug into the appropriate body compartment for the appropriate amount of time without seriously disrupting the rest of the organism functionality. The application of the polymeric materials for medical purposes is growing fast. Polymers have found applications in diverse biomedical fields such as drug delivering systems, developing scaffolds in tissue engineering, implantation of medical devices and artificial organs, prosthesis, ophthalmology, dentistry, bone repair, and many other medical fields[1]

The word “polymer” is derived from the Greek πολυ (Polu) for “many” and μερος (meros) for “part,” meaning a long-chain consisting of many parts. The combination of repeating units to form long chains with widely variable length and structure is essential in determining the properties and applications of the resulting polymers, as the diversity of polymer properties is attributed to the simple fact that each polymer molecule consists of many parts with individual variations in sequence of repeating units and chain length. In contrast to substances comprised of small molecules that are well defined and identified by a set of system variables, including basic physical properties, states, or characteristics with unique and discrete values, polymers are less well defined or characterized in the conventional sense. This applies to even the simplest of polymeric systems. For example, substances comprised of small molecules have a distinct molecular weight, with each molecule having exactly the same nominal mass, neglecting, for the moment, the multiple natural isotopes possible for the atomic constituents. Polymers, on the other hand, are characterized by a diverse population in which there is a broad distribution of molar masses across the entire chain population. This is well known and clearly understood, since polymers are simply chains of many monomeric residues covalently linked together. For small molecules, it can be clearly defined if a molecule is in solution or not. Such a clear distinction may not be applied to polymers. It is quite possible for extended segments of a long polymer chain to effectively reside in bulk solution, while other parts still reside in a bulk polymer solid phase. Conceptually, the polymer chain is not completely in solution, yet the behaviour of this system is

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clearly very different from the one where an unswollen polymer sample is sitting unsolved in a sea of solvent. The state of an unswollen polymer is not a fluid or solution by traditional definition. Distributions in properties, states, and characteristics are what set the behaviour of many polymers apart from small molecules in general. Understanding the operational impact of this difference is the first step in rational characterization and applications of polymeric materials. [17]

Current challenges for the development of degradable polymers include optimization of structure–property correlations in respect to the biological profile and performance that are expected to change with time due to degradation processes, and maintenance of an acceptable toxicity profile over time. While there are many other important issues (e.g. manufacturing biomedical polymers at pilot scale under GMP conditions), regardless of the application or whether the polymer is degradable or non-degradable, toxicological considerations are crucial. [2]

Polymers have an indispensable role from packaging to drug delivery systems (DDS) in pharmaceuticals. Their roles in DDS include either as a solubilizers, stabilizers, taste-masking, release-modifiers, bioavailability enhancers, carriers for drug payload or to provide mechanical supports as in bone scaffolds. A large number of naturally occurring and synthetic polymers such as starch, cellulose derivatives, polyesters, polyanhydrides, etc. are currently used in DDS. Some of the United States Food and Drug Administration (US FDA) approved biodegradable polymers are N-(2-hydroxypropyl) meth acrylamide (HPMA), polyethylene glycol (PEG), poly(L-lactic acid) (PLA), poly(glycolic acid) (PGA), poly(D,L-lactic-co-glycolic acid) (PLGA) and polycaprolactone (PCL). However, PEG is a benchmark and a polymer of choice1 . US FDA's Inactive Ingredient Guide (IIG) (also referred as Inactive Ingredient Database (IID)) lists use of PEGs in oral, topical and intravenous formulations, it also describes the maximum concentration of PEGs used in that composition.[3]

Excipients are inactive constituents they are deliberately , added to the formulation to produce effective dosage forms with desired properties and a robust manufacturing process. Principal examples of excipients include: fillers, binders, diluents, wetting agents, solvents, preservatives, Flavors, coating agents, colouring agent, ant adherents, glidants, sorbents, and surfactants. Although pharmaceutical excipients are not anticipated to provide any therapeutic effects, excipients often alter the performance of the delivery system. For example, some excipients may promote enhanced absorption of the API from the gastrointestinal (GI) tract while other excipients facilitate a tailor-made release of the APIs from the dosage form. In contrast, inappropriate selection of pharmaceutical excipients in the dosage form may hamper the performance of the dosage form and may thereby lead to a therapeutic failure. For instance, some excipients may affect the uptake of drugs from human transporting proteins.[4]

Excipients are additives used to convert the active pharmaceutical ingredients into dosage forms suitable for administration to patients, Synthetic polymers offer a broad range of properties that can be reasonably well ―built- in‖ by design and modified by altering polymer characteristics. Plant products are therefore, attractive alternatives to synthetic products because of biocompatibility, low toxicity, environmental ―friendliness and low price compared to synthetic products. Natural gums obtained from plants have diverse applications in drug delivery as a disintegrant, emulsifying agent, suspending agents and as binders. They have also been found useful in formulating immediate and sustained-release preparation[5]

Chitosan is a natural cationic biopolymer consequent commencing the hydrolysis of chitin. One perceptible improvement of this substance is that it can be obtained from ecologically sound natural sources, namely crab and shrimp shell wastes. Together with chitin, Chitosan is well thought-out the second most profuse polysaccharide subsequent to cellulose. However contrasting cellulose, the employ of Chitosan as an excipient in pharmaceutical formula is a pretty new development. But Chitosan has been widely premeditated in the biomedical field and has been found to be highly biocompatible. In addition to the good biocompatibility of Chitosan and the abundance of natural sources of the material, Chitosan has a number of enviable properties that put together study of it attention-grabbing[10]

Reversed-phase HPLC (RP-HPLC) is by far the most popular LC technique for pharmaceutical analysis , As the technique is characterized by the use of a polar stationary phase (SP) and a polar mobile phase (MP), retention increases with decreasing polarity of the analysed compounds and/or SP, and/or with increasing MP polarity. The most hydrophilic (polar) compounds elute first, and the most hydrophobic (a polar) last. The main drawback of RPHPLC is the insufficient retention of very polar compounds. Normal-phase LC (NPLC) , on the contrary, features a polar SP

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and a polar MP. Consequently, retention increases with increased polarity of the analysed compounds and/or the SP, and/or with decreased MP polarity. The elution sequence goes from the least to the most hydrophilic compound. The main drawbacks are the use of quite expensive, toxic, and environmental unfriendly MP solvents (e.g. heptane, hexane, pentane, cyclohexane), and the often-observed poor solubility of hydrophilic (pharmaceutical) components in these solvents[13]

➢ **Definition**

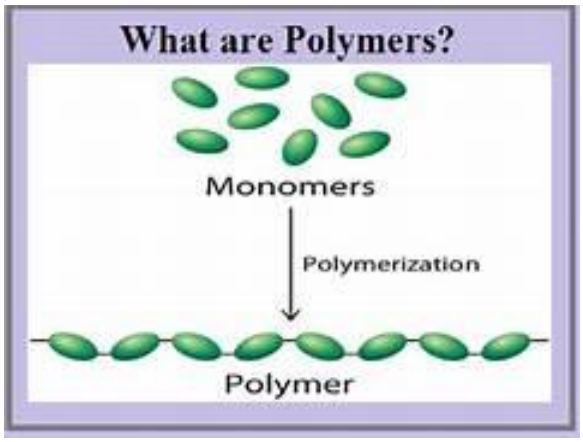

Fig no . 1: polymer [6]

The gross architecture of a polymer chain can be readily assessed by asking whether the chain or chain assembly can be mapped onto a one-(linear), two(branched), or three- (cross-linked network) dimensional object ,In general terms, these distinctions reflect the natural spatial connectivity imparted by these chains when placed into a volume element, either in formal solution, a melt, or the solid state.

How a polymeric chain mechanically couples to and transports within a medium comprised of either other polymeric materials or low molecular weight solvent is determined in part by the gross topology of the chain system. Ultimately, the key physical attributes are the length, scale, and nature of connectivity between volume elements in solution, gel, melt, or solid states and how that connectivity propagates through space.

If one takes a linear chain and stretches it, a simple line is obtained. By the same token, the lowest

Table no. 2 commonly used polymer in solid oral dosage [17]

Polymers	Majorfunctionality	Applications	Typical use levels (%)	IID or IIG limit
WATER-INSOLUBLE NATURAL/MODIFIED POLYMERS				
Cellulose, microcrystalline (MCC) $(C_6H_{10}O_5)_n$, n B220	Binder/filler	Tablet and capsules	1090	789.6 mg
Cellulose, powdered $(C_6H_{10}O_5)_n$	Filler	Tablet and capsules	540	391.7 mg
Cellulose, silicified, microcrystalline (SMCC), (C6H10O5)n. SiO2	Binder/filler	Tablet and capsules	1090	N/A
Cellulose acetate (CA) $(C_6H_7O_2(OH)_3)_n$	Coating for osmotic pump	Osmotic pump	120	47.49 mg
Ethyl cellulose (EC) C12H23O6(C12H22O5)nC12H23O5	Coating/binder	Extended-release coating/ matrix former	130	308.8 mg
Croscarmellose sodium (NaCMC) $(C_8H_{16}O_8)_n$	Disintegrant	Tablet and capsules	0.525	180 mg
Sodium starch glycolate (SGS) $(C_{24}H_{44}O_6N_a)_n$	Disintegrant	Tablet and capsules	28	876 mg
WATER-INSOLUBLE SYNTHETIC POLYMERS				

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Crospovidone $(C_6H_9NO)_n$	Disintegrant	Tablet and capsules	230	340 mg
Polyacrylic acid (carbomer; Carbopol), $(C_3H_4O_2)_n$	Rheology modifier/controlled release	Tablets, suspension	0.130	90 mg
Polymethacrylate, cationic	Coating/binder	Extended-release coating/ matrix former	550	161 mg
Polymethacrylate, neutral	Coating/wet binder	Extended-release coating/ matrix former	550	187.3 mg
WATER-SOLUBLE NATURAL/MODIFIED NATURAL POLYMERS				
Hydroxyethyl cellulose (HEC) $[C_6H_7O_2(OH)_x(OC_2H_5)_y[O(CH_2CH_2O)_mH]_z]_n$	Coating/rheology modifier	Tablet, suspension, pellets	250	400 mg
Hydroxypropyl cellulose (HPC) $(C_{36}H_{70}O_{19})_n$	Binder/coating/controlled-release matrix, extrusion aid	Tablet, capsules, pellets	150	240 mg
Hydroxypropyl methylcellulose (HPMC or hypromellose) $(C_{56}H_{108}O_{30})_n$	Binder/coating/controlled-release matrix	Tablet, capsules, pellets	175	480 mg
Methyl cellulose (MC) $C_6H_7O_2(OH)_x(OCH_3)_y$	Coating/binder/rheology modifier	Tablet, suspension, capsules	0.520	30 mg
Sodium alginate $(C_6H_7O_6Na)_n$	Coating/controlled-release matrix/ rheology modifier	Tablet, capsules, pellets	140	350 mg
Sodium carboxymethyl cellulose (NaCMC) (C8H15NaO8)n	Binder/coating/controlled-release matrix/rheology modifier	Tablet, capsules, pellets	0.190	2000 mg
WATER-SOLUBLE SYNTHETIC POLYMERS				
Polyethylene glycol (PEG), $C_{2n}H_{4n12}O_{n11}$	Plasticizer, solubility enhancer	Coating, tablet, softgel, capsules	140	960 mg
Polyethylene oxide (PEO), $C_{2n}H_{4n12}O_{n11}$	Mucoadhesion, tablet binder, matrix former, thickener	Tablets, coating	550	393.46 mg
Polyvinyl alcohol (PVA), $(C_2H_4O)_n$	Film former, thickener	Tablets, coating, microspheres	0.520	79.4 mg
Polyvinylpyrrolidone (PVP), $(C_6H_9NO)_n$	Coating, binder, solubility enhancement	Tablet, capsules, pellets	0.590	853.8 mg
POLYMERS WITH pH-DEPENDENT WATER SOLUBILITY				
Cellulose acetate phthalate (CAP)	Enteric coating	Tablet and capsules	0.59	75.6 mg
Hydroxypropyl methylcellulose acetate succinate (HPMCAS)	Enteric coating, solubility enhancement	Tablet and capsules	0.590	560 mg
Polymethacrylate, anionic	Enteric coating, solubility	Enteric coating, solubility	0.530	430.8 mg

Polymers in pharmaceutical drug delivery system

1. Rosin : Rosin a film-forming biopolymer and its derivatives have been extensively evaluated pharmaceutically as film- coating and microencapsulating materials to achieve sustained drug release. They are also used in cosmetics, chewing gums, and dental varnishes. Rosin has been used to prepared spherical microcapsules by a method based on phase separation by solvent evaporation. Rosin combination with polyvinyl

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pyrrolidone and dibutyl phthalate (30 % w/w) produces smooth film with improved elongation and tensile strength.

2. Chitin and Chitosan: Chitin a naturally abundant muco polysaccharide and consist of 2-acetamido-2- deoxy-b-D-glucose. Chitin can be degraded by chitinase. Chitosan is a linear polysaccharide composed of randomly distributed β-(1- 4)-linked D-glucosamine (deacetylated unit) and N-acetylD glucosamine (acetylated unit). The most important property of chitosan with regards to drug delivery is its positive charge under acidic conditions. This positive charge comes from protonation of its free amino groups. Lack of a positive charge means chitosan is insoluble in neutral and basic environments.

3. Zein :Zein an alcohol-soluble protein contained in the endosperm tissue of Zeamais, occurs as a by-product of corn processing. Zein has been employed as an edible coating for foods and pharmaceuticals for decades. Zein is an inexpensive and most effective substitute for the fast-disintegrating synthetic and semi synthetic film coatings currently used for the formulation of substrates that allow extrusion coating.

4. Collagen : Collagen is the most widely found protein in mammals and is the major provider of strength to tissue. It not only has been explored for use in various types of surgery, cosmetics and drug delivery, but in bioprosthetic implants and tissue engineering of multiple organs.

5. Starches :It is the principal form of carbohydrate reserve in green plants and especially present in seeds and underground organs. Starch occurs in the form of granules (starch grains), the shape and size of which are characteristic of the species, as is also the ratio of the content of the principal constituents, amylose and amylopectin. A number of starches are recognized for pharmaceutical use. These include maize (Zea mays), rice (Oryzasativa), wheat (Triticumaestivum), and potato (olanumtuberosum). To deliver proteins or peptidic drugs orally, microcapsules containing a protein and a proteinase inhibitor were prepared. Starch/bovine serum albumin mixed-walled microcapsules were prepared using interfacial cross-linking with terephthaloyl chloride. The microcapsules were loaded with native or amino- protected aprotinin by incorporating protease inhibitors in the aqueous phase during the cross-linking process. The protective effect of microcapsules with aprotinin for bovine serum albumin was revealed in vitro.

6. Polycaprolactone :Polycaprolactone (PCL) is biodegradable polyester with a low melting point of around 60°C and a glass transition temperature of about −60°C. PCL is prepared by ring opening polymerization of ε-caprolactone using a catalyst such as stannous octanoate. The most common use of polycaprolactone is in the manufacture of speciality polyurethanes. Polycaprolactones impart good water, oil, solvent and chlorine resistance to the polyurethane produced.

7. Polyorthoesters: These materials have gone through several generations of synthetic improvements to yield materials that can bepolyurethanes. Polycaprolactones impart good water, oil, solvent and chlorine resistance to the polyurethane produced. [1]

➢ **Polymers in Conventional Dosage**

Forms Despite the well-known advantages of controlled release dosage forms, conventional dosage forms are still more widely used, probably because they cost less to manufacture. More than three-quarters of all drug formulations are made for oral administration. Oral dosage forms such as tablets, capsules, and liquids are still most popular. Since tablet is one of the most widely used dosage forms and its preparation requires the incorporation of polymers, we will focus on polymers used in the tableting process.

➢ **Polymers Used in Controlled Release Dosage Forms**

One of the most important applications of polymers in modern pharmaceutics is the development of new, advanced drug delivery systems, commonly known as controlled release drug delivery systems. Controlled release formulations attempt to alter drug absorption and subsequent drug concentration in blood by modifying the drug release rate from the device. Polymer use in controlled release dosage is reduced fluctuations in the plasma drug concentration, less side effects, and increased patient compliance. Controlled release products consist of the active agent and the polymer matrix or membranes that regulate its release. Advances in controlled release technology in recent years have been possible as a result of advances in polymer science that allow the fabrication of polymers with tailormade specifications, charge density, such as molecular size, specific functional groups, hydrophobicity, biocompatibility, and degradability. Controlled release dosage forms refresh old drugs by reducing pharmaceutical shortcomings and improving biopharmaceutical properties of the drugs. Polymers used in controlled release dosage forms are an

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alternative to the development of new drugs, which is extremely costly. The controlled release dosage forms are also important in the delivery of newly developed protein drugs. Currently, most protein drugs are administered by injection. Although protein drugs have delicate bioactivity, its success in treating chronic illness largely depends on the development of new delivery systems for the routine administration other than injection.

The mechanisms of controlled drug delivery can be classified into the following five mechanisms: 1) diffusion; 2) dissolution; 3) osmosis; 4) ion-exchange; and 5) polymeric prodrug. In all cases, polymers function as a principal component that controls the transport of drug molecules and the way this process is utilized in the device determines the primary mechanism for each drug delivery system.

- **Polymers for Drug Packaging**

Many polymers are used as packaging materials for pharmaceutical products. The properties of the plastic packaging materials, such as gas permeability, flexibility, and transparency, are responsible for specific applications. Flexible packages are made by the use of thin and flexible polymer films. When they are wrapped around a product, they can easily adapt their shape to conform to the shape of the contents. The thin, flexible films are usually produced from cellulose derivatives, Polly(vinyl chloride) (PVC), polyethylene, polypropylene, polyamide (nylon), polystyrene, polyesters, polycarbonate, poly(vinylidene chloride), and polyurethanes. These polymeric materials are generally heat sealable and are also capable of being laminated to other materials. A tight package can be prepared by wrapping an article with these polymer films followed by a brief heat treatment. Rigid packages such as bottles, boxes, trays, cups, vials, and various closures are made from materials of sufficient strength and inflexibility. Widely used polymers are high-density polyethylene, polypropylene, polybutene, poly(vinyl chloride), acrylic copolymers, polycarbonate, nylon, and polyethylene terephthalate (PET)

- **Taste Masking**

Taste is an important factor in the development of dosage form. Taste masking becomes a requirement for bitter drugs to improve patient agreement especially in the paediatric and old population. Taste-masking technologies are increasingly paying attention on aggressively bitter tasting drugs like the macrolide antibiotics, non-steroidal anti-inflammatory drugs, and penicillin. Taste-masking technologies offer a great scope for invention and patents (Fig. 1). Undesirable taste is one of the significant formulation problems encountered with most drugs. The methods most commonly involved for achieving taste masking include various chemical and physical methods that prevent the drug substance from interaction with taste buds. The simplest method for taste masking is to use of flavour [16]

- **Analysis of polymer via HILIC method**

hydrophilic interaction liquid chromatographic (HILIC) applications for pharmaceutical analysis are discussed. The HILIC technique uses an aqueous/organic modifier mobile phase with a high organic modifier fraction and a hydrophilic stationary phase (SP). In general, the SPs are silica or polymer based. The silica-based columns are most often applied and are divided into bare-silica particle, chemically bonded silica particle, and monolithic phases. The bare-silica columns are most frequently used. The much less applied polymer-based columns are also divided into particle and monolithic phases. In this review, the applications are grouped and discussed according to the SP type used. Whenever possible, the considered HILIC application is compared with other HILIC methods, e.g. on other SPs, and/or with other separation modes, for that application. The advantages and drawbacks of HILIC are also discussed, as well as the method validation issues, when executed

In the past, bare-silica columns were used in HILIC to separate small polar components, e.g. pharmaceuticals, while applications on carbohydrates, peptides, or proteins were rather limited [9]. In pharmaceutical analysis, most HILIC applications still use underivatized bare-silica as SP. An advantage is that, in contrast to chemically bonded silica phases, these phases are not subject to bleeding of the bonded phase from the column . To analyse polar compounds, the bare-silica phases typically are reported to provide at least two to ten times sensitivity improvements over RP-HPLC [6]. The idea that bare-silica cannot be used to separate polar compounds is wrong, and finds its origin in NPLC, where fully organic MPs (often not miscible with water) are used. In contrast to NPLC, the addition of water in the HILIC MP deactivates the bare-silica sufficiently to obtain reproducible results , The absence of ligands on these columns has a major advantage, i.e. the absence of peaks in mass spectra from potentially detached ligands [6]. On bare-silica columns, basic analytes are strongly retained because of hydrogen bonding and ion-

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exchange (electrostatic) interactions with the silanol group [13]

Table 1. Conditions for HILIC analyses of pharmaceutical analytes on bare-silica particle stationary phases

Analyte	Sample clean-up procedure	Stationary phase[a)]	Mobile phase[b)]	Flow rate (mL/min)	Detection	Ref.
Atenolol in human plasma	PP	Hypersil SIL (ambient temp., 50 mm × 4.6 mm id, 5 μm)	ACN/water/acetic acid/TFA (85/15/0.5/0.04)	2.0	MS	[21]
Cetirizine in human plasma	SPE	Betasil SIL (30°C, 50 mm × 3.0 mm id, 5 μm)	ACN/water/acetic acid/TFA (93/7/1/0.025)	0.5	MS	[22]
Basic compounds (sildenafil, desmethyl sildenafil, fluconazole, isoniazid, ethionamide, pyrazinamide, nicotine, cotinine) in plasma or ultrafiltrate	SPE	Betasil SIL (ambient temp., 50 mm × 3.0 mm id, 5 μm)	ACN/water/acetic acid/TFA (92/8/1/0.025)	0.3	MS	[23]
Omeprazole and 5-OH omeprazole in human plasma	LLE	Betasil SIL (25°C, 50 mm × 3.0 mm id, 5 μm)	ACN/water/formic acid (95/5/0.1) with decreasing ACN gradient	1.5	MS	[24]
Levofloxacin in human plasma	LLE	Atlantis HILIC (30°C, 50 mm × 3.0 mm id, 5 μm)	ACN/100 mM ammonium formate (pH 6.5) (82/18)	0.5	MS	[25]
Muraglitazar in human plasma	LLE	Hypersil SIL (ambient temp., 50 mm × 3.0 mm id, 3 μm)	Methyl *t*-butyl ether/ACN/water/TFA (85/13.5/1.5/0.3)	0.3	MS	[26]
Pseudoephedrine.HCl, diphenhydramine.HCl, and dextromethorphan.HBr in cough–cold formulations	/	Supelcosil SIL (ambient temp., 250 mm × 4.6 mm id, 5 μm)	6.0 g/L ammonium acetate and 10 mL/L triethylamine (pH 5.2) in MeOH/water (95/5)	1.2	UV[c)] (254 and 280)	[27]
Carvedilol in human plasma	LLE	Atlantis HILIC (40°C, 50 mm × 3.0 mm id, 5 μm)	ACN/50 mM ammonium formate (pH 4.5) (90/10)	0.5	MS	[28]
Zanamivir in rat and monkey plasma	PP	Atlantis HILIC (50 mm × 2.1 mm id, 3 μm)	ACN/10 mM ammonium acetate in 1% MeOH (100/0) with decreasing ACN gradient	0.3	MS	[29]
Glucuroconjugate metabolites from propofol in human plasma	SPE	Atlantis HILIC (25°C, 150 mm × 2.1 mm id, 3 μm)	ACN/water/100 mM ammonium acetate (pH 5) (87/1/12)	0.2	MS	[30]
Adrenoreceptor agonists and antagonists (*e.g.* phenylephrine, propranolol, salbutamol, *etc.*)	/	Atlantis HILIC (40°C, 150 mm × 2.1 mm id, 5 μm)	ACN/10 mM ammonium formate (pH 3.0, 4.0, and 5.0) (75/25, 80/20, 85/15, and 90/10)	0.2	UV (225 or 300)	[31]
Fentanyl in dog plasma	PP and SPE	Atlantis HILIC (150 mm × 4.6 mm id, 5 μm)	ACN/10 mM ammonium acetate and 0.1% formic acid (100/0) with decreasing ACN gradient	0.6	MS	[32]
Ritodrine in human serum	SPE	Unison UK – Silica (30°C, 50 mm × 2.0 mm id, 3 μm)	ACN/10 mM ammonium acetate (pH 4.5) (90/10)	0.4	MS	[33]
Doxazosin in human plasma	LLE	Atlantis HILIC (50°C, 50 mm × 3.0 mm id, 5 μm)	ACN/100 mM ammonium formate (pH 4.5) (93/7)	0.5	MS	[34]
Sodium cromoglicate in ophthalmic solution	/	Atlantis HILIC (room temp., 250 mm × 4.6 mm id, 5 μm)	ACN/30 mM ammonium acetate (pH 3.0) (84/16)	2.0	UV (326)	[35]
4-(Aminomethyl)pyridine and its five related compounds	/	Atlantis HILIC (30°C, 150 mm × 4.6 mm id, 3 μm)	ACN/50 mM ammonium formate (pH 3.0) (95/5) with decreasing ACN gradient	1.5	UV (254)	[36]

Analyte	**Sample clean-up procedure**	**Stationary phase[)]**	**Mobile phase[)]**	**Flow rate (mL/min)**	**Detection**
5-Fluorouracil in mouse plasma and tissues	PP	Amine particle Asahi Pak NH_2 (451C, 150 mm 4.6 mm id)	ACN/10 mM ammonium formate (pH 3.5) (90/10) with decreasing ACN gradient	1.0	MS
Gaboxadol in human plasma	SPE	Amine particle Asahipak NH_2 (150 mm 2.0	ACN/20 mM ammonium acetate (pH 4.0) (70/30)	0.25	MS

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		mm id)			
Inorganic pharmaceutical counter ions in drug substances: nitrate, chloride, bromide, sodium, potassium, phosphate, and sulfate	/	Zwitterionic particle ZIC-pHILIC (301C, 150 mm 4.6 mm id, 5 mm)	ACN/0.1 M ammonium acetate (pH 7.0) (75/25)	1.0	CAD
Inorganic pharmaceutical counter ions in drug substances: sodium, potassium, chloride, and bromide	/	Zwitterionic particle ZIC-pHILIC (301C, 150 mm 4.6 mm id, 5 mm)	ACN/0.1 M ammonium formate (pH 3.5) (80/20)	1.0	CAD
Inorganic pharmaceutical counter ions in drug substances: calcium, magnesium, sulfate, and phosphate	/	Zwitterionic particle ZIC-pHILIC (301C., 50 mm 4.6 mm id, 5 mm)	ACN/0.1 M ammonium formate (pH 3.5) (70/30)	1.0	CAD

HILIC was used to analyse active pharmaceutical ingredients (APIs) in formulations in formulations, the sympathomimetic decongestivepseudoephedrine, the antihistaminicdiphenhydramine, and the antitussivumdextromethorphan were determined simultaneously . Initially RP-HPLC method development was tried. Different MPs and SPs were examined, but all resulted in an insufficient resolution between the three compounds and some excipients. The HILIC method (Supelcosil SIL) resulted in baselineseparated peaks. In an ophthalmic solution, the antiallergic agent sodium cromoglicate was analysed . In tablet formulations, the antidiabetic drug metformin and its related compound 1-cyanoguanidine were determined . For the experimental conditions Quantitative structure–retention relationship (QSRR) models to predict the retention of adrenoreceptor agonists and antagonists on a bare-silica column under HILIC mode were build using multiple linear regression or artificial neural networks The studied compounds were acebutolol, alprenolol, atenolol, bambuterol, betaxolol, carvedilol, isoxsuprine, metaproterenol, methoxamine, metoprolol, midodrine, nadolol, oxymetazoline, phenylephrine, pindolol, propranolol, ritodrine, salbutamol, sotalol, and timolol. These structurally related compounds are widely used to treat various diseases. Besides allowing retention prediction, these models (the included descriptors) provide information regarding HILIC retention mechanisms. By evaluating the models (descriptors), hydrophilic interactions, hydrogen bonding, and ionic interactions were suggested as mechanisms to retain compounds on the bare-silica SP [13]

➢ **Natural polymer :gums**

Gums are widely used natural excipients for conventional and novel dosage forms. With the increasing interest in polymers of natural origin, the pharmaceutical world has compliance to use most of them in the formulation.

➢ **Classification of Gums**

Gums are present in high quantities in a varieties of plants, animals, seaweeds, fungi and other microbial sources, where they perform a number of structural and metabolic functions; plant sources provide the largest amounts. The different available Gums can be classified as follows.[4]

➢ **According to the charge**

➢ **Anionic Polysaccharides**

- **Natural**: Alginic acid, pectin, Xanthan gum, Hyaluronic acid, Chondroitin sulfate, Gum Arabic, Gum Karaya, Gum Tragacanth
- **Semi-Natural**: Carboxymethyl, Chitin, Cellulose gum

➢ **Cationic Polysaccharides**

- **Natural**: Chitosan **Semi-Natural**: Cationic Guar gum.
- **Cationic**- Hydroxyethyl cellulose (HEC).

➢ **Non-ionic Polysaccharides**

- **Natural**: Starch, Dextrin's, Guar gum.
- **Semi-Natural**: Cellulose Ethers (e.g. hydroxyethyl cellulose, Methylcellulose, Nitrocellulose).

➢ **Amphoteric Polysaccharides**

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- **Semi-Natural**: Carboxymethyl chitosan, Nhydroxyl-Dicarboxyethylchitosan, Modified Potato starch.

➢ **Hydrophobic Polysaccharides**

- **Semi-Natural**: Cetylhydroxyethylcellulose, Polyquaternium.

➢ **According to the source**

➢ **Marine origin/algal (seaweed) gums:** Agar, Carrageenans, Alginic acid, Laminarin.

➢ **Plant origin**

- **shrubs/tree exudates**—Gum Arabica, Gum Ghatti, Gum Karaya, Gum Tragacanth, Khaya and Albizia gums;
- **Seed gums**—Guar Gum, Locust bean Gum,

Starch, Amylose, Cellulose **Extracts -** Pectin, Larch gum;

Tuber and roots—Potato starch.

➢ **Animal origin:** Chitin and chitosan, Chondroitin sulfate, Hyaluronic acid.

➢ **Microbial origin (bacterial and fungal):** Xanthan, Dextrin, Curdian, Pullulan, Zanflo, emulsan, Baker's yeast glycan, schizophyllan, lentinan, krestin, scleroglucan.

➢ **Prepared gums**

- Biosynthetic gums Xanthan, scleroglucan, dextrins.
- Starch and its derivatives, dextrins.
- Cellulose derivatives.

➢ ***Semi-synthetic***

- **Starch derivatives** — Heta starch, Starch acetate, Sarch phosphates.
- **Cellulose derivatives** — Carboxymethyl cellulose (CMC), Hydroxyethyl cellulose, Hydroxypropyl methylcellulose (HPMC), methylcellulose (MC), Microcrystalline cellulose (MC).

- **According to shape**

➢ Linear: Algins, Amylose, Cellulose, pectins.

➢ Branched [5]

➢ **Advantages of Natural Gums in pharmaceutical science**

➢ Biodegradable— Naturally available biodegradable polymers are produced by all living organisms. They represent truly renewable source and they have no adverse impact on humans or Environmental health (e.g. skin and eye irritation).

➢ Biocompatible and non-toxic—chemically, nearly all of these plant materials are carbohydrates composed of repeating sugar (monosaccharide's) units. Hence, they are non- toxic.

➢ Low cost—it is always cheaper to use natural sources. The production cost is also much lower compared with that for synthetic material. India and many developing countries are dependent on agriculture.

➢ Environmental-friendly processing—Gums from different sources are easily collected in different seasons in large quantities due to the simple production processes involved.

➢ Local availability (especially in developing countries) —in developing countries, government promote the production of plant like Guar gum and Tragacanth because of the wide applications in a variety of industries.

➢ Better patient tolerance as well as public acceptance-. There is less chance of side and adverse effects with natural materials compared with synthetic one. For example, PMMA, povidone. [5]

Application of gums in novel drug delivery system

Common name	Novel drug delivery system	Drug
Acacia	Osmotic drug delivery.	Water-insoluble naproxen.
Bhara gum	Microencapsulation	Famotidine.
Cordia gum	Novel oral sustained release matrix forming agent in tablets. Suspension.	Diclofenac sodium. Paracetamol.
Guar gum	Colon targeted drug delivery, Cross-linked microspheres.	Albendazole Metronidazole methotrexate

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Gellan gums	Ophthalmic drug delivery, Beads, Floating in-situ gelling.	Timolol propranolol Amoxicillin
Karaya gums	Mucoadhesive and buccoadhesive.	Nicotine
Locust bean gum	Controlled release agent.	Nimodipine, Glipizide,
Sodium alginate	Bioadhvesive microspheres,	Gatifloxin. MetforminHCL
Tamarind gum	Mucoadhesive drug delivery. Sustained releases.	Diclofenac. Verapamil.HCL
Xanthan gum	Pellets. Controlled drug delivery system.	Diclofenac sodium. theophylline

➢ **Need of herbal polymers**

1. Biodegradable – Naturally occurring polymers produced by all living organisms. They show no adverse effects on the environment or human being.

2. Biocompatible and non-toxic – Chemically, nearly all of these plant materials are carbohydrates in nature and composed of repeating monosaccharide units. Hence they are non-toxic.

3. Economic - They are cheaper and their production cost is less than synthetic material.

4. Safe and devoid of side effects – They are from a natural source and hence, safe and without side effects.

5. Easy availability – In many countries, they are produced due to their application in many industries

➢ **Disadvantages of herbal polymers**

1. Microbial contamination – During production, they are exposed to external environment and hence, there are chances of microbial contamination.

2. Batch to batch variation – Synthetic manufacturing is controlled procedure with fixed quantities of ingredients while production of natural polymers is dependent on environment and various physical factors.

3. The uncontrolled rate of hydration—Due to differences in the collection of natural materials at different times, as well as differences in region, species, and climate conditions the percentage of chemical constituents present in a given material may vary.

4. Slow Process – As the production rate is depends upon the environment and many other factors, it can't be changed. So natural polymers have a slow rate of production.

5. Heavy metal contamination – There are chances of Heavy metal contamination often associated with herbal excipients

➢ **Disadvantages of Synthetic Polymers in Pharmaceutical Sciences**

The synthetic polymers have certain disadvantages such as high cost, toxicity, environmental pollution during synthesis, non-renewable sources, side effects, and poor patient compliance.

1. Acute and chronic adverse effects (skin and eye irritation) have been observed in workers

handling the related substances methyl methacrylate and poly- (methyl methacrylate).

2. Reports of adverse reactions to povidone primarily concern the formation of subcutaneous granulomas at the injection site produced by povidone. There is also evidence that povidone may accumulate in organs following intramuscular injections

3. Acute oral toxicity studies in animals have indicated that carbomer-934P has a low oral toxicity at a dose of up to 8 g/Kg. Carbomer dust is irritating to the eyes, mucous membranes and respiratory tract. So gloves, eye protection and dust respirator are recommended during handling.

4. Studies in rats have shown that 5% polyvinyl alcohol aqueous solution injected subcutaneously can cause anemia and can infiltrate various organs and tissues.

5. Some disadvantages of biodegradable polymers used in tissue engineering applications are their poor biocompatibility, release of acidic degradation products, poor processing ability and rapid loss of mechanical properties during degradation. It has been shown that poly glycolides, polylactides and their co-polymers have an acceptcable biocompatibility but exhibit systemic or local reactions due to acidic degradation products. An initial mild inflammatory response has been reported when using poly-(propylene fumarate) in rat implant studies [5]

II. Conclusion:

In this review article we study about polymer and their different properties, also their important pharmaceutical applications, formulations concerns .

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