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Review Article

A Novel Approach on Role of Polymers Used In Sustained Release Drug Delivery System- A Review

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Abstract

Oral ingestion is the preferential route for various drugs, providing an acceptable technique to consummate both local likewise systemic effects. SRDDS designed to ease off drug at a fixed rate by upholding a constant drug level for a definite period of time with decrease side effects. The fundamental reasoning of SRDDS exemplifies the pharmacokinetic, pharmacodynamic and biopharmaceutical effects of a drug so that it utility is increased, reduced the side-effects and control the disease. Nowadays research and development are carried out on sustained release formulations due to its inherent benefits over conventional dosage form. The main objective of the review, we discuss the sustained release tablets, its rationale, challenges, advantages, disadvantages, various polymers used in the preparation, of these formulations. This system gets easy to adopt for designing to treat various diseases thereby it improves patient compliance.

Keywords: Sustained release drug delivery system (SRDDS), Polymers, Rationale, Merits, Demerits, Future treads.

INTRODUCTION

The oral route is determiner often route used for administration of drugs, due to its route of administration offers flexibility in two dosage form design than most other routes [1]. Drug release may be defined as the process where the drug is impose to pharmacokinetics study like absorption, distribution, metabolism and excretion, thereby drug is available for the efficient pharmacological action [2]. A number of terms used to describe the oral dosage forms that represent modified release properties, which include delayed release, repeated action, prolonged release, sustained release, controlled release, controlled release and other [3]. Each Active Pharmaceutical Ingredient delivery system, is focused on eliminating the repeated changes in plasma drug concentration seen after the administration of conventional delivery systems [4, 5]. Oral drug delivery as the often utilized ease of administered among compared to all the ease of administration, employed for systemic delivery of the drug from different pharmaceutical products of different dosage forms. The oral route of administration gets popularity due to its unique advantages [6, 7]. This article, make attempt to revisit the importance and recent advances in role of polymers in Sustained Release Drug Delivery System (SRDDS) treat various diseases thereby it improves patient compliance.

SUSTAINED RELEASE DRUG DELIVERY SYSTEM:

A sustained-release drug product is sustained release dosage forms designed to clemency a drug at a fixed rate by upholding a constant drug level for a definite period of time. Usually, the drug may be delivered in an initial therapeutic dose, followed by a slower and constant release [8]. They have certain advantages like increase the bioavailability of drugs, ease of administration often convenient, stability of the drug, maintain uniform drug concentration in plasma, reduce the gastrointestinal irritation and side effect, toxicity to be minimize [9], have some demerits like release rate are affected by different aspect as food and the amount of transit through the gut, high cost, high probability of drug tolerance and dumping [10], high rate of first pass metabolism, and poor invitro and invivo correlation [11].

Table-1: Parameters for dug selection parameter preferred value [12]

Molecular weight/size	<1000
Solubility	>0.1 mg/ml, pH1-7.8
Apparent partition coefficient	High
General absorbability	Form all GI segments
Release	Should not be influenced by pH and enzyme

RATIONALE OF DEVELOPING SUSTAINED RELEASE DRUG DELIVERY SYSTEM:

1. To enhance the period of drug action.
2. To scale down the frequency and inter and intra subject variability.
3. To reduce the fluctuations in plasma level and drug toxicity.
4. To improve drug utilization and duration.
5. To reduce side effects and cost of treatment.

ADVANTAGES:

i) Patient Compliance:
Patient compliance is overblown by numerous factors, like knowledge of ailment process, patient trust in treatment, and apprehension of patient related to a strict treatment plan. In addition to awkwardness of therapeutic regimens, the cost of therapy and local or systemic side effect of the dosage form. This issue start out to some degree by allocates sustained release drug delivery system.

ii) Reduced "See-Saw" fluctuation
Drug concentration in the body shows 'see-saw' pattern often when the drug given in conventional drug dosage form. The sizes of these variances essentially depend upon drug kinetics such as the amount of absorption, distribution, elimination and dosing intervals [13, 14].

iii) Total dose reduction
To treat a feeble condition less part of agitate drug is used in SRDDS. By reducing the total amount of drug, abate in systemic or local side effects are noticed. This would also lead to greater economy [15].

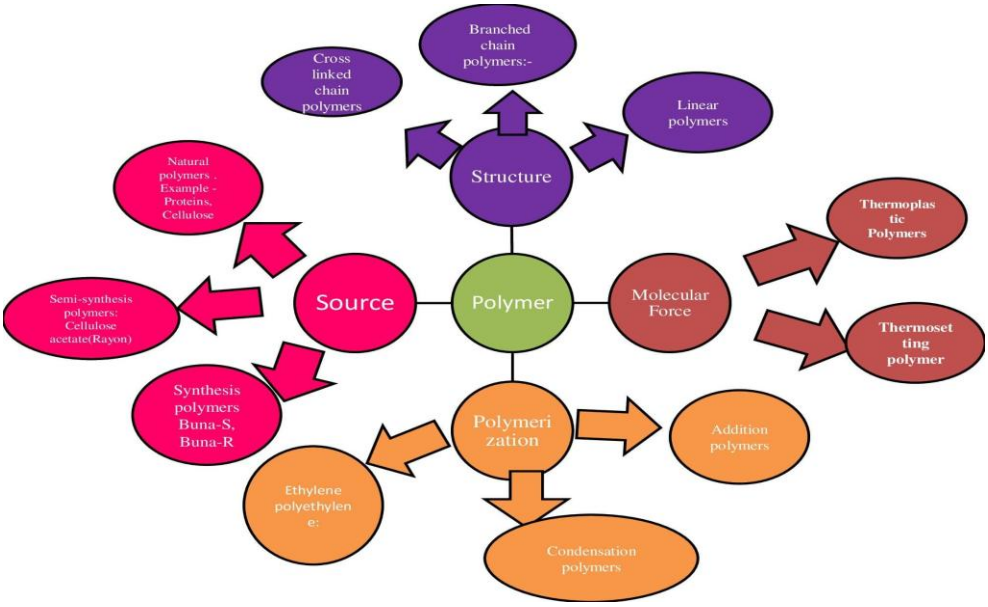
iv) Economy
The introductory cost of sustained release products is often furthermore of conventional dosage form because of the median cost of treatment above the long period of time [16].

Disadvantages of SRDDS:

(i) Highly expensive
(ii) Often poor bioavailability
(iii) Need for supplementary patient counseling and education.
(iv) Dose dumping [17]
(v) Often poor in vivo - in vitro correlation [18].

POLYMERS

Polymers are complicated and big molecules consistently with carbons building the backbone, differs from low weight molecular compounds. The small individual repeating units/molecules are known as monomers. A polymer with two different monomers is called as copolymer or homopolymer. It has characteristics like low density, good corrosion resistance, economical poor temperature resistance, and have transparent or in colors.



ROLE OF POLYMER IN PHARMACEUTICAL DRUG DELIVERY

Tablets

Polymers used as excipients in conventional immediate-release oral dosage forms for many years. Polymers including polyvinyl pyrrolidone and HPMC also find handling as binders that assistance the preparation of granules that improve the flow and convenient properties of tablets formulations prior to the tablet. Sporadically, dosage forms precondition be coated with a "non functional" polymeric film that one may protect a drug from degradation, mask the taste of a disagreeable drug or excipients, or increase the visual delicacy of the formulation without poignant the releasing rate of drug [19].

Capsules

Capsules are worn a proxy to tablets, trouble compressible materials, to mask the bitter taste or stepping up bioavailability. Gelatin used as a shell material for hard (two-piece) and soft(one- piece) capsules. HPMC has recently been evolve and believe as a surrogate material for the formulation of hard (two-piece) capsules.

POLYMERS IN PHARMACEUTICAL DRUG DELIVERY SYSTEM:

Rosin a film- forming biopolymer and its byproducts broadly used for film coating and micro-encapsulating materials to accomplish sustained drug release. They are more in cosmetics, chewing gums and dental varnishes. Rosin combination with polyvinyl pyrrolidone and dibutyl phthalate (30% w/w) contribute smooth film with magnifying elongation and tensile strength [20, 21].

Chitin and Chitosan: Chitin a naturally mucopolysaccharide and it disintegrated by chitinase. Chitosan is a linear polysaccharide consisits of β-(1-4)-linked D glucosamine (deacetylated unit) and N acetyl D glucosamine (acetylated unit). The significant property of chitosan in drug delivery it is positive charge under acidic conditions. This positive charge approach from the protoniation of its free amino groups. Lack of positive charge explain chitosan is precipitate in neutral and basic environments [22].

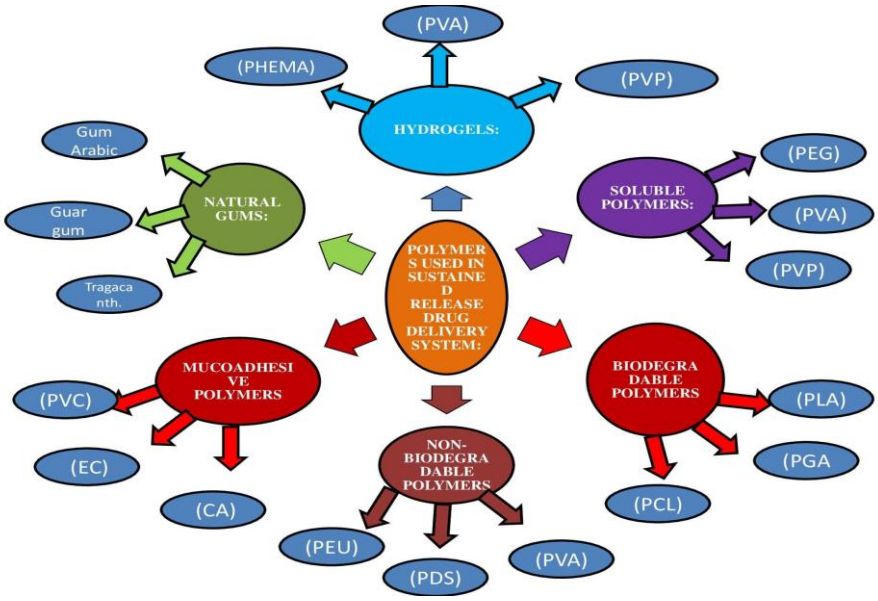
Zein: Zein is an alcohol-soluble protein emphasis in the endosperm tissue of Zea maize. Zein has been used as an edible coating for pharmaceuticals for two decades. Zein is an economical as well a substitute for rapid disintegrating synthetic and semi-synthetic film coatings currently used for the formulation of substrates that allow extrusion coating [23].

Collagen: Collagen is often found protein in mammals. It not only has been survey for use in various types of surgery, cosmetics and drug delivery, bio prosthetic implants, tissue engineering of multiple organs.

Polycaprolactone: Polycaprolactone (PCL) is biodegradable polyester along with around 60°C melting point Polycaprolactone is arranged by ring-opening polymerization of zeta-caprolactone using a catalyst such as stannous octanoate. The more often use of polycaprolactone is the formulations of polyurethanes. Polycaprolactones transmit good water, oil, solvent and chlorine resistance to the polyurethane produced [24].

POLYMERS USED IN SUSTAINED RELEASE DRUG DELIVERY SYSTEM

There are number of polymers which may be used to formulate matrix tablets controlling by the physicochemical properties of the drug substance and drug release profile required. Polymers used for matrix tablets may be classified as [25-31].



Legends:
PHEMA- Poly-hydroxyethyl methacrylate, **PVA-** Cross-linked polyvinyl alcohol, **PVP-** Cross-linked polyvinylpyrrolidone, **PEG-** Polyethylene glycol, **PVA-** Polyvinyl alcohol, **PVP-** Polyvinylpyrrolidone, **PLA-** Polylactic acid, **PGA-** Polyglycolic acid, **PCL-** Polycaprolactone **PDS-** Polydimethylsiloxane, **PEU-** Polyether urethane, **CA-** Cellulose acetate, **EC-** Ethyl cellulose.

ADVANCES IN HYBRID POLIMER – BASED MATERIALS FOR SUSTAINED RELAEASE DRUG DELIVERY SYSTEM [32]:

Table-2: Blended polymers as pharmaceutical form for Drug Delivery Systems

Sl. No	Polymeric blend	Form	Drug	Reference
01.	PEG-geletin	Nonoparticles	Ibuprofen	[33]
02.	PEG-geletin	Hydrogel	Ciproflaxin	[33]
03.	PLGA-gelatin	Nanofiber	Fenbufen	[33]
04.	PLGA-PEG	Micelle	Doxorubicin	[34]
05.	Chitosan-alginate	Beads	Bismuth Salicylate	[35]
06.	Chtin-Pluronic F108	Microparticles	Paclitaxel	[36]
07.	Chitosan-glucomannan	Hydorgel	Chloramphenicol	[37]
08.	Chitosan-silk fibroin	Film	Theophylline	[38]
09.	Chitosan-silk fibroin	Film	Salicyclic acid	[38]
10.	Chitosan-silk fibroin	Film	Amoxicillin	[38]
11.	Chitosan-silk fibroin	Film	Sodium diclofenac	[38]
12.	Alginate –gelatin	Film	Ciproflaxin	[39]
13.	Alginate-zein	Film	Ibuprofen	[40]

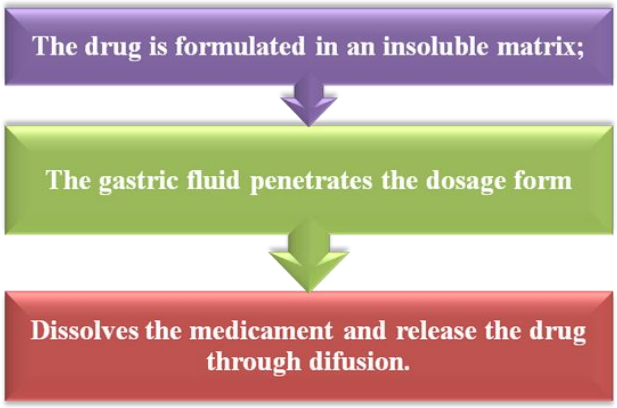
Table-3: Some published works regarding biohybrid systems for sustained drug delivery, listed in terms of kind, activity, and encapsulation efficiency (EE%)

Sl. No	Biohybrid systems	Therapeutic molecule	EE%	Ref
01.	SLN-PLGA-PEG-PLGA	2-Methoxyestradiol	91.3%	[41]
02.	PMMA-BSA	Camptothecin	11.0%	[42]
03.	Liposome-Chitosan	Doxorubicin	98.0%	[43]
04.	Liposome-cellulose	Quarcetin	40.0%	[44]
05.	Liposome-Gel	Lidocaine	21.6%	[45]
06.	Liposome-alginate	Benzocaine	63.2%	[46]
07.	Cyclodextrin/liposome	Quercetin	91.0%	[47]
08.	Cyclodextrin/PLGA	Oxaprozin	62.0%	[48]
09.	NE-alginate/chitosan	Capsaicin	68.0%	[49]
10.	SLN-hydorgel	Natural resin	-	[50]
11.	SLN-Polycarbophil	Cururmin	88.1%	[51]
12.	SLN-PLGA	Flurbiprofen	91.7%	[52]
13.	SLN-dextran	Ibuprofen	99.1%	[53]
14.	SLN-PLGA	DNA	93.1%	[54]
15.	NLC-Natural gum	Ondansetron	29.9%	[55]
16.	Liposphere-PLGA	Donopezil Hydrochloride	-	[56]
17.	Lipid nanocapsules	Quercerin	92.0%	[57]
18.	Lipid nanocapsules	Doxorubicin	90.0%	[58]
19.	Liposphere-PLGA	Albumin	90.8%	[59]
20.	SLN-PLGA	Salbutamol sulphate	30.0%	[60]

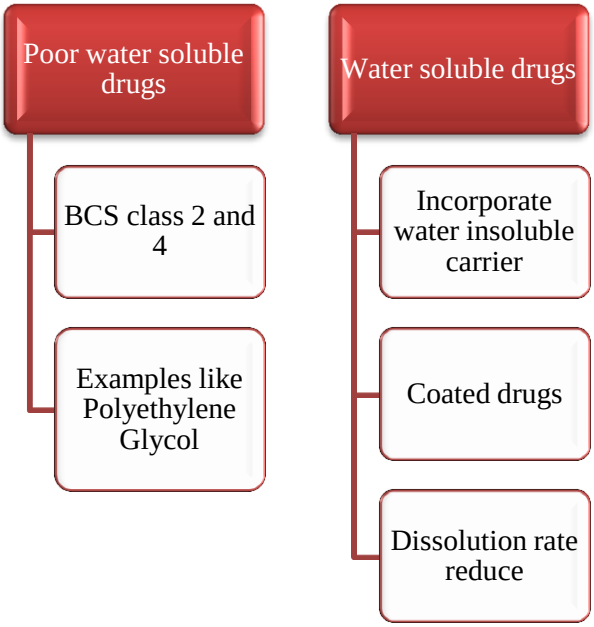
MECHANISMS OF DRUG RELEASE OF SRDDS [61, 62]

Diffusion is rate limiting

Diffusion may be defined as driving force where the movement of drug molecules occurs from high concentration in the tablet to lower concentration in gastro intestinal fluids [63]. This movement depends on diffusion pathway, diffusion coefficient, gastric acid, surface area and drug concentration gradient of the system. In practice we can follow either of the two methods,



Dissolution is rate limiting:



Osmotic pressure is rate limiting

Osmotic pressure is employed as the driving force to generate a constant release of drug. The delivery rate is constant provided that the excess of drug present inside the tablet. But, fate to deny to zero [64, 65].

Release is controlled by ion exchange

Ion exchangers are water in-soluble resinous materials that accommodate salt form in ganionicor cationic groups. While composing, the drug solution is meld with resin and dried to form beads which are tableted. The rate of drug release hang the thread on a high concentration of charged ions in the gastrointestinal tract whereas; the Active Pharmaceutical Ingredients are traded and spread into the enclosing fluid. This mechanism depends upon the resin environment but not pH or enzyme on the absorption site [66, 67].

Resin+ - drug - + X - resin+ - = X - + drug –

Conversely,

Resin- - drug+ + Y + resin- - = Y + + drug

Table-4: Sustained and Modified release formulations currently available in market [68-70]

Example	Drug	Type
Contifluo	Tamsolusin CRR beads	Diffusion an dissolution controlled beads
Co-Amoxyclav ER tablet	Amoxicillin and potassium clavulanate	Matrix type CR bilayer tablets
Cifran OD	Ciprofloxacin tablets (500 mg/g)	Effervescent matrix type floating tablets
Desval ER tablets	Divalproex sodium extended release tablets (250/500mg)	Matrix type diffusion controlled ER tablets

FUTURE TRENDS

The future of sustained-release drug products is promising, especially in the following areas that present high acceptability:

Particulate systems

The microparticle and nanoparticle access that draw in biodegradable polymers in which flawless drug-loaded particles via the Peyer's patches in the small intestine could be convient for delivery of peptide drugs that cannot, in often, be given orally [71].

Chrono pharmacokinetic systems

Oral sustained drug delivery with a pulsatile kindness regimen could satisfactory deliver drugs where a need exists to counter naturally transpire processes such as bacterial/parasitical growth patterns [72].

Targeted drug delivery:

Controlled drug delivery for oral route that targets regions in Gastro-Intestinal tract and clemency drugs only upon touching that site could offer effective treatment for assured disease states. E.g. colon-targeted delivery of Anti-neoplastics in the treatment of colon cancer [73].

Mucoadhesive delivery:

This is appropriate technique for the buccal and sublingual route, which can the rapid action and have greater bioavailability corresponding with simple oral delivery because it bypasses the first-pass metabolism in the liver [74].

CONCLUSION

The focus of this review article has been the formulation of sustained release drug delivery system, benefits of different types of Polymers, advantages, disadvantages, evaluation parameters. As compared to this system, may have better patient compliance, maintains plasma drug levels, reduce toxicity. The systems are very economical and these are designed by using the commonly available polymers. These systems are particularly useful, the patients those who are needed for a longer period of time.

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Conflict of Interest: The authors declare to have no conflict of interest.

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