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A Review of the Polymer's Role in the Development of a Cancer Formulation

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ABSTRACT:

Cancer is an extremely frequently disease, accounting for 10 million deaths worldwide. Because each cancer kind necessitates a unique treatment plan, an accurate cancer diagnosis is critical for appropriate and effective treatment. Radiotherapy, chemotherapy, or surgery are common treatments. The determination of treatment goals is a critical initial step. Polymers are significant in cancer therapy. Because of their tailor-made nature, polymers have been widely developed in the field of drug delivery systems, promoting the development of diverse systems such as implants, pastes, hydrogels, and micro or nanoparticles. Natural polymers such as arginine, chitosan, dextrin, polysaccharides, hyaluronan, and others, as well as synthetic polymers such as polyester, polyhydrides, and others, have a wide range of uses in the creation of cancer formulations. Polymeric nanoparticles derived from block co-polymers have proven to be a popular platform for the co-delivery of medication combinations due to the many functional compartments contained within such nanoparticles. Various polymeric nanoparticles have been utilised in cancer therapy to improve therapeutic index. However, the stated medication ratios employed in such systems frequently vary greatly. As a result, the same pharmacological combination can provide quite diverse treatment outcomes. We explored the role of various polymers in cancer treatment and the development of polymeric co-delivery methods to boost therapeutic impact in this review.

Cancer, Polymers, Chemotherapy, Tumour, Nanoparticles, and so forth

Introduction:

Cancer is now the leading cause of death in affluent countries and the second leading cause of death in developing countries [1]. Cancer killed 7.6 million people worldwide, and 12.7 million new cancer cases are reported each year [2]. The most frequent forms of cancer are breast, lung, oral, and uterine cancers, with the latter accounting for 1.6 million deaths worldwide.

For local and non-metastatic tumours, radiotherapy and surgery are the most commonly utilised treatments, but chemotherapy is the primary treatment for metastatic cancers. The three treatments are frequently combined. Chemotherapy is based on the employment of anti-cancer medications to stop the rapid proliferation of cancer cells, but the lack of selectivity will naturally damage healthy tissues, resulting in a number of adverse effects. Drugs also have limited half-life periods in the bloodstream and reduced bioavailability due to their chemical nature. These two facts typically lead to the necessity for greater drug dose administration, with concurrent issues linked to unexpected side effects [3, 4]. In this sense, drug delivery systems (DDS) can provide significant "breakthroughs" in the field of chemotherapy. In general, a DDS allows for the regulated delivery of an active chemical (time and release rate) and the maintenance of drug concentrations in the body within a more tolerable therapeutic window [5]. Drug Delivery Systems can be formulated in the form of particles such as microparticles, nanoparticles, micelles, and liposomes to be administered via common routes such as oral, pulmonary, or implantable like gels, microparticles, and surgical like sheets/films, foams, and scaffolds [6].

Content:-

1. Polymers used in cancer therapy.

1.1Natural polymers:

Natural polymers are derived from abundant herbal resources, and many of them are biocompatible and breakdown into non-toxic, non-immunogenic components. Polysaccharides and protein-based polymers are examples of these. Polysaccharides interact with living cells and are hemocompatible, whereas protein-based polymers create platforms that resemble the extracellular matrix and are thus kept at the site of administration . As explained below, natural polymer-based restricted cancer therapeutic delivery methods show considerable promise. However, there are certain drawbacks, including as purifying complications, immunogenicity, development challenges, the possibility of disease transfer from their source organisms to humans, and batch-to-batch inequalities.

Polysaccharides:

Polysaccharides are biopolymers comprised of simple sugar molecules. Polysaccharide-based polymers are created by varying the type, molecular weight, and structural formula of these units. These are not expensive since they are common in nature and can be obtained from algals (for example, alginate), plants (for example, pectin, guar gum), microorganisms (for example, dextran, xanthan gum), and animals (for example, chitin, chondroitin). They are stable, safe, and suitable for the development of biocompatible drug delivery technologies. The hydrophilic groups found in polysaccharides like chitosan, hyaluronan, and aliginates that produce bioadhesions with biological tissues may improve medication retention in tissues like malignant tumours.

Chitosan:

Chitosan is a linear natural polysaccharide comprised of -(14)-2-amido-2-deoxy-D-glucan (glucosamine) and -(14)-2-acetamido-2-deoxy-D-glucan (acetyl glucosamine) units formed by deacetylation of chitin found in crustaceans, insects, and certain fungi. Chitosan has high biocompatibility, low toxicity, immunostimulatory capabilities, antibacterial and antifungal activity, and anticoagulant qualities. Furthermore, the chitosan breakdown products (amino sugars) are non-toxic, non-immunogenic, and non-carcinogenic. Chitosan is appealing in cancer therapeutic applications because it exhibits antitumor activity. Unfortunately, clinical trials of chitosan-based localised delivery systems have not yet begun. Achieving high purity can be difficult, and impurities or unreacted cross-linking agents can have a major impact on chitosan's safety profile. Furthermore, natural enzymes do not breakdown some chitosan derivatives). Chitosan will most certainly have widespread clinical application once these and other difficulties are handled, as it has showed great promise in pre-clinical research.

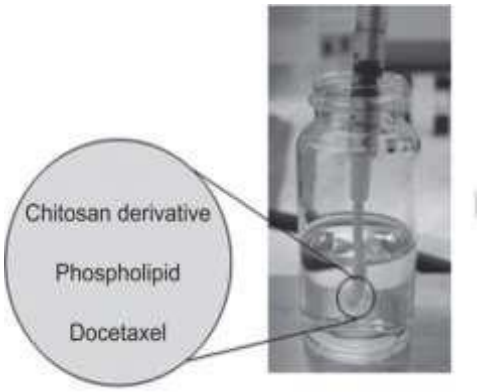

Fig. No.1: An injectable polymer-lipid docetaxel formulation.

Alginate:

Alginate is a natural linear anionic heteropolysaccharide composed of repeat units of -D-mannuronic acid (M) and its C-5 epimer, -L-guluronic acid (G), which are linked together via 1, 4-glycosidic connections. Alginates are derived from brown seaweed and have been shown in pre-clinical investigations to be non-toxic. Because of its remarkable adaptability, this polymer has a tremendous potential for use in medication administration. For example, depending on the pH of the preparation medium, neutral and charged gels can be created, allowing for the retention of medicines with a variety of physicochemical properties. However, like with other natural polymers, several contaminants are obtained with alginates, including endotoxins, heavy metals, and proteins.

Hyaluronan:

Hyaluronan, commonly known as hyaluronic acid, is a non-sulphated anionic glycosaminoglycan comprised of D-glucuronic acid and D-Nacetylglucosamine linked by interchanging -1,4 and -1,3 glycosidic linkages that is widely dispersed in connective, epithelial, and neural tissues. Because of its biocompatibility, unusual viscoelastic nature, and non-immunogenicity, hyaluronan and its derivatives have been created as topical, injectable, and implantable carriers for the transfer of biologically active compounds. However, its application in the development of localised anti-cancer medication delivery systems has been very limited. In 50 days, intra-tumoral injection of drug-loaded nanoparticles in female rats effectively reduced tumour growth in all treated rats. At 57 days following medication treatment, the mean tumour size rose linearly to a size that was 4.9-fold larger than the baseline volume in the free paclitaxel group.

Protein-based:

Proteins are three-dimensional folded amino acid polymers. Proteins, one of the most significant types of macromolecules, play a crucial part in practically every intracellular and extracellular function. Proteins and other amino acid-derived polymers are essential components of natural tissues; as such, they are promising biomaterials for the production of surgical seams, hemostatic agents, and scaffolds for tissue engineering. Furthermore, protein-based biomaterials are known to decompose naturally. They are biocompatible in general, thanks in part to their ability to mimic the extracellular matrix. One significant advantage of protein-based polymers over polysaccharides is the possibility to use recombination protein technology, which allows polymer characteristics to be carefully specified, reducing batch-to-batch inequalities. However, because proteins are easily decomposed, a fundamental limitation

in the therapeutic application of these polymers is the evaluation of stable formulations. Albumin, collagen, and gelatine are the most common proteinbased polymers utilised to create localised cancer formulations.

Albumin

Albumin is a protein with 584 amino acids that is larger, soluble, has a significant negative charge, and accounts for half of the normal intravascular protein content. Albumin is used in microsphere formulation for lipophilic drug administration due to its wide availability in nature, low toxicity and immunogenicity, and capacity to extend drug levels in the coronary circulation . One impediment to making albumin available for clinical use is that it is obtained from human or animal plasma, which raises the danger of blood-borne disease transmission. This can be avoided by using high-temperature pasteurisation, which may destroy the protein. However, albumin's favourable characteristics make it an appealing natural polymer for localised delivery of anti-cancer medicines.Albumin, for example, has been shown to accumulate in the tumour interstitium, resulting in high intra-tumoral concentrations of medicines bound to it .

Collagen:

Collagen is the primary structural protein in all animal bodies. Collagen has been utilised in suturing materials for many years due to its high profusion in the human body and high biocompatibility, and it is now employed worldwide in tissue engineering. Collagen has been underutilised in localised cancer therapeutic applications because to a number of factors, including its low mechanical qualities and fast disintegration after implantation. Crosslinking strategies are one way to combat this.

Gelatin:

Gelatin is a natural, biocompatible, and non-toxic macromolecule created by denaturing collagen from animal skin, white connective tissue, and bones. There are concerns about the transmission of infections such as prions that survive the high temperatures required for the degrading process. As a result, synthetic or plant-derived collagen is usually preferable in biomedical applications.

1.2 Synthetic polymers:

Because synthetic polymers may be customised or modified to provide desirable mechanical and chemical properties for specific purposes, they are frequently used in the development of innovative drug delivery systems. Importantly, unlike natural polymers, synthetic polymers represent a very low risk of immunogenicity and disease transmission. On the other hand, because of their manufactured character, these polymers cause mitigating responses, low clearance rates, and localised pH drops due to acidic breakdown products. However, formulations based on synthetic polymers for local chemotherapy have entered clinical trials. This means that the benefits of these polymers exceed the drawbacks .

Polyesters:

Polyester-based polymers are the most often employed type of biodegradable polymers for drug delivery applications, with poly (lactic acid-co-glycolic acid) (PLGA) alone receiving over 500 patents . The majority of marketable licenced pharmacological implants are based on PLGA. While these polymers have been chastised for producing acidic degradation products that can lead to local susceptibility and instability of the drugs being delivered, polyesterbased polymers such as PLGA are considered biocompatible and biodegradable, and are thus used in drug delivery systems.

PLGA has been utilised to create a variety of localised delivery methods, including microparticles, pastes, and implants. Because many medications and their carriers are unable to cross the blood-brain barrier, researchers created a wafer formulation for the treatment of gliosarcoma. The wafer was created by compressing PLGA with 1,3-bis(2-chloroethyl)-1-nitrosourea (carmustine, also known as BCNU) mixes, which release after 7 days. In a subcutaneous xenograft model of gliosarcoma, implanting near the tumour site proved beneficial. Because the development of BCNU resistance in the brain is a worry, Ranganath and Wang created a paclitaxel-loaded thin PLGA implant in 2008.

Polyanhydrides:

Polyanhydrides, like polyesters, are a class of synthetic polymers that have been extensively researched for drug delivery applications. Polyanhydrides have a significant advantage over polyesters in that they degrade into non-cytotoxic or inflammatory metabolites. These biocompatible polymers can be modified to produce medication release ranging from days to months. The polyanhydride poly(1,3-bis-(p-carboxyphenoxy propane)-co-(sebacic anhydride), or P(CPP-SA), which has been licenced by the FDA for drug delivery in brain cancer, is the most efficient application of polyanhydrides in localised chemotherapy. Gliadel®, a commercially available formulation, uses P(CPP-SA) in the form of a dime-sized wafer that is implanted at the site of tumour resection and slowly releases BCNU. Because PLGA is known to stimulate inflammatory reactions, this system outperforms the BCNU-PLGA wafer. Clinical experiments have demonstrated that when the wafer is implanted at the tumour resection site, it provides continuous drug release for 710 days after implantation, and patients with recurrent malignant glioma have a longer life duration .

Conclusion:

The review's findings and recommendations include the function of various polymers and polymer conjugates in the creation of cancer medications and cancer drug carriers, as well as the meaning of the polymers and polymer systems mentioned in this review. Have shown more potential in terms of enhancing cancer therapy efficacy and safety. Because they are customised, they have a higher therapeutic index and cause less damage to healthy cells.

As a result, the use of polymers in cancer treatment is strongly advised. There is little question that more Advanced Research on Polymers in Cancer Formulation Development would result in effective therapies for cancer treatment.

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