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Integrating A Role of Injectable Hydrogel for Localized Cancer Therapy

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Abstract: *Traditional intravenous chemotherapy is often associated with adverse effects in normal cells and tissues including liver or kidney dysfunction and neurotoxicity, myelosupression. As an alternative approach Localized chemotherapy can minimise the toxicity and side effects. As an alternative method, the injectable hydrogel can effectively reduce this type of adverse effects by releasing drugs topically at the tumor site . Based on the different types of stages of Cancer a number of Hydrogel based drug delivery have been developed that is thermo sensitive ,pH sensitive, photo sensitive and dual sensitive hydrogel. The recent advancement in this hydrogels and related drug discovery mostly injectable hydrogel for localised cancer therapy is used more effectively than traditional chemotherapy. This therapy is briefly discussed in this article.*

Keywords: Cancer, Hydrogel, injectable, localized cancer therapy, smart drug delivery

I. INTRODUCTION

Cancer is a deadly complaint produced by the limited proliferation of aberrant cells in a specific area of the body, performing in cell damage or death(apoptosis) and death of the host carrier. Cancer has traditionally been considered one of the scariest conditions. In 2018, 9.6 million people failed from cancer throughout the world. presently available cancer curatives include surgery, chemotherapy, radiation, and immunotherapy. Although chemotherapy may be successful in some cases, its general operation is limited because of adverse medicine responses, low remedial indicator, medicine forbearance, and shy targeting. To increase chemotherapy efficacity and drop side goods, colorful innovative medicine delivery ways have been developed in recent times, including nanotechnology, which can produce picky medicine

accumulation in excrescence towel via unresistant and active targeting routesAlthough nanoparticles have several benefits for targeted distribution, some suffer from burst release, poor adhesion, and endless distortion, making them infelicitous for long- term administration. Cancer is considered the world's alternate deadliest illness, counting for a significant portion of global mortality. Cancer caused 10 million deaths encyclopedically in 2020. In comparison to the fleetly rising global population, the death risk rate has reduced pragmatically from previous times. The death rate in 2018 was 9.6 million, compared to 7.6 million in 2007. 1 In 2012, 14.1 million. By 2025, new cancer cases are estimated to total 19.3 million. According to dependable statistical exploration, one in every eight males and one in every ten women suffer from these diseases. 2 Medicinal shops and their derivations have traditionally played an important part in drug development of colorful conditions.3 Different ypes of nanocarries are used as controlled delivery vehi cles in the cancer treatment, some of the main are-0-d material, 1- d material, 2- d material, mesoporous, iposomes, micelle, dendrimer, polymeric nanoparticles, and hydrogels. Hydrogels, a new medicine carrier, have been routinely employed to deliver excrescence medicines.

Novel drug delivery systems (NDDS) are a type of pharmaceutical device that has undergone much study and development in recent years. Hydrogel formulations allow for the creation of a variety of physical forms, including slabs, microparticles, nanoparticles, coatings, and films. Because hydrophilic moieties exist in hydrogels, which are hydrophilic polymers, the materials have a three-dimensional network structure, allowing them to absorb large volumes of water. Hydrogels have a wide range of applications for cancer therapy- Hydrogels are commonly utilized in cancer radiation, chemotherapy, immunotherapy, hyperthermia, photodynamic treatment, and photo-thermal therapy because of their high biocompatibility, biodegradability, drug loading, and controlled release properties.

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Hydrogel :

Van Bemmelen was the first to coin the term "hydrogel" in 1884. Wichterle and Lim introduced cross-linked hydroxyethyl methacrylate (HEMA) hydrogels in 1960 as a form of hydrophobic gel intended for biological applications. Some research has been conducted on hydrogels in regenerative medicine, medication delivery, tissue engineering, and agricultural applications.6 Hydrogels are classified into three sizes: macroscopic, micro-gels (0.5-10 μm), and nanogels (<200 nm). diverse sizes and architectures dictate the diverse activities of the hydrogels, as well as the delivery channel by which they are delivered for cancer therapy[1].

There are two types of hydrogels: synthetic and natural. Natural and manmade polymers are excellent drug-delivery polymers for target tissues. Polymeric nanoparticles remain in the bloodstream for an extended period before being removed, allowing them to reach the targeted tumor.They must be nontoxic, biocompatible, and biodegradable. Natural polymers such as starch, chitosan, alginate, hyaluronic acid, silk, gelatin, collagen, fibrin, and glycosaminoglycans have piqued researchers' attention due to their abundance, nontoxicity, biocompatibility, and biodegradability[2]. Cellulose is an abundant natural polysaccharide that is commonly utilized as a hydrogel due to its great biocompatibility and biodegradability. Cytokines, anticancer vaccines, checkpoint inhibitors, and CAR-T cells are the most widely utilized cancer immunotherapy drugs. One common feature of these medicines is that they target immune cells independent of their location or the presence of tumor cells. Systemic administration of such medicines, particularly checkpoint inhibitors, frequently leads to immune-related adverse events (irADs). Local administration considerably reduces the danger of irADs while ensuring that agents are targeted and effective in achieving the necessary degree of anti-cancer immunity[3].

7 Polyethylene glycol (PEG) is a common building element for biomaterials used in biomedical engineering, including tissue regeneration and medication delivery. PEG-based biomaterials have several notable advantages, including biocompatibility, no immune response stimulation, and high water solubility. 8 Chitosan is a natural polysaccharide generated from chitin. When utilized as a carrier, chitosan improves its solubility in water. Due to its muco-adhesive cationic nature, it can keep therapeutic materials at the tumour site, allowing for regulated medication administration. It is widely recognized for its regulated non-immunogenicity, biodegradability, and availability. Dextran is another essential polysaccharide that is often transformed into enzymatically biodegradable reactions and is pH sensitive. Because of their flowability, injectability, biocompatibility, and network-like structure, xyloglucan and collagen structures can also be employed for local medicinal drug administration. Gelatin is a highly biodegradable and biocompatible biopolymer protein that occurs naturally and has thermo-reversible properties. Gelatin in an aqueous solution hardens at temperatures below 25°C owing to the creation of triple helices and stiff three-dimensional networks, and it returns to liquid at temperatures over 30°C due to conformational shifts from a helix to a more flexible coil. When coupled with other polymers, gelatin produces thermal gelation close to body temperature, making it an efficient drug delivery agent. Some of the common hydrogel are classified in the (Table 1). 9 To far, an outstanding library of drug delivery vehicles has been produced with diverse sizes, topologies, and surface physicochemical features, as well as targeting techniques[4].

Source	Natural hydrogel	Collagen, chitoson,hyaluronic acid, gelatin.
	synthetic hydrogel	Polyethylene glycol (PEG), N-isopropyl acrylamide (PNIPAM), Poloxamer.
Crosslinking method	Physically crosslinked	Hydrogen bonding, Ionic interactions, hydrophobic interactions.
	Chemically crosslinked	Glutaraldehyde, epichlorohydrin, adipic dihydrazide, and polyaldehydes.
Response to environment stimuli	Environmentally sensitive hydrogels	Temperature sensitive Electric-field sensitive pH sensitive Light sensitive.

Figure 1: Classification of hydrogels

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There are some important properties of hydrogel

Swelling properties:

All polymer chains in hydrogels are physically or chemically bonded to one another and are thus treated as a single molecule, regardless of size. As a result, there is no idea of molecular weight for hydrogels, which are sometimes referred to as infinitely huge molecules or super macromolecules. One of the factors influencing water absorption capacity is the degree of cross-linking and the type of cross-linking agent utilized[5] .

A modest change in environmental circumstances can cause rapid and reversible alterations in a hydrogel. The amount of aqueous medium incorporated in a hydrogel is measured gravimetrically and represented as a swelling ratio.

Swelling Ratio = Ws - Wd/Wd

Where, Ws is the weight of hydrogel in swollen
Wd is the weight of hydrogel in when dry

Mechanical properties:

Hydrogel mechanical characteristics are critical for pharmaceutical and biological applications. The examination of mechanical properties is critical in a variety of biomedical applications, including ligament and tendon restoration, wound dressing material, and drug matrix development[6].

Hydrogel inhomogeneity:

It affects drug delivery, tissue engineering, and cartilage replacement materials. Hydrogels should have mechanical qualities that allow them to keep their physical texture while delivering therapeutic moieties for a set amount of time. By varying the degree of crosslinking, the desired mechanical characteristic of the hydrogel may be obtained. An increase in the degree of crosslinking results in a stronger hydrogel, which reduces the percentage elongation of the hydrogels and forms a brittle structure[7].

Inhomogeneity in hydrogels:

It influences medication delivery, tissue engineering, and cartilage replacement materials. Hydrogels should have mechanical properties that allow them to maintain their physical texture while delivering therapeutic moieties for a certain period of time[8]. By adjusting the degree of crosslinking, the desired mechanical property of the hydrogel may be achieved.

As the degree of crosslinking increases, the hydrogel becomes stronger, reducing its percentage elongation and forming a brittle structure. It was discovered that the scattering intensity from gels is always greater than that of the polymer solution. The gel's homogeneity grows with the cross-linking network across the gel polymer, but decreases with the gel's ionisation degree[9].

Biocompatible Properties:

In order to be used in the biomedical area, hydrogels must be biocompatible and non-toxic. Most polymers used for this purpose need to pass cytotoxicity and in-vivo toxicity studies. Biocompatibility refers to a material's capacity to respond appropriately to a host in a certain application. Biocompatibility studies include two parameters: biosafety and bio-functionality[10].

Type of Cancer	Hydrogel-based clinical products	Anti-cancer drugs	Delivery system	Company name	Approval year
Breast cancer & Ovarian cancer	Genexol-PM®	Paclitaxel	Micelle polymer	Samyang	2009
Esophageal cancer	Oncogel™	Paclitaxel	Thermal Sensitive ReGel polymer	Diatos	2007

Figure 2 : some hydrogel based anti-cancer nanomedicine

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THERMOSENSITIVE HYDROGEL :

Temperature-sensitive hydrogels are hydrogels that change in volume as the ambient temperature changes(Klouda, 2015; Chen et al., 2018). The gel always has a certain proportion of hydrophobic and hydrophilic groups. Temperature changes can affect the hydrophobic commerce of these groups. Thehydrogen relating between the macromolecular chains causes the gel structure to change, and volume changes do(Fanet al., 2015)[11].

The temperature at which the volume changes is appertained as lower critical result temperature(LCST)(Sapino et al., 2019). Under this temperature, the gel swells in waterless result. Once the temperature rises to LCST, the gel shrinks(Lei et al., 2012; Wang et al., 2015). Its unique parcels can be used as a medicine carrier, which is fitted into the body after being combined with a medicine at a low temperature(Le et al., 2018). Forming a colloidal state with the help of body temperature makes it a medicine sustained- release system, which simplifies not only medical treatment but also cases' suffering(Wang et al., 2015, 2016; Yang Y. et al., 2016)[12].

Main thermosensitive injectable hydrogels include chitosan/ glycerophosphate(C/ GP), hyaluronic acid(HA), PLGA grounded hydrogel, cut- grounded hydrogel, PECE, and PECT(Guo et al., 2012; Klouda, 2015; Huang et al., 2016; Le et al., 2018; Sapino et al., 2019).

In one study(Huang et al., 2016), injectable thermosensitive doxorubicin(DOX) delivery system was developed with PECT hydrogel. rather of hydrogel grounded on free DOX prolixity, which suffered from rapid-fire medicine concurrence and poor medicine penetration in excrescence towel, tone- polymerized medicine- loaded nanoparticles were reprised into PECT hydrogel(Huang et al., 2016)[13].

After in vivo injection, PECT gel displayed a transition phase between sol and gel. The density increased suddenly once the temperature is advanced than 28 ◦ C. With the loftiest density at 37 ◦ C, the hydrogel turned to gel from sol. Loaded nanoparticles were separated from hydrogel and diffused within excrescence towel by EPR effect. Intracellular chemical drugrelease limited its poisonous goods and enhanced itsanti-tumor effectiveness. varied with intravenous medicine injections(I.V.), a thermosensitive hydrogel with nanomedicine loaded is an effective medicine delivery system, which enabled nonstop medicine release around excrescence apkins(Huang et al., 2016)[14].

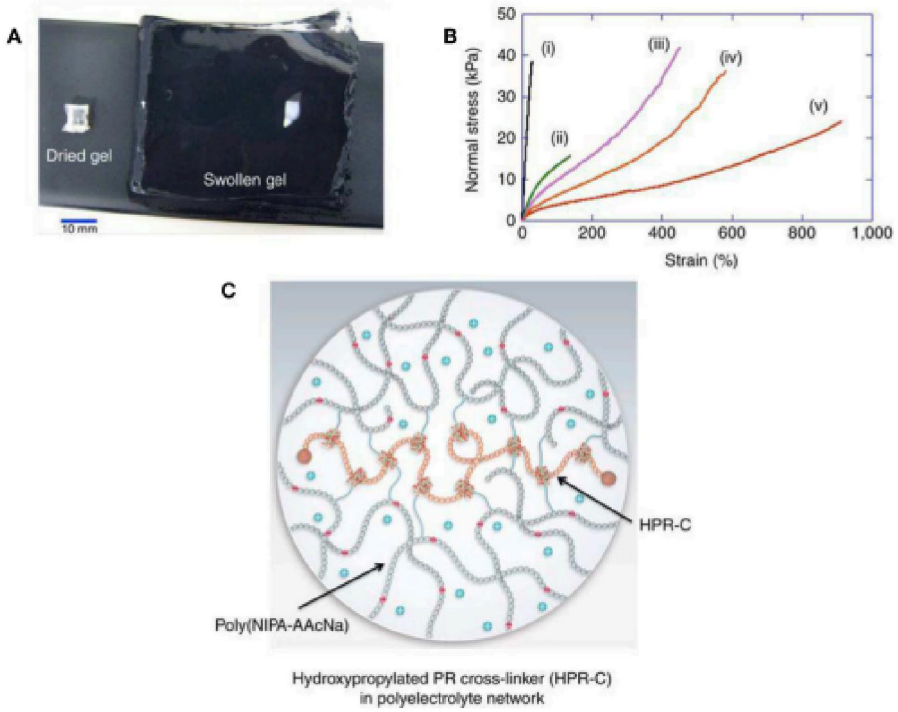

Figure 3 : Hydrogel forms crosslinked 3D network and shows excellent water absorption capacity.

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(A) Hydrogel swelling from 129 mg (dry gel) to 80,000 mg (water-swollen gel). (B) Stress-strain curves of different hydrogels (i–v).
(C) Schematic of swollen hydrogel (Bin Imran et al., 2014). Reproduced, with permission, from Main thermosensitive injectable hydrogel and drug delivery system[16]

Two or further rudiments loaded in one thermosensitive hydrogel has surfaced as a promising medicine delivery system for its superioranti-tumor efficacity. Polo- suchlike kinase 1(PLK1) gene is honored as a crucial controller of excrescence cell meiosis and mitosis(Ma et al. 2014). RNA hindrance- grounded on PLK1shRNA can specifically reduce the function of the target gene in the excrescence. A strategy of DOX and PLK1shRNA/ PEI- Lysco-delivery hydrogel was developed for the treatment of osteosarcoma(Ma et al., 2014). In this system, PLK1shRNA/ PEI- Lys in the hydrogel can greatl enhance theanti-tumor effect of DOX. With the synergistic effect from PLK1shRNA/ PEI- Lys and DOX, significant osteosarcoma. apoptosis was caused by theco-loaded hydrogel[15].

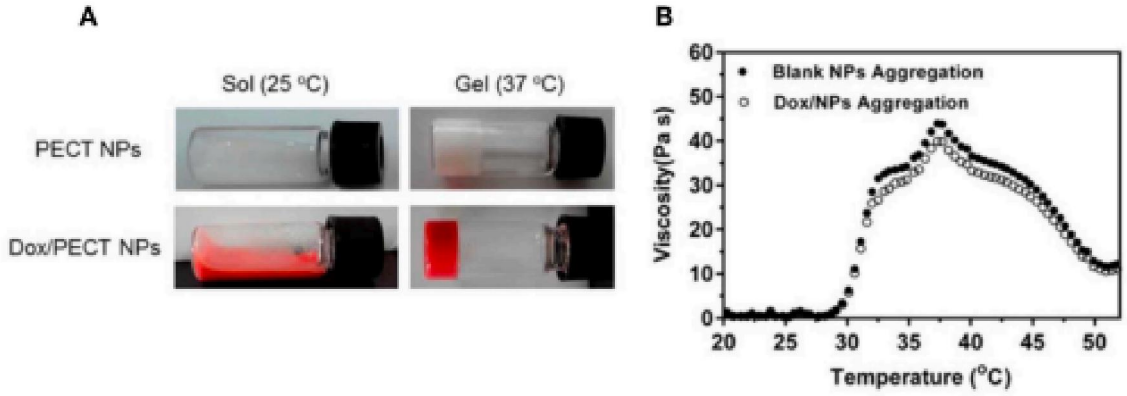

Figure 4 : The thermosensitive property of hydrogel
(A) State of the thermosensitive hydrogel at different temperatures (25◦C, 37◦C). (B) Hydrogel viscosity increase of aqueous solution as a function of temperature. Source: Reproduced, with permission, from Huang et al. (2016)

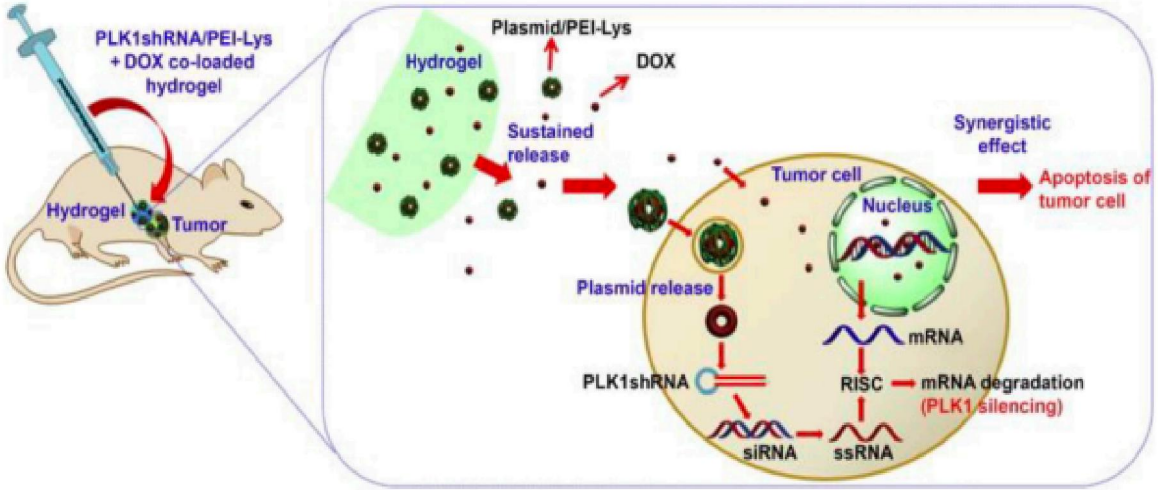

Figure 5 : Schematic for synergism of PLK1shRNA/PEI-Lys and DOX from the hydrogel promotes tumor apoptosis on osteosarcoma in nude mice[17]

PH-SENSITIVE HYDROGELS :

Glycolysis of excrescence cells can beget acidification in the terrain next to excrescence apkins, performing in lower pH value in the extracellular matrix than normal apkins(Kenney et al., 2018; Hu et al., 2019). A pH-sensitive hydrogel is a polymer gel in which the volume of the hydrogel changes depending on the pH of the external terrain and the ionic

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strength(Liao et al., 2017; Liu et al., 2019). similar gels contain a large number of readily hydrolyzable or protonated acids, base groups similar as carboxyl groups and amino groups(Lym et al., 2016). The dissociation of these groups is affected by the external pH. When the external pH changes, the degree of dissociation of these groups changes similarly, causing the internal and external ion attention to change(Norouzi et al., 2016).

In addition, the dissociation of these groups will destroy the corresponding hydrogen in the gel[18]. The bond reduces the cross linking point of the gel network, causing a change in the structure of the gel network and the degree of lump of the hydrogel(Qu et al., 2017; Oroojalian et al., 2018). With this property, the rate of prolixity and release of the medicine in the gel can be accessibly acclimated and controlled(Samanta et al., 2015).

A variety of rudiments for pH-sensitive hydrogel were explored in the once decades. One of the choices is grounded on chitosan- grafted- dihydrocaffeic acid (CS- DA) and oxidized pullulan(OP)(Liang et al., 2019). With classical medicine for anti excrescence remedy, DOX- loaded hydrogel was tested to explore its responses for the pH changes in the excrescence terrain. With glycolysis in the excrescence point, a drop of pH touched off the medicine release(Liang et al., 2019)[19].

Compared with the morphology of hydrogel at pH 7.4, significant decomposition of hydrogel redounded in larger severance size at pH 5.5(Liang et al., 2019). After 60 h at pH 5.5, further than 80 of DOX was released from the hydrogel. The hydrogel wasco-cultured with Hct116 cells(colon excrescence cells) to test itsanti-tumor effect(Liang et al., 2019). DOX is continuously stable released from hydrogel at pH 5.5 and 7.4. In both conditions, DOX can be effectively released for further than 3 days(Liang et al., 2019). In recent times, aspirin has been set up to inhibit carbon monoxide synthase, inhibit nitrite- intermediated DNA damage, reduce surviving, inhibit nuclear recap factors, proteasomes, and calcium- actuated neutral proteasome genes by inhibiting cyclooxygenase(Lu et al., 2008; Choi et al., 2013 [20].

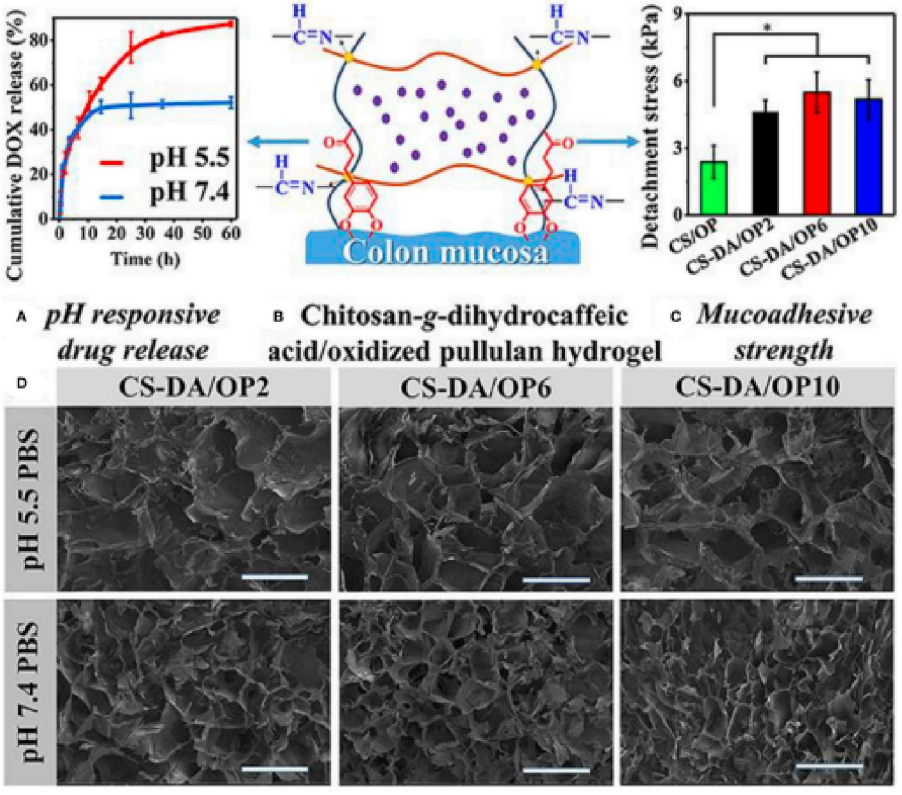

Figure 6 : Characters of the pH-sensitive hydrogel. (A) pH-responsive drug release. (B) Schematic for pH-sensitive hydrogel. (C) Mucoadhesive strength of different elements. (D) SEM images of the pH-sensitive hydrogel after swelling in PBS with different pH values. *P < 0.05[23]

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The expression and other mechanisms play ananti-tumor effect. After loading aspirin into the hemicellulose hydrogel, it was set up that 85 of the medicine could be released continuously for 5 – 6 h under pH 7.4(Choi et al., 2013). Sun et al. successfully prepared a series of acrylic acid and acrylamide copolymer grafted hemicellulose hydrogels by free radical polymerization(Sun et al., 2013). The combination of aspirin and the medicine showed that the release rate of the medicine in the dissembled gastric juice was slower, and the release rate in the dissembled intestinal fluid was significantly faster than that of the dissembled gastric juice. When the release time was 12 h, the accretive release rate reached 90, which shows excellent sustained release parcels(Sun et al., 2013)[21].

In addition, Wang et al. first fitted dexamethasone phosphate into molecularly ingrained polymer nanospheres and loaded the polymer onto a pH-sensitive hydrogel, making it a biosensor that inhibits inflammation(Wang et al., 2010). Since the seditious response can lead to an acidic terrain, this pH-sensitive hydrogel can fleetly release the medicine at pH 6.0 ~ 7.4 to inhibit the inflammation(Wang et al., 2010). This different system is resistant to pH-sensitive hydrogels. The operation of oncology Medicines has brought new ideas[22] .

PHOTOSENSITIVE HYDROGEL :

The mechanism of a light-sensitive hydrogel is divided into two types according to the properties of the photosensitive material (Chang et al., 2019). One is to directly add the photosensitive molecular material to the temperature-sensitive gel, and convert the light energy into heat energy to make the temperature inside the gel reach the phase transition temperature. In this way, hydrogel produces photosensitivity[24].

Another kind of chromophore is introduced into the gel structure (Norouzi et al., 2016). The physicochemical properties of the chromophore are changed when subjected to light stimulation. By changing the network structure, hydrogel macroscopically exhibits photosensitivity. Usually, a structure such as azobenzene, spiropyran, o-naphthoquinone, anthracene, nitrophenyl, and coumarin is introduced into the gel (Tam et al., 2017). Among them, ruthenium, nitrophenyl, and coumarin compounds mainly take advantage of photo-cleavage photosensitive groups, which are bonded to the hydrophobic end through an aryl methyl bond (Norouzi et al., 2016; Tam et al., 2017). Under ultraviolet light or near-infrared light, the ester group is broken. The photosensitive reaction is caused. The hydrophobic end is converted to a hydrophilic end, causing the gel to dissociate. The azobenzene compound is controlled by the conversion of the cis- trans structure[25].

One of the applications for photosensitive hydrogels is that platform for cell culture and 3D tumor micro-environment studies. With advantages of its photosensitive character, cell detachment on the surface of hydrogel was done layer-by-layer to form a 3D cell culture medium (Figure 5) (Wang et al.,2014).Photoinitiated copolymerization of P (OEGMA-co-VDT-co-SPAA) (POVSP) hydrogels happened with UV irradiation[26] .The compressive strengths of hydrogels were up to 5.1 MPa,which is strong enough for cell culture (Wang et al., 2014).

Its revealed that photosensitive hydrogel isuitable for 3D cell culture model, which is vital for the study of the mechanism for tumor development. To achieve the same purpose, a photocleavable terpolymer hydrogel was developed as the basic technique for 3D bio-printing. This hydrogel is capable of self-shaping directly to the UV irradiation. It is designable by using selective illumination to UV light with the specific area covered with darkness (Liao et al., 2015). The printable hydrogel is an inspiring design for controlled drug delivery with district distribution. It is a key technique for the realization of 4D drug delivery with both dimensions of time and space. With drugs loaded in the 3D space of hydrogels, dynamic drug release can be realized. In this process, different drug could be controlled to be released in different time with purpose (Xu et al., 2015; Chen Y. et al., 2016; Kim et al., 2017; Guo et al., 2018). This is the typical way of 4D drug delivery with additional dimensions of time[27].

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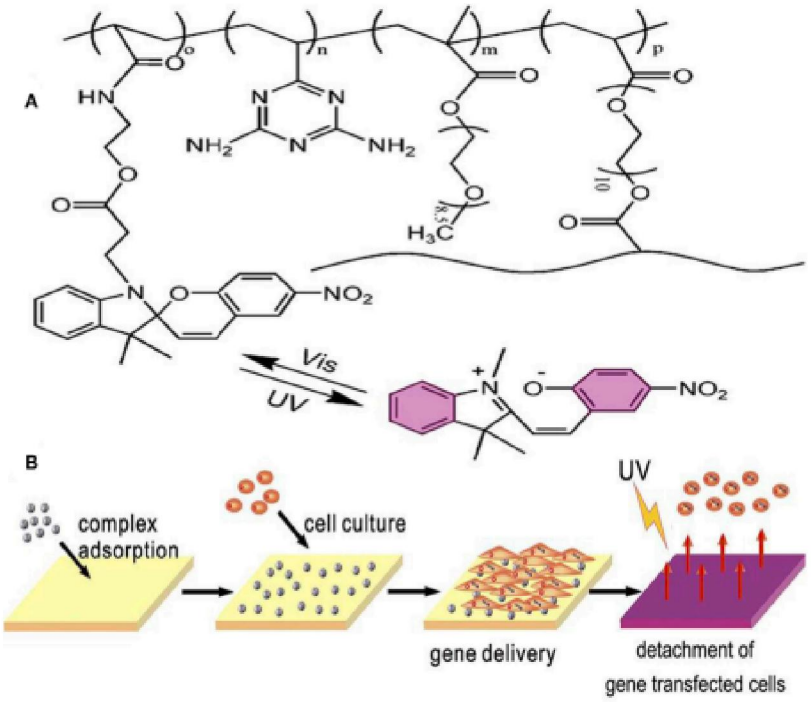

Figure 7: Schematic structure and mechanism of the photosensitive hydrogel. (A) Schematic molecular structure of hydrogel. (B) UV irradiation triggers the detachment of cells from the surface of the hydrogel. Reproduced, with permission, from Wang et al. (2014)[28].

DUAL-SENSITIVE HYDROGELS :

With the increasing requirements for the precision of controlled release of drugs, multi-sensitive hydrogels have received more and more attention (Bardajee et al., 2017). In particular, co-sensitive hydrogels for temperature and pH is widely researched. Temperature and pH are two important factors in physiological, biological, and chemical systems (Bardajee et al., 2017; Fathi et al.,2019). The temperature-pH double-sensitive hydrogel consists of a temperature-sensitive and pH-sensitive two-part hydrophilic polymer network (Lym et al., 2016). Usually formed with two or more monomers or polymers, which respond to temperature and pH, respectively[29].

The combination of temperature and pH sensitivity is crucial for the management of locoregional tumor recurrence(Mackiewicz et al., 2019). A novel pH-sensitive thermosensitive hydrogel loaded with modified doxorubicin-based prodrug nanoparticles (PDNPs), which is more efficient for tumor management than free DOX (Liu et al., 2019). Good biocompatibility and anti-tumor activity were verified by in vitro uptake and cell toxicity. For in vivo experiment,4T1 cells with luciferase-tagged expression were implanted into mice. Management by temperature and pH co-sensitive hydrogel was remarkable (Liu et al., 2019). It is a promising strategy for preventing the locoregional recurrence of the tumor[30]. Co-sensitive hydrogel with dual photoluminescence was developed with PL and PNIPAM (Zhao et al., 2016). This hydrogel contains a core which was made up of a red-emission complex and a blue-emission d-TPE. This nanoparticle is sensitive to the change of temperature and pH (Zhao et al., 2016). This hydrogel is stimulated by both temperature and pH and is more adaptable to the complex environment of human body fluids. In addition, the application of two or more materials, through their interaction, not only can improve the mechanical strength of the hydrogel, but also improve the precision of controlled release. With this character, the stimuli-responsive hydrogel has a wide application in medical imaging, cancer diagnosis, and advanced antitumor drug delivery (Zhao et al., 2016).[31]

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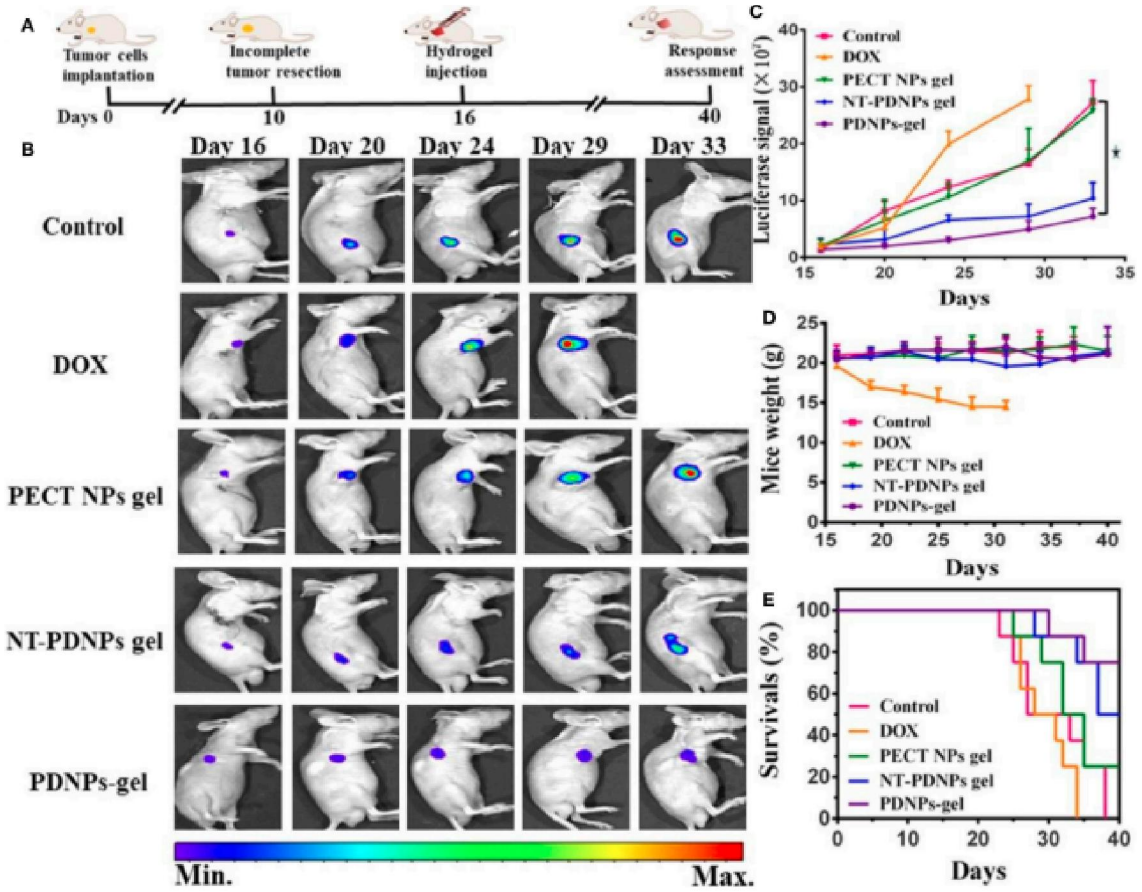

Figure 8 : In vivo luciferase-tagged tumor model with the management of hydrogel. (A) Experiment process. (B) Bioluminescence images of mice treated with different formulations, (C) Quantified bioluminescence for tumors in mice. (D) Mice weight changes. (E) Survival rates of mice treated with different methods. Reproduced, with permission, from Liu et al. (2019) [32].

Benefits of Hydrogels in Drug Delivery :

- Hydrogels have been defined in a variety of ways throughout the years, but they are most commonly described as a crosslinked polymeric network generated by the conjugation or reactivity of one or more monomers and exhibiting waterswollen properties. Though hydrogels are three-dimensional networks, they have the potential for water absorption due to the presence of hydrophilic capabilities that may fill the gap between macromolecules and have a higher affinity for biological fluids[33].
- Hydrogel-based advanced dressings have been demonstrated to be extremely successful in wound healing because of their moisture-retaining properties at the application site, which prevent fluids from spreading to adjacent healthy skin regions. Commercially available hydrogels include DermaFilm®, Condress®, Kaltostat®, and Sofargen®. [34]
- Hydrogels are being used for drug delivery due to their unique physical features. Controlling cross-link density in the gel matrix and hydrogel affinity for the aqueous environment can help to fine-tune their extremely porous structure. This permits medications to be placed into their gel matrix and subsequently released in an amount determined by the diffusion coefficient of small molecules or macromolecules. Because of their pharmacokinetic features, hydrogels can be employed for drug administration with the primary goal of

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maintaining a high local concentration of the drug in the surrounding tissues for a longer length of time, as well as for systemic distribution.[35]

- Hydrogels are biocompatible and can be employed in the peritoneum and other parts of the body. The high water content of hydrogels, along with their physical resemblance to the natural extracellular matrix and mechanical qualities, promotes biocompatibility. It is possible to create biodegradable or dissolvable hydrogels by environmental, hydrolytic, or enzymatic means, albeit this may not be desired depending on the timing and location of the drug delivery device[36].
- Hydrogels, on the other hand, are somewhat malleable and may be shaped to fit any surface. Some hydrogels' muco- or bio-adhesive properties might be useful when applying them to non-horizontal surfaces or immobilizing them at the application site[37]. Hydrogels' effectiveness in biomedical applications led to the hypothesis that they may be employed for medication delivery in cancer therapy. Local medication delivery may be particularly effective in situations of nonsquamous or incompletely excised tumors, although most cancer therapy research focuses on systemic and oral administration.
- Injectable hydrogel systems provide certain advantages over systemic chemotherapy, including lower toxicity in normal tissues, localised and prolonged drug administration in the tumour region, more effective cell death, and tumour growth suppression. The efficacy of these hydrogels for localised chemotherapy has been thoroughly investigated in highly structured and regulated in vitro settings[38].
- Proof-of-principle studies on their action in numerous rodent cancer models are also promising. However, much of the in vivo investigations to date have focused on hydrogels in subcutaneous ectopic tumour models. The benefits of ectopic tumour models include simplicity of monitoring tumour growth and, because the majority are subcutaneous, direct placement of hydrogel near or into the tumour mass is simple[39].
- The hydrogel-based medication delivery methods offer distinct benefits in postoperative radiotherapy. Traditional medication formulations (such as radioisotopes, radio-sensitizers, chemotherapeutic medicines, or immune-modulators) were studied by encapsulating them in hydrogels and combining them with postoperative radiation to prevent tumor reoccurrence[40] . This local drug delivery strategy avoids the nonspecific dispersion of standard medications, sensitizes radiation, and allows for the combination of several treatment options. 12 Hydrogels can be used in the cancer treatment as Radiotherapy, Immunotherapy, hyperthermia, photothermal and photodynamic therapies.
- Postoperative concurrent chemo-radiotherapy, which administers chemotherapeutics and radiotherapy after surgery, is now the standard treatment for solid tumors such as lung, esophageal, gastrointestinal, and brain cancers. Radiotherapy exposes normal tissues to radiation as well. Radioactive necrosis occurs when the radiation exposure surpasses the normal tissue's maximal tolerance threshold. Traditional chemotherapeutic drugs have been shown to make radiation more effective in solid tumors, however, their nonspecific tissue distribution causes significant harm to other tissues and organs[41].
- Hydrogel has been widely used in postoperative chemoradiotherapy due to its unique properties, including intraoperative delivery, prolonged drug release, and high drug loading. Doxorubicin (DOX), a broad-spectrum anticancer medication, can efficiently limit the production of RNA and DNA, hence eliminating tumour cells. However, doxorubicin's harmful side effects, including as myelosuppression and cardiac damage, severely limit its utilization in clinical settings[42] .

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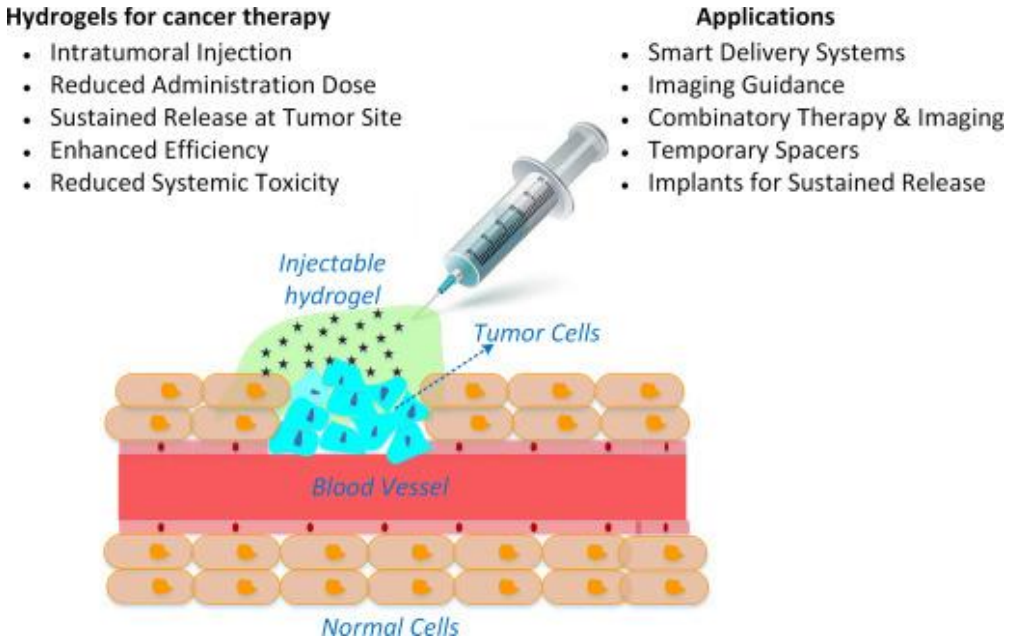

Figure 9 : some benefits of hydrogel in cancer therapy

II. CONCLUSION

The unique character of hydrogel makes it an effective functional medium for medicine delivery. Given the limits from chemical medicine toxin for normal towel and organs, localized medicine delivery system by hydrogel has been a pivotal system for canceroperation. Affiliated studies substantially concentrated on the delivery function and the styles of stimulants- response The smart hydrogel was developed with accurate responses to bitsy changes in temperature, pH, and light.

For now, medicines can be fluently delivered to cancer towel at the right time point. In the future, co-loaded medicines, including DNA, RNA, protein, and related products, would be a crucial point. The constantly accurate drudelivery system can realizeanti-tumor medicines release followed by towel form factors. In this way, demission of time and space for medicine delivery would be mixed in one hydrogel, making it a 4D functional hydrogel. It can make hydrogel a perfect choice for original chemotherapy and cancer operation.

The utilisation of hydrogels to transport diverse medications is thus particularly appropriate for the present development of melanoma immunotherapy and has a wide range of applications. It is expected that as hydrogel research advances and immunotherapy improves, hydrogels will become a viable drug carrier, leading to new advancements in cancer treatment and encouraging future development.

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