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Review Article

An Updated Review on Nanoparticle Based Approach for Nanogel Drug Delivery System

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ABSTRACT

Nanocomposite hydrogels or nanogels (a nanoparticles composed of a hydrogel) are nanomaterial filled, swollen nanosized networks of deliquescent or amphiphilic compound chains. It may be developed by drug - polymer interactions and to create 3D advanced networks. Nanogel may be ready by many strategies just like the particle gelation, Inverse mini emulsion, Dispersion, Chemical cross linking, fabrication of biopolymers and so on. It can be characterized by SEM, DSC, FTIR, Drug content, Particle size, Zeta potential and drug efficiency. Further, it can be evaluated by in vitro drug release and in vivo study in suitable animal modeling. In this review article, we have focused on basic methodology of nanogels, evaluation terms, their application in industry with future prospects for the researchers.

Keywords: Nanogel; methods of nanogel preparation; evaluation parameters and their applications.

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1. INTRODUCTION

1.1 Drug delivery system: Drug delivery is the technique or method of administering a pharmaceutical compound to attain a therapeutic impact on humans or animals. The most common strategies of delivery stands for the well-liked non-invasive per oral (through the mouth), topical (skin), trans-mucosal (nasal, buccal, sublingual, vaginal, ocular, and rectal) and inhalation routes.

1.2 Why can we like NDDS?

The conventional indefinite-quantity kinds offer drug unharness instantly and it causes fluctuation of drug level in blood bank upon indefinite quantity form. Therefore, to take care of the drug concentration among therapeutically effective vary would like the novel drug delivery system.

1.3 Novel drug delivery system

“Novel Drug delivery System (NDDS) refers to the approaches, formulations, technologies, and systems for transporting a pharmaceutical compound within the body as requisite to securely bring home the bacon it's desired therapeutic effects. NDDS is an advanced drug delivery system that improves drug efficiency, management drug unharness to convey a sustained therapeutic impact, offer bigger safety, finally, it's to focus on a drug specifically to the desired tissue.

1.4 Modes of NDDS -

- Targeted drug delivery system
- Controlled drug delivery system
- Modulated drug delivery systems.
- It has been shown in **Fig.1**

1.5 List of drug carriers within the NDDS (Fig.2)

- Nanosome
- Liposomes
- Niosomes
- Nanospheres
- Nanoparticles (Nanogel)
- Microspheres
- Microparticle
- Nanosuspension
- Micelles.

It has been shown in **Fig.3**

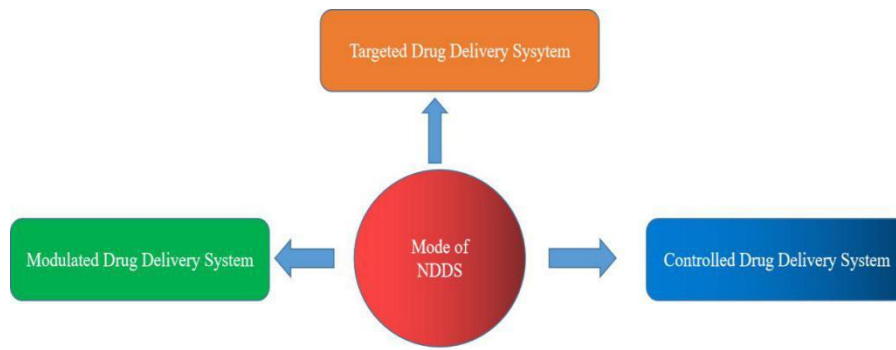


Figure 1: Mode of NDDS

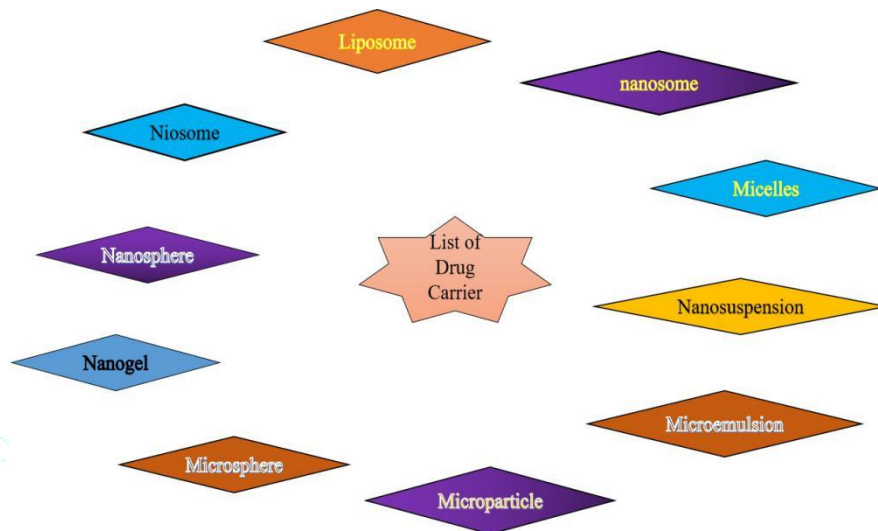


Figure 2: List of Drug Carrier

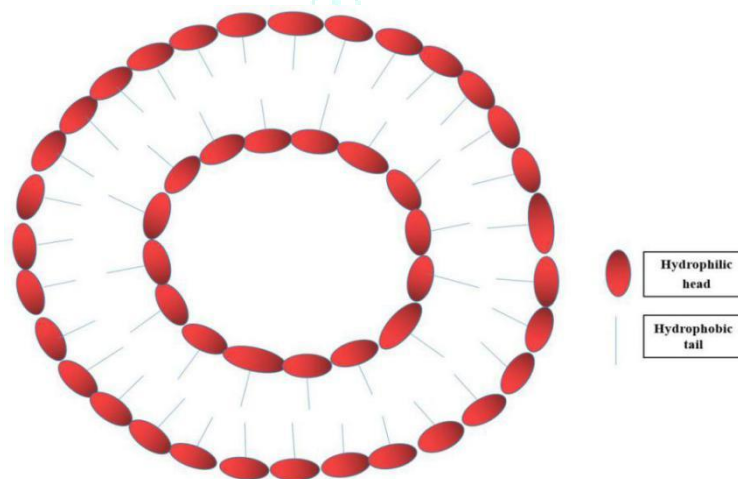


Figure 3: Nanoparticle micelle without loaded drug

1.6 History

The term ‘nanogel’ outlined because the nanosized particles shaped by physically or with chemicals cross-linked compound networks that swells in a very sensible solvent (Fig. 4). The term, “nanogel” (NanoGel™) was 1st introduced to outline cross-linked bi-functional networks of a poly ion and a non-ionic compound for the delivery of polynucleotides (cross-linked polyethyleneimine (PEI) and polyethylene glycol) (PEG)¹

The characteristics of “nanogels” is derived from their parent “hydrogels.” The best options of nanogels be their optimum size (ranging from ten to two hundred nm), tunable degradation, high practicality, bio-compatibility glorious drug loading capability, sensible unharness characteristics, high binary compound dispersion, prolonged blood circulation, and immunocompatibility².

Diclofenac sodium nanogel that provides prolonged unharness, increase the continuance of drug on the skin thereby enhance bioavailability³.

Table 1: Examples of Nanogels Formulations

SN.	Drug	Additives	Method	Treatment
1	Zno	Acetic acid , chitosan, ethanol, sodium tripolyphosphate	Ion gelation method	Liver
2	Gum arabic aldehyde	Gelatin, borax, sodium chloride, span20, trinitrobenzene sulphonic acid, sodium meta periodate, sodiumdihydrogen phosphate, disodiumhydrogen phosphate, sodium bicarbonate, isopropanol, sodium hydroxide, cyclohexane, acetone, methyl orange, Hydroxylamine Hydrochloric acid	Inverse mini emulsion method	Breast cancer
3	Beta sitosterol	Carbapol 934, Polyethylene -glycol, glycerin,Triethanolamine, eudragitRL100, poloxamer 407	Dispersion method	TDDS
4	5flurouracil	Lysozyme, trypsinase, pepsin, sodium CMC, di-sodium hydrogen phosphate, potassium dihydrogen phosphate, Hydrochloric acid	Convenient method, [polyelectrolyte- complex coacervation] via-electrostatic- interactions	Epithelial cancers
5	Carboxymethyl	Chitosan, PVA, N, N'- methylene bisacrylamide, Tetramethylenediamine, KPS, sodium hydroxide, acetic acid , methanol, monochloroacetic acid	Surfactant free method	Antimicrobial activity
6	Cyclodextrin	HPMC, EGDE, dichloromethane, span80, cross linker BIS, N-vinylcaprolactam, Acetoacetoxyethylmethacrylate	W/O emulsion Emulsification / Solvent-evaporation process	---
7	Al ₂ O ₃	Sodium hydroxide, Ethanol, aluminium nitrate, urea	Sol gel auto combustion syn. Chemical precipitation	----
8	Deferoxamin	Lecithin, streptozotocin, Bovine serum albumin, Aminoethylcarbazole, chloroform, pentobarbitone sodium		Intraperitoneal
9	10-hydroxy camptothecin	Ferricchloride hexahydrate, Ferrouschloride tetrahydrate, N-isopropylacrylamide, Methacrylic acid, Polyethyleneglycol, methacrylate, Acrylamide, 2,20- Azoisobutyronitrile, Cetyltrimethylammonium bromide, Methylthiazolyl tetrazolium, Fetal bovine serum	Emulsion polymerization method Emulsification evaporation method	Inhibit tumor growth and alleviate metastasis
10	Myricetin	Beta glycerol phosphate, Beta glucuronidase, Sulfatase, Formic acid, MTT[3-(4,5-dimethyl-2-thiazolyl)-2, 5- diphenyl-2H-tetrazolium bromide], Acetonitrile, Methanol	Sol gel method	oral
11	Methotrexate	Carbopol, EDTA, Propyl paraben, Methyl paraben, Butylated hydroxyl anisole, Glycerol, Propylene glycol	Hot homogenization method	Skin
12	Diclofenac sodium	Eudragit S-100, Carbopol 940, Glycerol, Tween 80, Triethanolamine, Water	Emulsion solvent- diffusion method	Topical
13	Nickel	Chitin, Calcium chloride, Methanol, Sodium hydroxide, Triethanolamine, Nickel chloride	Hydrothermal method	
14	PVA/1-VI	Methylene bisacrylamide, Potassium persulfate, Tetramethylenediamine, Acetone	Polymerization of PVA nanoparticles with vinylimidazole monomer	Skin
15	Polyherbal formulation i.e. ADJ6	Soluble starch, Porcine pancreatic alpha amylase, Alpha glucosidase, 3,5- dinitrosalicylic acid, 2,4-dinitrophenyl hydrazine, P-nitrophenylalpha-D glucopyranoside, Gallic acid, Quercetin, Ascorbic acid, acarbose	Traditional Ayurveda method	Pancreas and digestive system

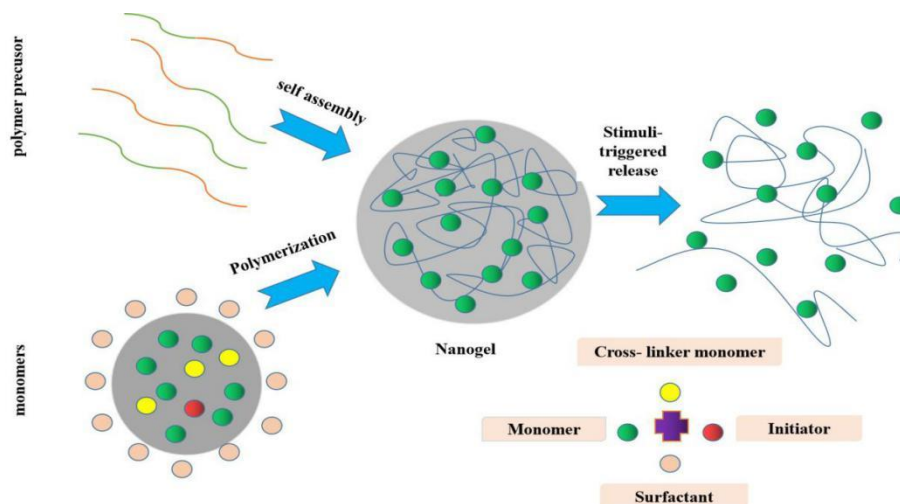


Figure 4: Nanogel formation

1.7 Features of nanogel

1.7.1 Size control: Nanogel size and surface properties are frequently with chemicals obsessed to limit the rate of clearance by somatic cells furthermore to modify either passive or active cell targeting. Nanogels should be sufficiently small to traverse capillaries and penetrate tissues through either paracellular or transcellular pathways⁴.

1.7.2 High encapsulation stability: Drug molecules loaded into the nanogel ought to be maintained and not to be transported out or leak untimely whereas current so as to supply most therapeutic effects and minimum toxicity or facet effects

1.7.3 Controlled and sustained drugged release: Drug transport ought to occur at the target website, thereby providing each therapeutic effectively and reduced facet effects. Drug loading ought to be sufficiently high to attain therapeutic goals

1.7.4 Targeting: Site specific delivery of nanogels carriers are often achieved via either coupling to their surface affinity ligands binding to focus on determinants of victimization responsiveness to native factors as on top of, or via “passive” targeting approaches together with extrapolation within the pathological sites and retention within the microvasculature

1.7.5 Low toxicity: The nanogels themselves ought to be extremely biocompatible and free from toxicity, and may be perishable with non-toxic degradation merchandise that area unit pronto cleared from the body⁴

1.8 Ideal characteristics of drug for Nanogel⁵

- The drug ought to be of low weight unit. Wt (<500 da)
- The drug ought to be compatible with the polymers wont to prepare nanogels
- The charge density on a drug ought to below
- Hydrophobic or hydrophilic drugs will be incorporated in nanogel

1.9 Ideal characteristics of polymers⁵

- Polymers ought to be biocompatible to be employed in oral nanogel drug delivery

- Polymers ought to be compatible with the drug used
- The compound ought to be capable of forming a gel
- Polymers ought to be sensitive to the physiological stimuli (PH, Enzyme, Glucose) to be used for drug delivery.

1.10 Advantages of nanogel

- Nanogels have high bio-compatibility and biodegradability
- Each deliquescent and hydrophobic medication will be developed in nanogels formulation⁵
- Macro molecular medical specialty like DNA, siRNA, amide & proteins will be incorporated into nanogel⁶
- Good for specific target and transport characteristics⁷
- Reticuloendothelial area unit invasion in nature which might be prevented by nanogel
- Target or site-specific delivery to be achieved
- Helps in enhancing oral and brain bio-availability of low relative molecular mass medication and biomacromolecules⁸.

1.11 Disadvantages of Nanogel

- Surface-active agent & Monomers will impart toxicity to the tissues
- Polymerization reactions for the preparation of the nanogels area unit terribly harsh.

2. RELEASE MECHANISM OF DRUG FROM NANOGEL⁹:

The discharge of the drug from nanogels within the site of the action happens by following ways that¹⁰

- Easy diffusion of the drug from the nanogel
- Degradation of nanogel
- pH stimulant
- Ionic exchange with the surroundings
- External energy supply.
- It has been shown in fig.5

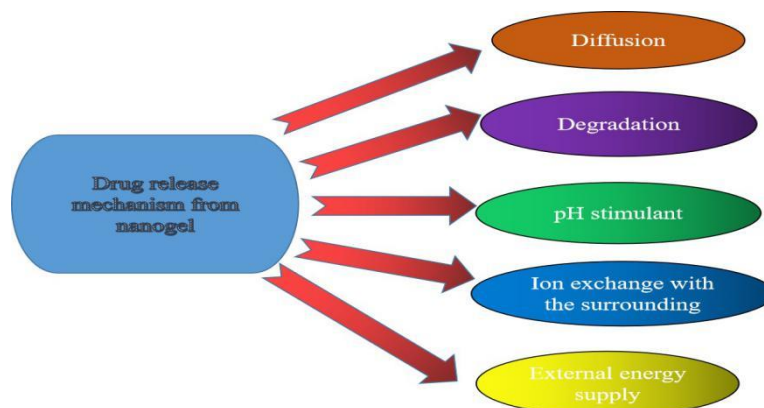


Figure 5: Drug release mechanism from Nanogel

3. CLASSIFICATION OF NANO GEL:

Basically, nanogels are classified into three types (fig.6)

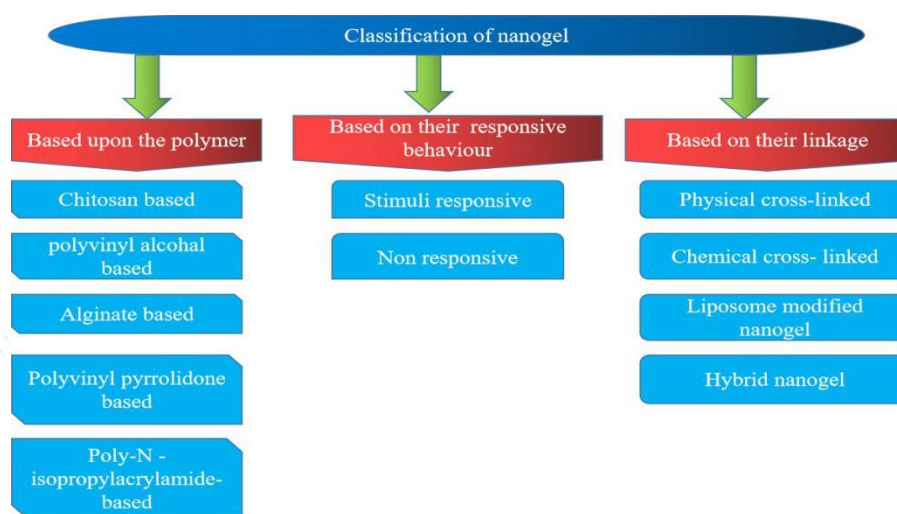


Figure 6: Classification of Nanogel

3.1 Based upon the polymers

3.1.1 Chitosan-based nanogel

Chitosan, α (1-4)-2 amino-2-deoxy β -D-glucan, is a polyose which is a deacetylated form of chitin and present in crustacean shells¹¹. The polymer chitosan having a positive charge and easily hydro-soluble in the nature of these properties permit interacting with negatively charged polymers and have contact with polyanions in an aqueous state of affairs¹².

3.1.2 Poly (vinyl alcohol) - based nanogel

PVA plays an essential role in nanogel studies. It has the cross-linking characteristics that are administrated using physical and chemical ways. Physical ways like e.g.: (freezing/ thawing) ways and chemical ways like e.g.: cross-linking agents, ray, γ - irradiation). Even though the cross-linking method is challenging but it is helpful for various applications in medical and pharmaceuticals fields¹³. Biodegradable polymers having short polylactone chains grafted to PVA or amendment sulfobutyl- PVA was ready and used as a completely unique category of water-soluble comb-like polymers¹⁴.

3.1.3 Alginate - based nanogel

The prepared alginate nanoparticles{ metal alginate drug carrier} with a wide range of particle sizes (250 – 850 nm), by using the sodium alginate and calcium chloride and resulted by polylysine. The anti-tubercular chemotherapy increases the bioavailability by using the alginate nanoparticles and of all drug encapsulated in alginate nanoparticles were significantly higher than those with free drugs¹⁵.

3.1.4 Poly (vinyl pyrrolidone)-based nanogel

Polyvinyl based mostly colloidal gel nanoparticle with final length is a smaller amount than a hundred nm, using the aqueous center was reverse micellar depicted by Baharali¹⁶. These reverse micellar are highly monodispersed, the droplet sizes can be well- controlled and size can be softened by controlling the size of the reverse micellar droplets¹⁷.

3.1.5 Poly-N-Isopropylacrylamide-based nanogel

Dextran containing hydrogel has been developed by G. Huang¹⁸. In this study, covalent cross-linking is formed by the PNIPAM -co-allylamine nanoparticles network.

Thermoresponsive core-shell PNIPAM nanoparticles via seeding and feeding precipitation polymerization are described by Gan & Lyon¹⁹.

3.2 Based on their responsive behavior²⁰

3.2.1 Stimuli-responsive

In this form of nanogel, it may be swelling or deswell. It depends upon exposure to environmental changes like temperatures, PH, magnetic field and ionic strength. The nanogels which have the multi-responsive character have more than one environmental stimulus

3.2.2 Non-responsive

These have a characteristic like absorbing water and swelling.

3.3 Based on their linkages present in the network chains: Based on their linkage it has a capacity like to form a gel structure, polymeric gels (including nanogel) and these divided as follows:

3.3.1 Physical Cross-linked Gels

These types of gels are also known as pseudo gels. They are formed by weaker linkages through Vander-Waal forces, hydrogen bonding, hydrophobic or electron static interactions.

3.3.2 Chemically cross-linked Gels

These types of gels are permanently linkages through the covalent bonds. It has properties like a crosslinked gel system and depends on the functional group present in the gel system. By the polymerization of vinyl monomers in the presence of multifunctional cross-linkers the deliquescent polymers and deliquescent-hydrophobic copolymers are obtained.

3.3.3 Liposome Modified Nanogels

When liposomes are mixed with the succinylated poly (glycidol)s; these liposomes can be expeditiously delivered calcein to the cytoplasm by nuclear reaction to the chain below pH 5.5. Liposomes which area unit the Thermo and pH-responsive nanogel like as poly (N isopropyl acrylamide) area unit being examine for transdermic drug delivery.

3.3.4 Hybrid Nanogels

When the nanogel particles dispersed in organic and inorganic matrices are thought of as hybrid nanogels. These sorts of nanogel formation take place in equal degree watery medium by self-assembly or accumulation of chemical compound amphiphiles, like pullullan-PNIPAM, hydrophobic polyoside, and hydrophobic pullan²¹⁻²². These forms of hybrid nanogel are shaped physical cross-linking and capable to deliver the hypoglycemic agent and anti-cancer medication additional efficaciously²³⁻²⁴.

4. METHODS FOR NANOGEL PREPARATION:

By the employment of Isostatic ultra-high pressure (IUHP), cross, water, and important conditions of drying, nucleophilic substitution reaction, gelling agents and irradiation, and freeze-thawing, we will additionally prepare nanogel.

4.1 Heterogeneous atom polymerization

Various heterogeneous chemical action reactions of deliquescent or soluble monomers inside the presence of either dysfunctional or multifunctional crosslinkers are chiefly in use to arrange the well-defined artificial microgels. They embody precipitation, inverse (mini) emulsion, inverse small emulsion, associate degree dispersion chemical {process|chemical change|chemical action} utilizing an uncontrolled atom chemical action process²⁵. Photocrosslinked perishable photoluminescent polymers

(PBPLPs) nanogel was ready by atom cross-linking of a vinyl-containing fluorescent polymer for drug delivery and cell imaging. Development of PBPLPs nanogel shows a brand-new era to develop nanomaterials in therapeutic nanomedicine for drug delivery and cell imaging²⁶⁻²⁷.

4.2 Inverse (mini) emulsion method

A W/O emulsion is created from a combination consisting of binary compound biopolymer droplets and never-ending lipid portion exploitation either a homogenizer or a high-speed mechanical stirrer. Resulting binary compound droplets of biopolymers area unit then cross-linked with applicable cross-linking agents. Then cross-linked microgel particles area unit primed as dispersion in organic solvents. Sublimate by precipitation, natural process, laundry with organic solvents like isopropyl alcohol, and dehydration.

4.3 W/O heterogeneous emulsion method

W/O emulsion strategies involve typically Two steps: emulsification of binary compound droplets of water-soluble biopolymers in continuous oil section with associate degree aid of oil-soluble surfactants and cross-linking of biopolymers with soluble crosslinkers. The water-in-oil emulsion method has recently been custom-made to organize γ -cyclodextrin (γ CD) or hydroxypropyl- β -cyclodextrin (HP β CD) nanogels inside which the crosslinking takes place at the same time with an associate degree in emulsification/solvent evaporation method²⁸.

4.4 Precipitation polymerization²⁹⁻³⁸

Precipitation chemical process involves the formation of a uniform mixture at its initial stage, and therefore, the incidence of initiation and chemical process within the homogeneous solution. Because the designed polymers don't seem to be swella however soluble within the medium, employment of a cross-linker is critical to cross-link chemical compound chains for the isolation of particles. As a result, the ensuing cross-linked particles typically have equal degree casual form with high polydispersity (PDI).

The preparation of microgels and nanogels supported PNIPAM and its derivatives by precipitation chemical process in water has been extensively explored for medical speciality applications.

4.5 Inverse microemulsion polymerization

While inverse (mini) emulsion chemical process forms kinetically stable macroemulsions at, below, or close to the essential micellar concentration (CMC), inverse microemulsion chemical process produces thermodynamically stable microemulsions upon any addition of surfactant higher than the essential threshold. Poly(vinylpyrrolidone)-based nanogels incorporated with Dex as a soluble organic compound macromolecule drug were ready³⁹⁻⁴⁰ cationic nanogels of poly (HEA-co-AETMAC) were ready within the presence of oligo(ethylene glycol) dimethacrylate (OEGDMA) as a cross-linker.

4.6 Heterogeneous controlled/ living radical polymerization

C-reactive protein has been explored as a tool for the preparation of well-controlled polymer- protein/peptide bioconjugates. Varied ways for C-reactive protein are developed; but, the foremost successful techniques embrace atom transfer radical chemical process (ATRP), stable a tom chemical process (SFRP), and reversible addition-fragmentation chain transfer (RAFT) chemical process.

4.6.1 Atom transfer radical polymerization

ATRP is one of the foremost successful C-reactive protein techniques, sanctionative the preparation of a good spectrum of polymers with planned relative molecular mass and comparatively slender relative molecular mass distribution ($M_w/M_n < 1.5$)⁴¹⁻⁴². ATRP additionally permits for the preparation of copolymers with completely different chain architectures, like block, random, gradient, comb-shaped, brush, and multimedia star copolymers⁴³⁻⁴⁵

Colloidal gel NPS of PNIPAAm were ready by precipitation chemical process via ATRP in water⁴⁶. OEOMA, AN analog of PEG has been polymerized by AGET ATRP in undiversified binary compound solution⁴⁷ and in heterogeneous conditions⁴⁸.

4.6.2 Nanogel synthesis by RAFT chemical process in water

The primary example of nanogel synthesis by direct RAFT chemical process below precipitation/dispersion chemical process condition was reported by AN and co-workers in 2007⁴⁹. Two sorts of poly(N, N'-dimethyl acrylamide)s (PDMA)s bearing a tri-thiocarbonate cluster were first synthesized by RAFT answer chemical process and were afterward used as an each stabilizer and RAFT agents for nanogel synthesis by RAFT precipitation/dispersion chemical process.

4.7 Dispersion polymerization: In the method, most ingredients as well as monomers, chemical compound stabilizers and initiators area unit soluble in an organic solvent as a continual section. At the onset, chemical process occur in an extremely jelled reaction mixture; but, the shaped polymers become insoluble within the continuous medium, ultimately resulting in the formation of stable dispersion of chemical compound particles with an aid of mixture stabilizers.

5. EVALUATION PARAMETERS

5.1 Appearance: The ready gel bases were inspected visually for clarity, colour, and presence of any particles.

The Diclofenac sodium nanogel using {carbopol 940 as a gelling agent and Eudragit S-100 has shown higher flux improvement with humectant as permeation enhancer} was ready and evaluated by emulsion solvent diffusion methodology. The appearance of Diclofenac sodium were found that **clear**.

The nanosized dispersion of Beta-sitosterol {One Chronicles of carbopol 934} by nanoprecipitation methodology was ready and evaluated. The appearance of beta-sitosterol nanogel was found that **White**.

5.2 Homogeneity: All developed gels were tested for homogeneity by visual review when the gels are set within the instrumentality.

The Diclofenac sodium nanogel using {carbopol 940 as a gelling agent and Eudragit S-100 has shown higher flux improvement with humectant as permeation enhancer} was ready and evaluated by emulsion solvent diffusion methodology. The homogeneity of Diclofenac sodium was found that **homogenized**.

The nanosized dispersion of Beta sitosterol {One Chronicles of carbopol 934} by nanoprecipitation methodology was ready and evaluated. The homogeneity of beta-sitosterol nanogel was found that **homogenized**.

5.3 Particle size and polydispersity index (PDI): The mean size of the chosen nanogels was determined by exploitation Malvern Master sizer 2000 MS. The mean particle size was recorded.

The anti-inflammatory nanogel {propylene glycol as permeation enhancer} was ready and evaluated by the emulsion solvent diffusion technique. The particle size(nm) of anti-inflammatory was found that=**165 nm**.The marketed product (serrini Gel) was evaluated. The particle size of this gel was found: **168 nm**.

The Chitosan primarily based nanogel for oral delivery of myricetin was prepared and evaluated. Particle diameter, polydispersity index (PDI), and letter of the alphabet potential of the blank and Myr-loaded nanogels were determined by an optical device. The mean particle size of the blank CS/ β -GP nanogels was some 107.43 ± 11.86 nm, but the PDI approached, the foremost a pair of peaks was 288.3 nm (66. 2%) and 31.44 nm (27. 0%), indicating that the blank CS/ β -GP nanogels was associate in Nursing heterogeneous system⁵⁰.

The immunosuppressant loaded nanostructured super-molecule carrier (MTX-NLC) was prepared and evaluated {throughout a mix of Precirol ATO Five and Captex 300 (1:1) at seventy zero C} by Hot mix technique. The particle size of MTX-NLC was found that **278 ± 10 nm**, PDI of **0.231 ± 0.05** ⁵¹.

The polyose nanogel(CNGs){0. 5% polyose solution}, Act loaded polyose nanogel(ActCNGs), AE loaded polyose nanogels (AECNGs) were prepared {wood alcohol to induce a quantity of 2. 5mg/5mL that was intercalary to polyose resolution for regeneration of AE loaded CNGs}and evaluated and the particle size was found to be **98 ± 10 , 138 ± 8 and 238 ± 6 nm** severally with spherical morphology⁵².

5.4 pH measurement:

The Acyclovir gel was prepared {by exploitation Acyclovir nanoparticles with Eudragit RS a hundred as a chemical compound, carbopol 934P (1%) as gel reservoir}and evaluated. Once evaluating this, the pH worth of Acyclovir gel was found that: **6. 8**⁵³

5.5 Drug content:

The drug concentration in nanogel was measured by high-performance skinny layer natural action. Beta-Sitosterol content in nanogel was measured by dissolving the best-known amount of nanogel in Phosphate buffer (pH-7. 4) by sonication. Space beneath curve was measured once appropriate dilution at 550 nm in HPTLC⁵⁴

The Acyclovir gel was prepared by using {Acyclovir nanoparticles with Eudragit RS an one hundred as chemical compound, carbopol 934P (1%) as gel reservoir}and evaluated. Once evaluating this, the drug content value of Acyclovir gel was found that **$98.2-99.12$ %**.

5.6 Spreadability: Spreadability is set by equipment advised by Mutimer. Spreadability was calculated by exploitation of the formula,

$$S=M. L/T,$$

Where, S=spreadability, L=Length of glass slide, M=weight tied to higher slide, T=Time taken to separate the slides.

The nanosizes dispersion of Beta-sitosterol by using {1% of carbopol 934} by nanoprecipitation technique was ready and evaluated. The spreadability of varied concentrations of carbopol 934 is been, out of that F2 showed

higher spreadability than opposite formulations. The spreadability of beta-sitosterol was found that **20.35 (\pm 0.05)**

5.7 Extrudability

The Diclofenac sodium nanogel {1% carbopol 940 as gelling agent and Eudragit S-100 has shown higher flux sweetening with propylene glycol as permeation enhancer} was ready and evaluated by emulsion solvent diffusion methodology. The extrudability of Diclofenac sodium was found that **279 \pm 0.7**

5.8 Fourier transform infrared spectrometry (FT-IR)-

From the FTIR spectrum, it was terminated that the drug sample was in pure type⁵⁵⁻⁵⁷

The polyose nanogel(CNGs){0.5% polyose solution}, Act loaded polyose nanogel (ActCNGs), AE loaded polyose nanogels (AECNGs) were ready and evaluated. After evaluating this we tend to determine that, FTIR spectra of polyose and CNGs have characteristic peaks at 3500-3400, 1640 (amide I region) and 1070 cm⁻¹(-C-O-stretching. Act was defined by peaks around 1700-1500 and 1300-1000 cm⁻¹.

5.9 Differential scanning calorimetry(DSC)

Differential scanning measurement (DSC) was performed in DSC 60-Plus Shimadzu to characterize the physical state of the drug. From the DSC, it will be concluded that the excipients and drugs don't have any interaction with one another.

The CS-ZnO-NC was prepared {(0.01 M) to 100³centimeters of metallic element acetate (0.01 M) solution} and evaluated by the average phase transition methodology. The differential scanning measuring instrument (DSC) represented in shows a peak at around **257 °C** for ZnO⁵⁸.

5.10 UV-spectroscopy

The NSAID nanogel using {carbopol 940 as a gelling agent and Eudragit S-100 has shown higher flux sweetening with humectant as permeation enhancer} was ready and evaluated by emulsion solvent diffusion methodology. After evaluation, it had been found that the drug shows absorbances at 226 and 276 nm So, **276 nm** was thought-about as λ_{max} .

5.11 Entrapment efficiency⁵⁹

EE of MTX in NLC made up our minds by associate degree indirect methodology. Briefly, the NLC suspension was centrifuged at 22,000 revolutions per minute for ten minutes at 40°C The obtained supernatant was diluted with methyl alcohol and also the quantity of the free MTX endue within the supernatant was quantified mistreatment by HPLC method. The application was calculated mistreatment by the subsequent formula.

Entrapment efficiency = $\frac{1}{4}$ (Amount of MTX added in formulation-amount present in supernatant) /Amount of MTX added in formulation \times 100

The MTX-NLC nanogel was ready and evaluated by a hot-homogenization method. When evaluating this, we determined the EE of MTX-NLC was **22.29 \pm 1. 23%**.

5.12 Rheological property (viscosity)

Brookfield measuring device was used for the studies. First, the spindle was unfit into the gel until the notch on the spindle touched the gel surface. 3gm every of gel I and gel II

(Stability chamber and space temperature) was employed in the study. The spindle no. 61, 63, 64 was selected supported consistency of the gel. The dial readings were taken at 50, 100, 150, 250rpm and consistency was measured⁶⁰⁻⁶⁴.

The Diclofenac sodium nanogel{carbopol 940 as a gelling agent and Eudragit S-100 has shown higher flux improvement with humectant as permeation enhancer} was ready and evaluated by emulsion solvent diffusion technique.The viscosity(in cp at fifty (rpm)) of Diclofenac sodium was found: **9563**.

The nanosizes dispersion of Beta-sitosterol using {1% of Carbopol 934} by nanoprecipitation technique was ready and evaluated. When evaluating this we tend to find that the consistency of beta-sitosterol nanogel was **35,956 \pm 5. 50**

5.13 Swelling study: The nickel nanoparticle was ready {5 mg of nickel nanoparticles was another to 10 milliliters of 0.5% polyose solution and sonicated with amplitude of seventy-fifth for twenty minutes}and evaluated by victimization Hydro-thermal methodology.

Swelling quantitative relation = $(W_w - W_d)/W_d \times 100$

where, W_w (wet weight) and W_d (dry weight) of Ni-Chitin NGs were calculated severally⁶⁵⁻⁶⁶

5.14 In-vitro evaluation

5.14.1 In-vitro drug release and kinetic study- The *in-vitro* drug release behavior of drug-loaded nanogel particles, placed within the qualitative analysis tube (molecular weight cut-off 8–12 kg/mol), was examined in 3 totally different media at 67.0 \pm 0.5°C. The 3 media were 0.1 mol/l HCl (simulated stomachal fluid, pH 1. 0, I = 0. 1), phosphate buffer (simulated enteric fluid, pH 6.8, I = 0. 1) and phosphate buffer (simulated colon fluid, pH 7. 2, I = 0.1). The number of drug-free made up our minds exploitation an Uv-vis photometer at specific nm. The accumulative drug release was calculated as follows.

Accumulative drug release = $(M_t/M_0) \times 100\%$,

wherever M_t is the quantity of drug-free on time t and M_0 is the quantity of drug-loaded in nanogel particles.

The nonsteroidal anti-inflammatory drug nanogel {by exploitation carbopol 940 as a gelling agent and Eudragit S-100 has shown higher flux improvement with antifreeze as permeation enhancer} was ready and evaluated by emulsion solvent diffusion methodology. After analysis, we tend to get the drug to release values of nonsteroidal anti-inflammatory drug was **96.72 \pm 0. 0784**

5.14.2 In-vitro hemolysis:

The acitretin and Aloe-emodin loaded polyose nanogel was ready and evaluated for the treatment of skin disease. In this study, recent human blood was wont to assess the blood compatibility of formulations by *in vitro* hemolysis. The optical density (OD) values were scanned exploitation microplate reader at 450, 380 and 415 nm. The plasma Hb was calculated exploitation the equation given below⁶⁷.

Plasma Hb = $\{(2A_{415}) - [A_{380} + A_{450}] - 76.25\}$

The obtained values of samples compared therewith of positive management (Triton X) and negative management (normal saline). The values were triplicated⁶⁸. The results from *in vitro* hemolysis assay unconcealed there's no risk of hemolysis or activity even though general delivery of ActCNGs or AECNGs at a high concentration is achieved through the transdermic route. Once the encapsulation of drug in CNGs, the hemolytic proportion was found to be but

five-hitter, that is the margin of error for biomaterials per ISO/TR 7406⁶⁹⁻⁷⁰.

5.15 *In-vivo* Pharmacokinetics

5.15.1 Experimental protocol: within the experiment, a complete of twenty-four rats (18 diabetic extant rats, half-dozen traditional rats) were used. The rats were divided into four teams of half-dozen every. The experimental amount was twenty-eight days starting when the induction of polygenic disease.

- Group 1: traditional untreated rats
- Group 2: Diabetic management rats (STZ group).
- Group 3: were diabetic rats given CS-ZnO-NC (100 mg/kg body weight) for twenty-eight days
- Group 4: Diabetic rats given medical care drug [Glibenclamide] (600 µg/kg bodyweight).

5.15.2 Biochemical data analysis: The assorted organic chemistry parameters were analyzed on completely different teams.

Fasting blood sugar estimation was done weekly on tail prick blood by mistreatment ACCU-CHEK device glucometer.

Insulin concentration in bodily fluid was calculable by enzyme-linked-immunosorbent serologic assay. The macromolecule profile parameters like total steroid alcohol by CHOD-PAP methodology⁷¹

All the estimations were dole out on fast bodily fluid samples mistreatment business kits.

5.16 Stability studies:

The nanogels systems were stuffed in glasswares and incubated at 2-8°C (refrigeration condition), temperature (30±2°C) and at 40°C/65% RH (accelerated condition) for ninety days⁷². The physical stability of the formulation was examined visually for look, color, and odor in every thirty days.

6. APPLICATION:

Nanogel-based drug delivery formulations improve the effectiveness and safety of sure anti-cancer medicine, and plenty of different medicine (**Fig.7**), thanks to their chemical composition that is confirmed from *in vivo* study in animal models.



Figure 7: Application of Nanogel

6.1 Local anesthetics

Local anesthetics field are an unit one in all the categories of medication that induces physiological condition, and eliminate pain. A delivery system of procaine, that is Associate in Nursing amino organic compound native anesthetics loaded into acid alkyl group salt nanogel via hydrophobic and gas bonds exhibited a high unharness rate at high pH. The mechanism of unharnessing is predicated on the deprotonation of the acid on the nanogel that ends up in a rise within the pressure, and therefore, the swelling of the entire system that will increase the porousness, so promoting the discharge of the procaine⁷³.

6.2 Neurodegenerative disease

Currently, neurodegenerative disorders like Alzheimer's & Parkinson's malady haven't any well-known cure, therefore,

once oligonucleotides showed a possibility to be used as a diagnostic or therapeutic tool for these diseases, they became the main target of many studies. So far, the applying of oligonucleotides within the treatment of neurodegenerative malady is considerably hindered by their instability against metabolism, their inability to penetrate the blood-brain barrier, and their fast clearance by urinary organ excretion. To assist the performance of oligonucleotides they were incorporated into nanogel delivery systems. The novel properties of nanogels permit oligonucleotides to cross the blood-brain barrier, thereby aiding their delivery into the central system⁷⁴

6.3 Anti-inflammatory⁷⁵⁻⁷⁷

Nanogels have found associate in Nursing application medicine and cosmetology as topical delivery systems of

non-steroidal anti-inflammatory medicine (NSAIDs) and for the treatment of allergic dermatitis and psoriatic plaque. Nanogels are a unit ideal for this application since they will overcome the most important limitation of topical delivery systems, that is the comparatively shortened contact time between active medicine and therefore, the application site. This can be done by retaining water into the gel matrix and forming a consistent dispersion of the nanogel.

The PLGA/chitosan topical nanogel enhances the transdermal drug delivery of Oruvail and spantide II and shows smart therapeutic activities with low toxicities.

6.4 Vaccine delivery

Vaccination is predicated on the induction of an immune response that is antigen-specific. To assist the efficiency and therefore, the performance of vaccines, compound nanogels are a unit being used as a novel, different approach to immunogen delivery. The advantage of nanogels over standard immunogen lies within the ability of the nanogel network to guard the vaccine antigens from catalyst degradation⁷⁸.

6.5 Transdermal drug delivery system

Transdermal route of administration has raised over different routes therein it bypasses 1st pass impact improves the potency of medication, provides steady-state drug concentration in plasma and will increase patient compliance. Through the emulsion solvent diffusion technique, a dispersion of aceclofenac was shaped and incorporated into a gel matrix to formulate a nanogel for the stratum delivery of the drug⁷⁹.

6.6 Ophthalmology

Dexamethasone containing eye drop was readied by solvent evaporation or emulsification technique using 2-hydroxypropyl- γ -cyclodextrin (HP γ CD) medium containing γ CD nanogel for sustained unharmed. PH-sensitive polyvinylpyrrolidone-poly [acrylic acid] (PVP/PAAc) nanogels, developed by γ radiation-induced polymerization of propenoic acid (AAc) in an aqueous solution of polyvinylpyrrolidone (PVP) acting as a model, were accustomed to encapsulate alkaloid, so enhancing the bioavailability yet because of the stability of alkaloid in an aqueous solution maintaining an adequate concentration of the drug at the location of action for prolonged amount of time⁸⁰⁻⁸¹.

6.7 Diabetics

An injectable Nano-Network that responds to aldohexose and releases internal secretion has been developed. It contains a combination of oppositely charged nanoparticles that attract one another. To form the nanogel reply to enhance acidity dextran, a changed saccharide was used. Every nanoparticle within the gel holds spheres of dextran loaded with internal secretion associated in an aqueous solution a catalyst that converts aldohexose into gluconic acid. aldohexose molecules will simply enter and diffuse through the gel. So once levels are unit high, a lot of aldohexose passes through the gel and triggers unharmed of the catalyst that converts it to gluconic acid. This will increase acidity, which triggers the discharge of the internal secretion⁸².

6.8 Nanogel in Cancer⁸³⁻⁸⁷

Nanogel in cancer is employed for the particular targeted drug delivery with low toxicities with high therapeutic power and very good wound healing properties.

Polymeric nanogel plays a vital role in transporting the macromolecules:

Peptides: RGD, cyclosporin, and vasoactive

Proteins: hormone, cytokines, and elcatoninso

Glycoproteins: glycoprotein a sequence, peptidase substance peptides, and globulins

Oligosaccharides: anticoagulant medication and globulins

Amino-acids: l-arginine, glutamine, and essential amino acid.

7. FUTURE PROSPECTS AND CHALLENGES

Nanogels have already been used as DDS *in vivo* and in clinical trials, primarily for cancer medical care. CHP nanogels have additionally evidenced their prospects for clinical trials by reducing the toxicity of system cells by showing increase in the binding capability to A β oligomer in treating Alzheimer's disorder. Recent prospects in polygenic disorder management by optical sensitive hormone loaded silver nanoparticle nanogel of poly(4-vinylphenylboronic acid-co-2-(dimethylamino) alkyl group acrylate) are designed gap new era within the field of run.

The cholesteryl-HER - a pair of immunizing agent was administered to Nine patients with three hundred μ g with booster doses double every week. From this shown that skin sensitivity at the positioning of S. C injection & CD4+ & CD8+ T- cell shows the higher therapeutic effectiveness. Cholesterin pullulan nanogels show the cut back the toxicity to the system cells and increase the binding capability to AB oligomer in treating Alzheimer's illness⁸⁸⁻⁹².

Recently the new development of controlled polygenic disorder by optical sensitive hormone loaded silver nanoparticle nanogel of poly (four — vinyl phenyl chemical element acid - co - a pair of - (dimethylamino) alkyl group acrylate) are designed.

8. CONCLUSION

Nanogel is one of the fascinating fields of analysis in approaching the future, which may be helpful in delivering the drug in a controlled manner with minimizing the aspect result of typical nanogel. It has versatile advantages and properties that make them competent of economical delivery for biologically active molecules, significantly biopharmaceuticals. They will even be used as a carrier, or chaperoned to treat inheritable diseases such as cancer, neurodegenerative sickness etc. Nanogel seems to be a wonderful candidate for the treatment of varied diseases (including polygenic disease also)

9. REFERENCES

1. Sultana F, Manirujjaman, Imran-Ul-Haque Md, Arafat M, Sharmin S. An Overview of Nanogel Drug Delivery System, Journal of Applied Pharmaceutical Science. 2013; 3(8 Suppl 1):S95-S105.
2. Kumar N, Ashwin, sanoj Rejinold N, P Anjali, Balakrishnan A, Biswas R, R Jayakumar. Preparation of chitin nanogels containing nickel nanoparticles. Carbohydrate Polymer. 2013; 469-474.
3. Talele S, Nikam P, Ghosh B, Deore C, Jaybhav A, Jadhav A. A Research Article on Nanogel as Topical Promising Drug Delivery for Diclofenac sodium. Indian Journal of Pharmaceutical Education and Research. 2017; 51(4S):S580-587.
4. Yashashri I, Bhushan R, Jain Ashish. preparation and evaluation of beta sitosterol nanogel: a carrier design for targeted drug delivery system, Asian Journal of Pharmaceutical Research and Development. 2018; 6(3):81-87.

5. Sheikh T, Abrar M, Ansari D, Chaos S, Bagwan R, Kulkarni K. Nanogel: A versatile nanoscopic platform for oral drug delivery, *World Journal of Pharmacy and Pharmaceutical Sciences*. 2018; 7(9):2278 – 4357.
6. Sharma A, Garg T, Aman A, Panchal K, Sharma R, Kumar S, Markandeywar T. Nanogel - an advanced drug delivery tool: Current and future, *Artificial Cells. Nanomedicine and Biotechnology*, 2014.
7. Adhikari B, Cherukuri S, Reddy CS, Haranath C, Bhatta HP, Naidu Inturi R. Recent advances in nanogels drug delivery systems, *World Journal of Pharmacy and Pharmaceutical Sciences*. 2016; 5(9):505-530.
8. Arun Kumar Singh , Anita Singh. Phyto-Phospholipid Complexes: A Potential Novel Carrier System for Improving Bioavailability of Phytoconstituents. *Research Journal of Pharmacy and Technology*. 2020; 13(2):1059-1066.
9. Viswanathan B, Meeran IS, Subramani A, Sruthi, Ali J, TK shabeer. Historic review on modern herbal nanogel formulation and delivery, *International Journal of Pharmacy and Pharmaceutical Sciences*. 2018; 10(10):0975-1491.
10. Kabanov AV, Serguei V, Vinogradov. Nanogels as pharmaceutical carriers: Finite networks of infinite capabilities, *Advanced Drug Delivery Reviews*. 2009; 48:5418-29.
11. Kato Y, Onishi H, Machida Y. Application of chitin and chitosan derivatives in the pharmaceutical field, *Current Pharmaceutical Biotechnology*. 2003; 4(5): 303-9.
12. Shutava TG, Lvov YM. Nano-engineered microcapsules of tannic acid and chitosan for protein encapsulation, *Journal of nanoscience and nanotechnology*. 2006; 6(6):1655-61.
13. Knapczyk J, Krowczynski L, Krzck J, Brzeski M, Nirnberg E, Schenk D. Requirements of chitosan for pharmaceutical and biomedical applications, *Chitin and Chitosan: Sources, Chemistry, Biochemistry, Physical Properties and Applications*. Elsevier, London. 1989: 657-63.
14. Li JK, Wang N, Wu XS, Poly (vinyl alcohol). nanoparticles prepared by freezing–thawing process for protein/peptide drug delivery, *Journal of controlled release*. 1998; 56(1):117-26.
15. Rajaonarivony M, Vauthier C, Couarraze G, Puisieux F, Couvreur P. Development of a new drug carrier made from alginate. *Journal of pharmaceutical sciences*. 1993; 82(9):912-7.
16. Zahoor A, Sharma S, Khuller G. Inhalable alginate nanoparticles as antitubercular drug carriers against experimental tuberculosis, *International journal of antimicrobial agents*. 2005; 26(4):298-303.
17. Bharali DJ, Sahoo SK, Mozumdar S, Maitra A. Cross-linked polyvinylpyrrolidone nanoparticles: A potential carrier for hydrophilic drugs. *Journal of colloid and interface science*. 2003; 258(2):415-23.
18. Guowei D, Adriane K, Chen X, Jie C, Yinfeng L. PVP magnetic nanospheres: Biocompatibility, in vitro and in vivo bleomycin release, *International journal of pharmaceutics*. 2007; 328(1):78-85.
19. Huang G, Gao J, Hu Z, John JVS, Ponder BC, Moro D. Controlled drug release from hydrogel nanoparticle networks, *Journal of Controlled Release*. 2004; 94(2):303-11.
20. Gan D, Lyon LA. Tunable swelling kinetics in core-shell hydrogel nanoparticles. *Journal of the American Chemical Society*. 2001; 123(31):7511-7517.
21. Akiyoshi K, Sasaki Y, Sunamoto J. Molecular chaperone-like activity of hydrogel nanoparticles of hydrophobized pullulan: Thermal stabilization with refolding of carbonic anhydrase B. *Bioconjugate chemistry*. 1999; 10(3):321-4.
22. Akiyoshi K, Kang E-C, Kurumada S, Sunamoto J, Principi T, Winnik FM. Controlled association of amphiphilic polymers in water: Thermosensitive nanoparticles formed by self-assembly of hydrophobically modified pullulans and poly (N-isopropylacrylamides), *Macromolecules*. 2000; 33(9):3244-9.
23. Nishikawa T, Akiyoshi K, Sunamoto J. Macromolecular complexation between bovine serum albumin and the self-assembled hydrogel nanoparticle of hydrophobized polysaccharides. *Journal of the American Chemical Society*. 1996; 118(26):6110-5.
24. Kuroda K, Fujimoto K, Sunamoto J, Akiyoshi K. Hierarchical self-assembly of hydrophobically modified pullulan in water: Gelation by networks of nanoparticles, *Langmuir*. 2002; 18(10):3780-6.
25. Khoe S, Asadi H, Nanogels: Chemical Approaches to Preparation. *Encyclopedia of Biomedical Polymers and Polymeric Biomaterials*. 27 Jan 2016: 5266-5293.
26. Yadav HKS, Al Halabi N, Alsalloum GA. Nanogels as Novel Drug Delivery Systems - A Review, *Journal of Pharmacy and Pharmaceutical Research*. 2017; 1(1:5): 1-8.
27. D Manry, D Gyawali, J Yang. Size optimization of biodegradable fluorescent nanogels for cell imaging, *High School Res* 2011; 2:1.
28. Deore Samadhan K, Surawase Rajendra K, Maru Avish . Formulation and Evaluation of O/W Nanoemulsion of Ketoconazole. *Research Journal of Pharmaceutical Dosage Forms and Technology*. 2019; 11(4):269-274.
29. Guha S, Ray B, Mandal BM. Anomalous solubility of polyacrylamide prepared by dispersion (precipitation) polymerization in aqueous tert-butyl alcohol. *Journal of Polymer Sciences. A* 2001; 39(19):3434–3442.
30. Liu T, Desimone JM, Roberts GW. Continuous precipitation polymerization of acrylic acid in supercritical carbon dioxide: The polymerization rate and the polymer molecular weight, *Journal of Polymer Sciences. A* 2005; 43(12):2546–2555.
31. Bai F, Yang X, Zhao Y, Huang W. Synthesis of core-shell microspheres with active hydroxyl groups by two-stage precipitation polymerization. *Polymer International*. 2005; 54(1):168–174.
32. Li W.-H, Stover HDH. Mono- or narrow disperse poly(methacrylate-co-divinylbenzene) microspheres by precipitation polymerization. *Journal of Polymer Sciences. A* 1999; 37 (15):2899–2907.
33. Duracher D, Elaissari A, Pichot C, Preparation of poly(N-isopropylmethacrylamide) latexes kinetic studies and characterization, *Journal of Polymer Sciences, A* 1999; 37(12):1823–1837.
34. Hazot P, Chapel JP Pichot C, Elaissari, A, Delair T. Preparation of poly(N-ethyl methacrylamide) particles via an emulsion/precipitation process: The role of the crosslinker. *Journal of Polymer Sciences. A* 2002; 40(11):1808–1817.
35. H William, Blackburn L, Lyon A. Size-controlled synthesis of monodisperse core/shell nanogels. *Colloid Polymer Sciences*. 2008; 286(5):563–569.
36. Jones C.D, Lyon, LA. Synthesis and characterization of multiresponsive core-shell microgels. *Macromolecules*. 2000; 33(22):8301–8306.
37. Jones CD, Lyon LA. Shell-restricted swelling and core compression in poly(N-isopropylacrylamide) core-shell microgels. *Macromolecules*. 2003; 36(6):1988–1993.
38. Huang X, Lowe TL. Biodegradable thermoresponsive hydrogels for aqueous encapsulation and controlled release of hydrophilic model drugs. *Biomacromolecules*. 2005; 6(4):2131–2139.
39. Gaur U, Sahoo SK, De TK, Ghosh PC, Maitra A, Ghosh PK. Biodistribution of fluoresceinated dextran using novel nanoparticles evading reticuloendothelial system. *International Journal of Pharmacy*. 2000; 202(1–2):1–10.
40. Bharali DJ Sahoo SK, Mozumdar S, Maitra A. Cross-linked polyvinylpyrrolidone nanoparticles: A potential carrier for hydrophilic drugs. *Journal Colloid Interface Sciences*. 2003; 258(2):415–423.
41. Braunecker WA, Matyjaszewski K. Controlled/living radical polymerization: Features, developments, and perspectives. *Progress in Polymer Science*. 2007, 32 (1):93–146.
42. Matyjaszewski K and Xia J. Atom transfer radical polymerization. *Chemical Reviews*. 2001; 101(9):2921–2990.
43. Sheiko SS, Sumerlin BS, Matyjaszewski K. Cylindrical molecular brushes: Synthesis, characterization, and properties. *Progress in Polymer Science*. 2008; 33(7):759–785.
44. Yagci Y, Tasdelen MA. Mechanistic transformations involving living and controlled/living polymerization methods. *Progress in Polymer Science*. 2006; 31(12):1133–1170.
45. Hadjichristidis N, Iatrou H, Pitsikalis M, Mays J. Macromolecular architectures by living and controlled/ living polymerization. *Progress in Polymer Sciences*. 2006; 31(12):1068–1132.
46. Kim KH, Kim J, Jo WH, Preparation of hydrogel nanoparticles by atom transfer radical polymerization of N-

- isopropylacrylamide in aqueous media using PEG macro-initiator, *Polymer*, 2005; 46(9):2836-2840.
47. Oh JK, Min K, Matyjaszewski K. Preparation of poly(oligo(ethylene glycol) monomethyl ether methacrylate) by homogeneous aqueous AGET ATRP. *Macromolecules*. 2006; 39(9):3161-3167.
 48. Oh JK, Tang CB, Gao HF, Tsarevsky NV, Matyjaszewski K. Inverse miniemulsion ATRP: A new method for synthesis and functionalization of well-defined water-soluble/cross-linked polymeric particles. *Journal of American Chemical Society*. 2006; 128(16):5578-5584.
 49. An Z, Shi Q, Tang W, Tsung CK, Hawker CJ, Stucky GD. Facile RAFT precipitation polymerization for the microwave-assisted synthesis of well-defined, double hydrophilic block copolymers and nanostructured hydrogels. *Journal of the American Chemical Society*. 2007; 129(46):14493-14499.
 50. Yao Y, Xia M, Wang H, Li G, Shen H *et al*. Preparation and evaluation of chitosan-based nanogels/gels for oral delivery of myricetin. *Pharmaceutical sciences*. 2016; 30228-7(16):S0928-0987.
 51. Avasathi V, Pawar H, Dora CP, Bansod P, Gill MS, Suresh S. A novel nanogel formulation of methotrexate for topical treatment of psoriasis: Optimization, in vitro and in vivo evaluation. *Pharmaceutical development and technology*. 2015: 1-9.
 52. G Divya, Panonnummal R, Gupta S, R Jayakumar, M Sabitha. Acitretin and Aloe-emodin loaded chitin nanogel for the treatment of psoriasis. *European Journal of Pharmaceutics and Biopharmaceutics*. 2016; 107:97-109.
 53. Parchuri DB, Kumar GS Shantha, Goli D, Karki R. formulation and evaluation of nanoparticulate drug delivery system of acyclovir for topical drug delivery. *World Journal of Pharmacy and Pharmaceutical Sciences*. 2013; 2(6):5602-5617.
 54. Kaur LP, Guleri TK. Topical Gel: A Recent Approach for Novel Drug Delivery. *Asian Journal of Biomedical and Pharmaceutical Sciences*, 2013; 3(17):01-05.
 55. Xin, Hai-Shu L, Thenmozhiyal JC, YC Sui, paul CHO. Inclusion of Acitretin into Cyclodextrins: Phase Solubility, Photostability, and Physicochemical Characterization. *Journal of Pharmaceutical Sciences*. 9(2003):2449-2457.
 56. PR Sarika, Rachel James N. Preparation and characterisation of gelatin-gum arabic aldehyde nanogels via inverse miniemulsion technique. *International Journal of Biological Macromolecules*. 2015; 76:181-187.
 57. Abu-Dalo M, Othman A, Al-Rawashdeh N. *International Journal of Electrochem. Sciences*. 2012; 7.
 58. Chauhan P, Mahajan S, Prasad GBKS. Preparation and characterization of CS-ZnO-NC nanoparticles for imparting anti-diabetic activities in experimental diabetes, *Journal of Drug Delivery Science and Technology*, 2019; 52:738-747.
 59. Hao J, Fang X, Zhou Y *et al*. Development and optimization of solid lipid nanoparticle formulation for ophthalmic delivery of chloramphenicol using a Box-Behnken design. *International Journal of Nanomedicine*. 2011; 6:683-692.
 60. Kumar JA, Pullakanda N, Prabu SL *et al*, Transdermal Drug Delivery System: An Overview. *International Journal of Pharmaceutical Sciences. Review and Research* 2010; 3 (2):49.
 61. Dinda SC. *Advances in Pharmaceutical Technology. School of Pharmaceutical Education and Research*, 2011: 69-82.
 62. Phatak A, Jorwekar P, Chaudhari P. Nanosuspension a promising nanocarrier as a drug delivery system. *Research Journal of Pharmaceutical Dosage Forms and Technology*. 2011; 3:176.
 63. *The Merck Index*, 13th edition, 2001: 6909.
 64. Williams AC, Barry BW. Penetration Enhancers, *Advanced Drug Delivery Reviews*. 2004; 56:603-18.
 65. N Sanoj Rejinold, M Muthunarayanan, VV Divyarani, PR Sreerekha, KP Chennazhi, S V Nair, H Tamura, R Jayakumar, Curcumin-loaded biocompatible thermoresponsive polymeric nanoparticles for cancer drug delivery, *Journal of Colloid Interface Sciences*, 360(2011):39-51.
 66. Murray SB, Neville AC. The role of pH, temperature and nucleation in the formation of cholesteric liquid crystal spherulites from chitin and chitosan. *International Journal of Biological Macromolecules*. 22(1998): 137-144.
 67. J Smith, E Wood, M Dornish. Effect of chitosan on epithelial cell tight junctions. *Pharmaceutical Research*. 2004; 21:43-49.
 68. J Gibson, An evaluation of the effects on ProZ92 on proliferation of skin cells in culture. www.proz92.com/psoriasis/research. Cited 2014 January 16.
 69. M Sabitha, R N Sanoj, N Amrita, L Vinothkumar, SV Nair, R Jayakumar. Curcumin loaded chitin nanogels for skin cancer treatment via the transdermal route. *Nanoscale* 2012; 4:239-250.
 70. KT Smitha, A Anitha, T Furuiki, H Tamura, S V Nair, R Jayakumar. In vitro evaluation of paclitaxel loaded amorphous chitin nanoparticles for colon cancer drug delivery. *Colloids and Surfaces B- Biointerfaces*. 2013; 104:245-253.
 71. MF Lopes-Virella, P Stone, S Ellis, JA Colwell. Cholesterol determination in high-density lipoproteins separated by three different methods. *Clinical Chemistry and laboratory medicine*. 1977; 23:882-884 [PMID: 192488].
 72. *International Journal of Pharmaceutics*. 2007; 332:185-191.
 73. Tan JP, Tan MB, Tam MK. Application of nanogel systems in the administration of local anesthetics. *Local reg*. 2010; 3:93-100
 74. Vinogradov SV1, Batrakova EV, Kabanov AV, Nanogels for oligonucleotide Delivery to the Brain, *Bioconjugate Chemistry*, 2004; 15:50-60.
 75. Sahu P, Das D, Kashaw V, Iyer AK, Kashaw SK. Nanogels: A New Dawn in Antimicrobial Chemotherapy. *Antimicrobial Nanoarchitectonics*, 2017: 101-137.
 76. Chahrazad Bakka, Ouanissa Smara, Hadjadj Mohamed, Hocine Dendougui, Salha Mahdjar, Benzid Amina . In vitro Anti-inflammatory activity of Pistacia atlantica Desf. extracts. *Asian Journal of Research in Chemistry*. 2019; 12(6):322-325.
 77. Shah PP, Desai PR, Patel AR, Singh M (2012), Skin permeating nanogel for the cutaneous co-delivery of two anti-inflammatory drugs, *Biomaterials*, 33: 1607-1617.
 78. Ferreira SA1, Gama FM, Vilanova M. Polymeric nanogels as vaccine delivery systems. *Nanomedicine* 2013; 9:159-173.
 79. Phatak AA, Praveen DC, Development and Evaluation of Nanogel as a Carrier for Transdermal Delivery of Aceclofenac. *Asian Journal of Pharmaceutical Technology*. 2012; 2:125-132.
 80. Larsson M, Bergstrand, A, Mesiah, L, Vooren CV, Larsson SA. Nanocomposites of polyacrylic acid nanogels and biodegradable polyhydroxybutyrate for bone regeneration and drug delivery. *Journal of Nanomaterials*. 2014: 1-9.
 81. Moya-Ortega MD, Alves TF, Alvarez-Lorenzo C, Concheiro A, Stefánsson E *et al*. Dexamethasone eye drops containing γ -Cyclodextrin based nanogel. *International journal of pharmaceutics*. 2013; 441:507-515.
 82. HA1 Abd E1-Rehim, Swilem AE, Klingner A, Hegazy el-SA, AA Hamed. Developing the potential ophthalmic applications of pilocarpine entrapped into polyvinylpyrrolidone-poly[acrylic acid] nanogel dispersions prepared by γ radiation, *Biomacromolecules*. 2013; 14:688-698.
 83. Rezkita Fianza, Kadek, Wibawa G.P, P Alexander. Nugraha. Curcumin loaded Chitosan Nanoparticle for Accelerating the Post Extraction Wound Healing in Diabetes Mellitus Patient: A Review. *Research Journal of Pharmacy and Technology*. 2020; 13(2):1039-1042.
 84. Telrandhe Roshan. Anti-Cancer Potential of Green Synthesized Silver Nanoparticles- A Review. *Asian Journal of Pharmacy and Technology*. 2019; 9 (4):260-266.
 85. D Sushil. Patil, Gupta J Mukul, Kote Kaustubh S. , Mr. Rajendran R. Formulation of Novel Medicated Jellies for Treatment of Mouth Ulcer. *Asian Journal of Pharmacy and Technology*. 2019; 9(4):241-243.
 86. N T. Nistane. Herbal Nanoparticles against Cancer. *Research Journal of Pharmaceutical Dosage Forms and Technology*. 2019; 11(4):247-252
 87. Kailas M. Karande, Shivaji P. Gawade. Synthesis of Nanosilver and its Comparative Evaluation of Cytotoxic Activity. *Research Journal of Pharmacy and Technology*. 2020; 13(2):659-663.
 88. Sahu Pooja, Jangade Rajendra. An Updated Review on Mechanism of Novel Carrier System for Wound Healing. *Research Journal of Topical and Cosmetic Sciences*. 2019; 10(2):65-78.
 89. Nukolova NV, Oberoi HS, Cohen SM, Kabanov AV, Bronich TK. Folate-decorated nanogels for targeted therapy of ovarian cancer. *Biomaterials*. 2011; 32(23):5417-26.

90. Park W, Park S-j, Na K. Potential of self-organizing nanogel with acetylated chondroitin sulfate as an anti-cancer drug carrier. *Colloids and Surfaces B: Biointerfaces*. 2010; 79(2):501-8.
91. Nukolova NV, Oberoi HS, Cohen SM, Kabanov AV, Bronich TK. Folate-decorated nanogels for targeted therapy of ovarian cancer. *Biomaterials*. 2011; 32(23):5417-26.
92. Wu W, Mitra N, Yan EC, Zhou S. Multifunctional hybrid nanogel for integration of optical glucose sensing and self-regulated insulin release at physiological pH. *ACS Nano*. 2010; 4(8):4831-9.

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