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REVIEW

Pectin-Based Nanomaterials: Synthesis, Toxicity and Applications

MANDEEP KAUR, ADITYA WADHWA and VINEET KUMAR*

Department of Biotechnology, School of Bioengineering and Biosciences, Lovely Professional University, Phagwara-144111, India

*Corresponding author: E-mail: vineetkumar22@gmail.com; vineet.21644@lpu.co.in

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Nanomaterials of biological origin are very useful for drug delivery applications. The stability, biodegradability and biocompatibility of pectin nanomaterials in the human body make them an effective drug carrier. This review focus on different aspect of synthesis, drug encapsulation, drug release and safety of pectin-based nanomaterials. The nanomaterials can be used for the delivery of different hydrophilic and hydrophobic drugs to various organs. The release kinetics of drug loaded pectin-based nanoparticles can be studied *in vitro* as well as *in vivo*. The pectin-based nanomaterials have good pharmaco-kinetics and can ensure controlled drug delivery. However, the toxicity of pectin-based nanomaterials to human body needs to be evaluated carefully before industrial scale application.

Keywords: Pectin nanomaterials, Drug loading, Drug release kinetics, Biomedical applications, Toxicity.

INTRODUCTION

Nanotechnology is a versatile area in the field of biomedicine and drug delivery. Pectin is a natural polysaccharide extracted from the cell wall of various vegetables and fruits that consist of 1,4 linked α-D-galactopyranosyluronic acid and 1,2-linked α-L-rhamnopyranose residues. Pectin comprises of large amount of arabinose, galactose, and xylose. Pectin is a polyanion with 3.5 pK_a value. Esterification is a crucial property that helps in determining the charge density of pectin. The degree of esterification is defined as the percentage of galacturonic acid residues that are esterified. On the basis of degree of methyl esterification, pectin can be classified into high methoxyl (HM) pectin with degree of esterification more than 50% and low methoxyl (LM) pectin having degree of esterification less than 50% [1,2]. Hydrophobic property of pectin can be increased by the addition of methoxy groups which reduces the interfacial tension between an oil phase and a water phase easing the formation of emulsion [3]. Hence, the pectin with high methoxy (HM) esterification get easily emulsified [4]. Amidation of the low methoxyl-pectin alters their properties by producing amidated low methoxyl-pectin [5,6]. The presence of carboxyl group in the pectin enables the formation of amide bond between the drug and pectin that is disintegrated by the lysosomal enzyme in the target cells to release the drug [7-9]. The stability of pectin in the gastrointestinal tract and synergistic action of normal flora of gastrointestinal tract makes it useful for colon drug delivery. Pectin acts as gelling agent, thickening agent, emulsifier and stabilizer [10-12]. The galactouronic content of pectin provides innate anti-inflammatory property [13]. Pectin has been reported as an effective oral, vaginal and nasal drug delivery agent [14-21].

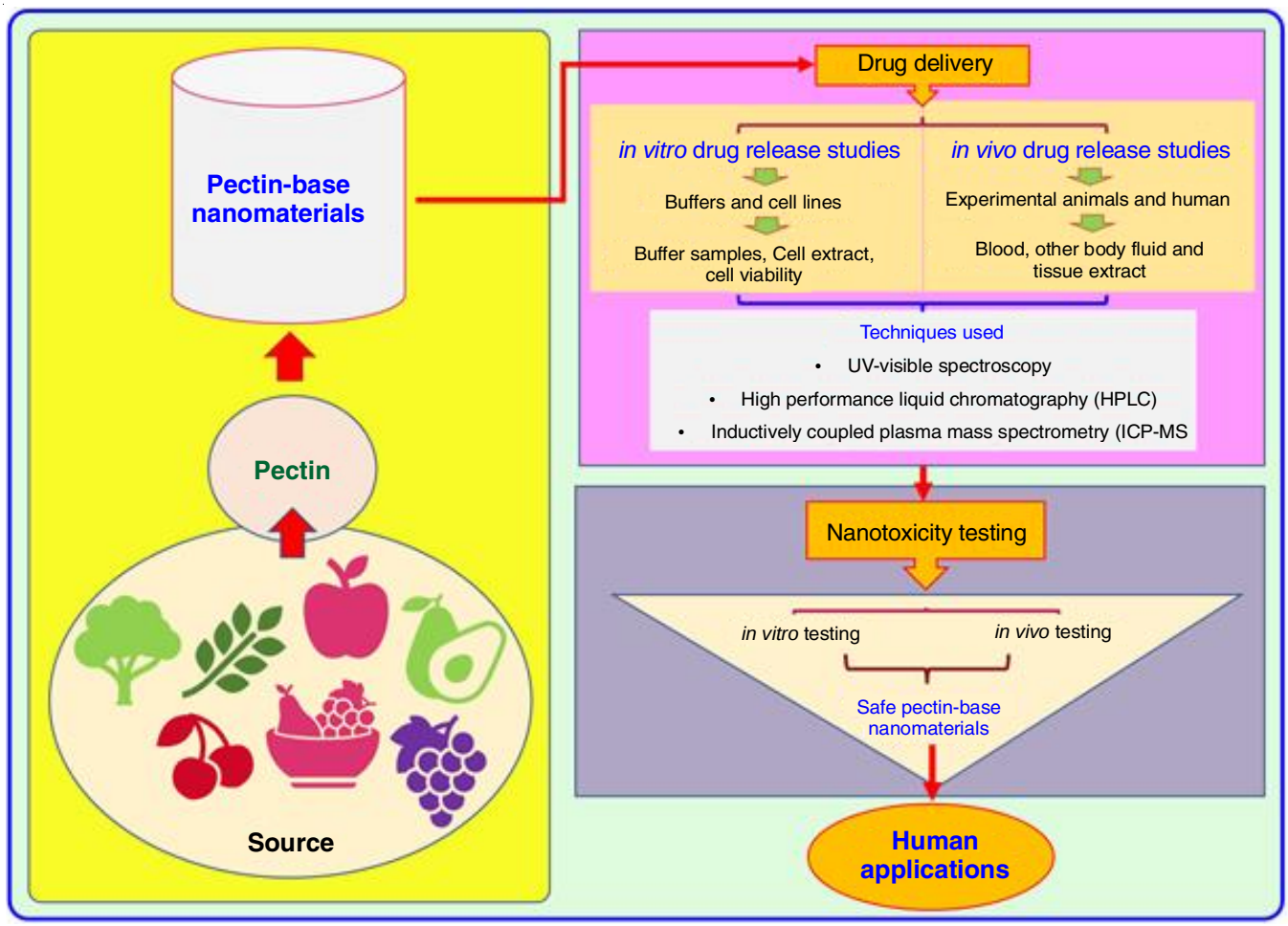
Pectin nanoparticles exhibit anticancer properties by blocking the growth of cancerous cells and inhibiting metastasis [22-26]. Pectin can also act by inducing apoptosis in cancerous cells [27-33]. The galacturonic acid and sugar chain components of pectin have been reported as a cure for colon cancer and liver cancer [34-39].

Chemotherapy has played a significant role in curing cancer but it has huge side effects. Most of the side effects arise due to availability of toxic chemotherapeutic drug to normal cells along with cancerous cells. Thus, the side effects can be mitigated by the use of nanoparticles-based drug carrier [40]. Pectin-based nanomaterials are preferred due to their properties like high surface area, biodegradability, cytocompatibility, extended drug half-life and controlled drug release [34,41]. Good water solubility of pectin-based nanomaterials makes them useful for drug delivery to gastrointestinal region [15,42-44]. In addition, characteristics like muco-adhesiveness,

ease of dissolution in basic environments and the ability to form gels in acidic environments makes pectin-based nanomaterials suitable for drug delivery [45-49]. The pectin-based nanoparticles owing to their nanometric size can easily enter the tumors thus making them more vulnerable to anticancer drugs [50,51]. This review focus over the synthesis of pectin-based nanomaterials, their drug release behavior and toxicity aspects of pectin-based nanomaterials with focus on drug delivery application (**Scheme-I**).

Types of sources used for pectin nanomaterial: Pectin is a natural polysaccharide that can be isolated from the cell wall of the plant tissue. It is used for pharmaceutical and nanomaterials synthesis applications. Pectin isolation from different bioresources is well documented. Some of these sources include burdock (genus Arctium), sunflower, Amaranth, Mandarin orange peel and berries of *Prunus dulcis* [52]. Pectin can also be procured from different commercial sources as listed in Table-1.

Methods used for preparation of pectin-based nanomaterial: Pectin-based nanomaterials can be prepared using nanoemulsion, ionotropic gelation, thermal, sonochemical, co-precipitation, microwave hydrothermal and solvent displacement methods [67-73]. Nanoemulsions are liquid in liquid dispersion of 100 nm droplets. A typical nanoemulsion consists of oil, water and emulsifier. Oil and water are the two phases that are emulsified in presence of emulsifier using low and high energy approaches. High energy approaches use high pressure homogenization and ultrasonication to break macrosize emulsion drops into nanosized droplets. Low energy methods use phase inversion to lower the interfacial tension thus breaking the macroscopic emulsion particles into nanoscale droplets. The mixture is cooled in case of phase inversion temperature method while the mixture is diluted with water to induce phase inversion in emulsion inversion method [74]. Burapapadh *et al.* [53] used high pressure homogenization approach to encapsulate poorly water-soluble drug itraconazole in pectin nanoparticles. Drug was dissolved in chloroform while pectin was prepared in water. The mixture was subjected to high pressure homogenization where pectin acts as an emulsifier. The nanoemulsion was subjected to solvent evaporation thus removing chloroform and dissolving itraconazole loaded pectin nanoparticles in water phase. Lyophilization is commonly used method to obtain nanoparticles in dry powder form. Reis *et al.* [75] reported two-step nanoemulsion droplet method for the synthesis of hollow sphere pectin nanoparticles. In first step, the modification of pectin is done with addition of modifier and in second step the pectin hydrogels are synthesized. Rangelova *et al.* [76] carried out pectin homogenization in hot water followed by cooling and mixing with SiO_2 precursor prepared in acidic ethanol. The mixture was stirred using magnetic stirrer to obtain transparent sol. The sol was dried at



Scheme-I: Schematic presentation of pectin-based nanoparticles and their applications

TABLE-1
COMMERCIAL SOURCES OF PECTIN THAT CAN BE USED FOR NANOPARTICLE SYNTHESIS

Pectin source name; country	Nanomaterial size (nm); shape	Drug used; Drug source; vector	Ref.
Herbstreith and Fox KG Germany	500–1000; Spherical with smooth surface	Itraconazole (ITZ); Antifungal	[53]
High-methoxylated pectin (citrus); P.C. Drug, Thailand	390; Spherical	Methotrexate; Anti-cancer drug	[54]
Quzhou Pectin company limited, Quzhou, China	100; Regular spherical	Honokiol (HK); Anti-tumor	[55]
Sigma Chemicals company, USA	300–350; Oval shape	Paclitaxel; Anti-cancer	[56]
Sigma-Aldrich, Shanghai, China	263–465; Spherical shape	DOX–HCl; Anticancer drug	[57]
Sigma-Aldrich, Shanghai, China	98; –	Dihydroartemisinin (DHA); Anticancer	[58]
Hi-Media lab, India	100–200; Spherical	Oxaliplatin; Colorectal metastatic pancreatic cancer	[59]
Sigma Chemicals company, USA	50–500; Regular spherical	5-Fluorouracil (5-FU); Antineoplastic	[60]
Burzin and Leons Agenturen private limited Mumbai, India	237; –	Timolol maleate; Beta-adrenergic blocker	[61]
HIMEDIA laboratories private limited, Maharashtra, India	29–110; Irregular	Ceftizoxime; Antibacterial	[62]
Herbstreith and Fox KG Neuenburg, Germany	14; Spherical	Doxorubicin; Anticancer	[63]
Sigma-Aldrich, Mumbai, India	174-218; Spherical	5-Fluorouracil; Anticancer	[64]
Copenhagen Pectin, Lille Skensved, Denmark	450-500; Agglomerated irregular shape	Insulin (Diabetes)	[65]
CPKelcoApS Company, Denmark	266; Spherical	Doxorubicin; Anticancer	[66]

50 ºC to obtain pectin nanocomposite. The use of nanoemulsification method for the synthesis of various types of nanoemulsions has been discussed in detail elsewhere [74].

Ionotropic gelation method involves spontaneous aggregation of precursors with multivalent counter ions [77]. Jonassen *et al*. [78] reported the formation of pectin nanoparticles using ionotropic gelation method. Two types of pectin nanoparticles were synthesized: LM pectin and amidated LM pectin of which amidated LM pectin nanoparticles were found to be comparatively better drug delivery agents. In this method, treatment of LM-pectin and AM-pectin with zinc chloride allows the gelation of pectin in the presence of divalent ions which crosslink the negatively charged carboxyl group to positive charged divalent ions. Furthermore, hydrophobic interactions and hydrogen bonding has significant effect over gelation process. Furthermore, the type of cation and concentration of two reactants also affects the nanoparticle size [79]. Carbodiimide chemistry approach was applied to load methotrexate over pectin nanoparticles. Carboxylic acid group present in the pectin can easily bind with amine group of the drug methotrexate [54]. Thiolated pectin nanomaterial has been prepared for ocular drug delivery application using magnesium chloride as a ionic crosslinker [61].

Precursor decomposition under thermal treatment is the basic behind thermal treatment method. It utilizes heat stable surfactant to stabilize the nanoparticle as the temperature involved in the synthesis process is high [80]. A mixture of pectin and β-lactoglobulin was exposed to temperature higher than thermal denaturation temperature of the supposed biopolymer, leading to the synthesis of biopolymeric nanoparticles [81].

Sonochemical method uses high intensity ultrasound to prepare novel pectin-based nanomaterials. The advantages of sonochemical method include short reaction time and no need of high temperature and pressure. Dai *et al*. [82] prepared pectin coated Fe_3O_4 magnetic nanospheres by ultrasonic treat-ment of a mixture of pectin and sodiumdodecyl benzene sulfonate followed by addition of Fe_3O_4 and calcium chloride under stirring condition. Xu *et al*. [83] has discussed sono-chemical method of nanomaterial synthesis in detail.

Co-precipitation method involves reaction between salt having difference in their water solubility leading to the precipitation and production of water insoluble material. The precipitation actually involves different chemical processes like nucleation and growth followed by agglomeration. In case of nano co-precipitation method, the insoluble products formed essentially has at least one dimension in nanometer range [80]. Pectin-iron oxide magnetic nanocomposite has been synthesized by iron salt co-precipitation upon mixing with pectin. Likewise, pectin-CuS nanocomposite and pectin-CdS nanocomposite were prepared by simply varying the metallic salt components [84,85]. The precipitation and co-precipitation methods for nanomaterial synthesis are well documented [86,87].

Microwave hydrothermal technique combines the benefits of hydrothermal and microwave methods. It can attain high temperature in a short time and hence has been used for the synthesis of wide range of nanomaterials reported by Meng *et al*. [88]. Pectin being a good reducing and stabilizing agent has been used for the synthesis of silver nanoparticles using microwave hydrothermal method [89].

In case of solvent displacement method the polymer, drug and surfactant are prepared in organic solution containing partially polar water soluble solvent like acetone or ethanol and precipitated with surfactant saturated aqueous solution. Rapid solvent diffusion is mainly responsible for pectin nanoparticle synthesis [90]. Ceftizoxime loaded pectin nanocarriers has been prepared by dropwise addition of pectin and ceftizoxime mixture to dioctyl sodium sulfosuccinate containing

dichloromethane solution under constant stirring. Further, polyvinyl alcohol and calcium chloride was added and the mixture was sonicated. The mixture was centrifuged and the pellets were dried to obtain ceftizoxime loaded pectin nanocarriers [62]. Likewise, dropwise addition of calcium chloride prepared in propyl alcohol to a mixture of sodium bis(2-ethylhexyl)sulfosuccinate, oleic acid and pectin induced the gelation of pectin. The reaction mixture was centrifuged to obtain supernatant that was further treated with anhydrous ethanol to obtain pectin nanoprecipitates [66]. The use of solvent displacement method for the synthesis of pectin nanomaterial and nanocomposite has been documented elsewhere [86,91].

Drug delivery application of pectin-based nanomaterials: Pectin-based nanomaterials has been used to deliver various types of the drugs to target tissue. Pectin-based nanoparticles loaded with different drugs were subjected to *in vitro* drug release assay in phosphate buffer. The pH of phosphate buffer was maintained at 7.4 which is similar to human blood while the buffer was incubated at 37 ºC mimicking human body temperature. Samples drawn from phosphate buffer containing suspended methotrexate loaded pectin nanoparticles were centrifuged. The supernatant containing methotrexate released from pectin nanoparticles absorbs at characteristic 372 nm in UV-visible region and hence was quantified by recording UV-visible absorption intensity at 372 nm [54]. Honokiol loaded pectin nanomaterials were stored in dialysis bag under constant stirring to mimic blood circulation that allows passage of honokiol to phosphate buffer. The phosphate buffer samples were withdrawn at regular intervals to study the amount of drug released using UV-visible spectroscopic analysis at 292 nm [55]. Likewise, dialysis method was used for the quantitative assessment of doxorubicin released from pectin nanoparticles. The dialysis bag was incubated at 37 ºC in phosphate buffer circulated at 100 rpm in an air bath oscillator. The samples were analyzed using UV-vis spectroscopy at 480 nm [66]. Kumar *et al*. [62] studied the release of ceftizoxime from pectin nanocarriers in phosphate buffer saline. Ceftizoxime released from nanomaterials was quantified by recording UV-visible spectra at 298 nm. Borker *et al*. [92] studied the release of doxorubicin from pectin nanomaterials in phosphate buffer saline and sodium acetate buffer by UV-visible spectroscopic analysis at 298 nm. In contrast, Subudhi *et al*. [64] used the Souder and Ellenbogen extraction technique along with dialysis bag technique to study the *in vitro* drug release of 5-fluorouracil in simulated gastric fluid or intestinal fluid maintained at 37 ºC and agitated at 100 rpm. The quantification of drug released was conducted using UV-visible spectrophotometer at 266 nm [65]. Verma *et al*. [56] studied the release of anticancer drug paclitaxel at pH 7.4 and 5.8. The amount of drug released was measured by UV-visible spectroscopic analysis at 227 nm. Maximum 96 % release was achieved at 5.8 pH while only 81% drug was released at pH 7.4. Likewise, the release of paclitaxel from pectin nanomaterial was studied using UV-visible analysis at 488 nm [57]. Yu *et al*. [60] performed the dialysis of 5-fluorouracil loaded pectin nanoparticles in various buffers namely hydrochloric solution, hexamine-hydrochloric acid buffer and tris-hydrochloric buffer. The buffer solutions were replaced with the freshly prepared solution and analyzed at 267 nm using UV-visible spectrophotometer.

However, in some of the studies more accurate analytical technique, high performance liquid chromatography (HPLC) has been used for in vitro drug release analysis. Burapapadh *et al*. [53] used HPLC for the quantitative analysis of itraconazole from pectin nanomaterials. Quantitative analysis of dihydroartemisinin, an anticancer drug released from loaded pectin nanoparticle at different pH has been conducted using HPLC [58]. The *in vitro* release analysis of oxaliplatin encapsulated in superparamagnetic iron oxide-pectin nanomaterials has been carried out using inductively coupled plasma mass spectrometry (ICP-MS) [59].

Drug release assay has also been studied using *in vitro* cell culture. Chauhan *et al*. [93] designed pectin-tannic acid nano-complexes for the delivery of drugs targeting pancreatic cancer. Various anticancer drugs such as 5-fluorouracil, gemcitabine and irinotecan were used to treat pancreatic adenocarcinoma. Microscopy and flow cytometry techniques revealed better delivery of drugs to cancerous cell in case of use of pectin-tannic acid nano-complexes. Hussien *et al*. [94] reported lower cytotoxic response of chemotherapeutic drug by using pectin-conjugated magnetic graphene oxide nanomaterial as compared to direct administration of drug. Devendiran *et al*. [95] prepared pectin-gold nanoparticle complex for the delivery of doxorubicin to HT-29 colon cancer cell. The nanocarrier showed better stability at different pH due to the loading of positively charged drug on the negatively charged pectin-gold nanoparticle. Tian *et al*. [96] prepared pectin nanoparticles for the delivery of doxorubicin to cancerous MDAMB-231, A549 and NCI-H1299 cells. Faster uptake and increased accumulation of drug has been observed in case of drug loaded pectin nanoparticles as compared to free drug. Resveratrol loaded pectin nanoparticles has been reported to cure growth of Caco-2 a colon cancer cell line [97]. In addition, cetuximab modified pectin-chitosan nanoparticles were reported to deliver curcumin to target colon cancer Caco-2 cells and exert anticancer effect by cell phase arrest at G2/M stage [98]. Likewise, increase in the anticancer activity against hepatocellular carcinoma with increase in amount of doxorubicin loaded pectin-gold nanomaterials have been reported by Devasvaran *et al*. [99]. Kumar *et al*. [100] documented biocompatible pectin-chitin/nano $CaCO_3$ composite scaffolds as a drug delivery system for the osteoporosis. Fosamax drug loaded nano-scaffold were found to induce bone regeneration without any sign of toxicity in NIH3T3, L929 and human dermal fibroblast cells. Few other applications of pectin nanoparticles in various diseases targeted drug delivery system are summarized in Table-2.

The release of drug from pectin-based nanomaterials has also been studied *in vivo*. Dhanya *et al*. [101] reported quercetin encapsulation in a zein-pectin nanocomplex *in vivo*. A self-assembled pectin-eight-arm polyethylene glycol nanoparticles have been designed for the co-delivery of two hydrophobic drugs ursolic acid and 10-hydroxycamptothecin in mice models. The nano assembly was found to demonstrate controlled release of drug with better chances of survival in tumor-bearing mice model [102]. Ouyang *et al*. [103] documented that doxorubicin

TABLE-2
APPLICATION OF PECTIN NANOPARTICLES IN VARIOUS DISEASES TARGETED DRUG DELIVERY SYSTEM

Drug delivery system	Drug	Disease	Ref.
PEC-conjugated magnetic graphene oxide nanocarrier	Paclitaxel	Cancer	[94]
Zein-pectin nanoparticle	Quercetin	Cancer	[101]
Pectin-eight-arm polyethylene glycol-ursolic acid/hydrooxycampothecin nanoparticle	Hydrophobic drugs ursolic acid and 10-hydroxycamptothecin	Cancer	[102]
Pectin-chitin-$CaCO_3$ nanocomposite scaffold	Fosamax	Osteoporosis/ bone regeneration	[100]
Pectin nanocarriers	Ceftizoxime	ENT infections	[62]
Pectin-gold nanoparticles	Doxorubicin	Colon cancer	[95]
Pectin nanocell	Doxorubicin	Cancer	[103]
Pectin nanoparticles	Doxorubicin	Cancer	[104]
Pectin nanoparticles	Doxorubicin	Cancer	[96]
Pectin and tannic acid nanocomplex	Gemcitabine; irinotecan; 5-fluorouracil	Pancreatic cancer	[93]
Cetuximab-conjugated modified citrus pectin-chitosan nanoparticles	Curcumin	Colorectal cancer	[98]
Chitosan-pectin nanoparticles	Insulin	Diabetes	[105]
Pectin-based nanoparticles	5-Fluorouracil	Hepatocellular carcinoma	[106]
Pectin-coated gold nanoparticles	Curcumin	Cancer	[107]
Pectin coated iron oxide nanocomposite	Curcumin	Colon cancer	[108]
Pectin/gellan gum nanoparticles	Resveratrol	Colon cancer	[97]
Pectin nanoparticles	*Ambystoma mexicanum* (AmbLOXe)	Wound healing	[109]
Butylglyceryl-modified pectin	Doxorubicin	Cancer	[110]

loaded pectin nanocell possess better anticancer activity with ability to cure multidrug resistant cancer in H22 tumor-bearing mice. Furthermore, pectin-based nanomaterials have been used for the delivery of other drugs. Pectin-gold nanomaterials have been used to deliver antiretroviral drug zidovudine to macrophages *in vitro* and HIV infected Wistar rats *in vivo*. The nanomaterials have been found to deliver drug to infected cells without toxicity to surrounding normal cells [92]. Oveissi *et al.* [109] has reported loading of *Ambystoma mexicanum* enzyme to alginate hydrogel enriched pectin nanoparticles and *in vivo* drug release in skin wound Wistar rat models. The *Ambystoma mexicanum* is an epidermal lipooxygenase enzyme that help in tissue regeneration process. The pectin nanocomplex was found to improve wound healing leaving minimum scar and avoiding the chances of abnormal scarring.

Fasted eight weeks old male Wister rats were orally administered with itraconazole loaded pectin nanomaterials to check the therapeutic effect of drug loaded nanoparticles. Blood plasma samples collected after different time interval were quantified for the presence of drug using HPLC. Phosphate buffer: acetonitrile (40:60) was used as mobile phase and drug was quantified at 263 nm wavelength [53]. Likewise, plasma samples of rats with intravenous administration of 5-bromouracil loaded pectin nanoparticles were collected and analyzed using 5% acetonitrile and 95% water as mobile phase and detected at 267 nm [106].

Plasma and gastrointestinal tract extracted samples from overnight fasted Wister rat albino strain orally administrated with 5-fluorouracil were analyzed using mobile phase methanol: water (10:90) adjusted to pH 3.2 using perchloric acid [64]. Sharma *et al.* [61] documented an *ex vivo* method to analyze drug released from timolol maleate-loaded thiolated pectin nanoparticles in cornea tissue isolated from the freshly excised goat eyeballs. One milliliter of the test formulation was placed over the cornea and samples were collected after 2 h of exposure for analysis. The amount of timolol maleate released *ex vivo* was spectrophotometrically measured at 294 nm. Further, the pectin may be used as a reducing and coating material for silver and gold nanoparticles synthesis. The pectin coated nanoparticles can be used for photothermal treatment of cancerous HeLA cells in presence of ultraviolet-A light.

Toxicity assessment of pectin nanomaterials: Nanomaterials possess unique properties that makes them unpredictable in term of their unwanted side effect towards human. Nanomaterials are a useful tool to maximize the delivery of drug to a target tissue. However, the translocation of nanoparticle from target organ to other organs is a matter of concern. Unwanted accumulation of nanomaterials or their residues may lead to improper tissue functioning and toxicity [111,112]. Non-biodegradable nanomaterials have more chances of hyper-accumulation in body and inducing toxicity than biodegradable nanomaterials [113,114]. Although biodegradable nanomaterials can also induce toxicity and therefore needs to be thoroughly investigated before labelling them safe for drug delivery application [115-117].

Cost-effectiveness and non-toxic behavior make pectin a suitable carrier for drug delivery application [56,118,119]. Dhanya *et al.* [101] isolated low methoxy pectin from *Coccinia indica* and documented its non-toxic behaviour during drug delivery application. Oral administration of drug conjugated pectin nanoparticles has been reported to effectively deliver drug without any side effects [120]. Pectin-coated gold nano-

materials have been reported to possess less cytotoxicity as compared to non-coated gold nanoparticles [63,92,121]. Pallavicini *et al*. [122] revealed the non-toxic behaviour of pectin-silver nanoparticles on the fibroblast cells. Pectin-based nanomaterials used for antitumor application have been reported to possess good efficacy and biocompatibility [51,108]. The stabilization of pectin-based nano-formulations by electrostatic interactions like hydrogen bonding, ion dipole forces and hydrophobic interactions is one of the major reasons for their biocompatible behaviour [93]. These interactions are also responsible for good stability of pectin-based nanomaterials in artificial media thus showing no sign of turbidity, agglomeration, precipitation and toxicity [120,123]. Furthermore, it has been found that the pectin nanoparticles retain stability up to a week without any change in zeta potential [93]. Pectin-gold nanoparticles even exhibited better stability at different pH with no sign of toxicity in rat models [124].

Toxicity testing using zebrafish embryos also revealed the non-toxic behavior of pectin-gold nanoparticles [95]. Likewise, acute and sub-acute nanotoxicity evaluation of pectin-gold nanoparticles in Sprague-Dawley rats model confirmed their non-toxic nature. Likewise, no sign of acute toxicity, inflammation and pro-angiogenic effect were observed in chicken embryos exposure to chitosan-pectin nanoparticles [125]. Liu *et al*. [102] suggested that the pectin nanoparticles have the capacity to reduce the chances of hematologic hypersensitivity up to zero percent. Pectin-based nanoparticles has also been recommended for human nutraceutical application [126].

Food, agriculture and environmental applications of pectin: Pectin nanoparticles are emerging as better anti-microbial agents in the food industries. Nisin-loaded pectin nanoparticles show remarkable antimicrobial activity against Gram-positive bacteria like *Arthrobacter* sp. and *Bacillus subtilis* and Gram-negative bacteria namely *Escherichia coli* and *Klebsiella* sp mainly helpful in long term preservation of food. At neutral pH, nisin-loaded nanoparticles functions better than sodium benzoate [127]. In food packaging, the nanocomposite film of pectin based cocoa puree fortified with chitosan nanoparticle decreased the water vapor permeability, considered best for food packaging material.Three percent content of pectin in the nanocomposite showed significant results when strengthen with chitosan nanoparticles [128]. Food protection is a crucial factor in food packaging being a determinant of shelf-life time of food. Edible bio-nano pectin hybrid with LDH-salicylate coatings is prepared for the apricots increased the preservation period as well as act as antimicrobial agent to such fruits or foods [129,130]. A cinnamaldehyde nanoemulsions hybrid with pectin edible films beneficial to inhibit the growth of various microorganisms like *E. coli*, *Salmonella enterica*, *Listeria monocytogenes* and *Staphylococcus aureus*. These nanoemulsions are considered as good packaging material as well as natural preservative [6,131]. Furthermore, curcumin nanoemulsion hybridized with pectin used to increase the shelf-life time of chicken for 12 days at 4 ºC. These edible coatings stabilize the water holding capacity with better antimicrobial activity against mold and fungi [131,132]. Sasaki *et al*. [133] described the newly nanoemulsified edible films of pectin as packaging material. These edible films have greater antibacterial activity against *E. coli* and *S. aureus*. Better mechanical and water vapour permeability property of these films made them a better packaging material. To protect the DHA retardation due to oxidation in non-fat foods, the pectin nanocomplex with the β-lactoglobulin (b-Lg) act as a nano-encapsulation for omega-3 fatty acids. A study showed that the 80% loss of omega-3 fatty acids(DHA) can be prevented when DHA is encapsulated in pectin nanocomplex. Moreover, it acts as nanovehicle which transparently disperse the DHA in enrichment of acid non-fat drinks [134]. Sahoo *et al*. [135] also stated various applications of nanotechnology in the food industry along with the role of nisin-coated pectin nanoparticle in antimicrobial action. Pectin coated ZnO nanocomposite considered as a promising tool in the food fortification. The staple food fortified with pectin capped ZnO nanocomposite have better survival in the acidic environment of gastrointestinal tract, which enables the greater absorption of zinc at the intestine [67]. The pectin-silver nanocomposite showed strong antibacterial activity against food-borne pathogenic bacteria, *E. coli* and *Listeria monocytogenes*. The nanofilm increased the water vapour barrier properties and thermal stability for better food packaging [136]. Biodegradable pectin based nanofilms prepared for strawberry wrapping having the better mechanical properties. These mesoporous silica nanoparticles have reduced Young's modulus and enhanced tensile strength, helpful to increase the shelf-life time of strawberry for 80 days [137]. Pectin based nanoencapsulated flavonoids results into better anti oxidant activity in the gastrointestinal tract [138].

Pectin is highly preferable in the agriculture for nanoparticle synthesis [139]. Paraquat-loaded pectin nanoparticles can be a futuristic tool in the agriculture to combat with herbicidal toxicity and mutagenicity. The nanoformulation containing the herbicide loaded with pectin nanoparticle increases the effect of herbicide and decreases the deeper penetration of paraquat for mustard and maize crops leading to better sustainable environment [140]. Pectin based biopolymeric nanocarrier encapsulating carbendazim is known for its controlled and sustained release with good efficiency and highly deteriorating effect on fungal strains, *Fusarium oxysporus* and *Aspergillus parasiticus*. Furthermore, the pectin based nanocarrier also enhanced the seed germination along with root growth of *Zea mays* and *Cucumis sativa* [141]. Cedarwood (*Cedrus deodara*) essential oil embedded pectin nanocapsules showed significant larvicidal activity against the malaria vector, *Anopheles culicifacies*. The pectin nanocapsules are packed into small tea bags. Their ready to use application at the sites reduce the pesticide application providing clean environment and cost-effective technique [142]. Pectin based nanocarrier also used for sustained irrigation in arid or semi-arid areas to combat with drought. Areas where rainfall is very less, pectin nanocarriers release the water with reduced amount for longer time for enhanced crop production [143]. A dual responsive delivery system containing pectin conjugated silica microcapsules used to deliver kasugamycin against the *Erwinia carotovora*. The delivery system known for its sustained controlled release and high antimicrobial effect [144].

Pectin has been reported for reversing the obesity induced by environmental pollutant *p*,*p*′-dichlorodiphenyldichloroethylene (*p*,*p*′-DDE) [145]. Chromium ions in the waste water can be selectively removed with the aid of pectin-graphene oxide nanocomposite. These nanocomposites have the tendency to degrade the 80% of methylene blue and 87.5 % of methyl orange dye. The toxic dyes can be removed from the wastewater [146]. Pectin-CuS nanocomposites are efficient in the removal of organic dyes. The nanocomposite adsorbs the dye molecules on the surface and destruct the adsorbed dye molecules with high recycling activity [87]. Kulal & Badalamoole [147] found the magnetite nanoparticle embedded pectin-graft-poly(*N*-hydroxyethylacrylamide) hydrogel able to adsorbs the dye and heavy metal ions for wastewater treatment. The copper and mercury ions can also be removed and destructed. The adsorbent capacity of the pectin nanoparticle was higher than the simple particles. Pectin based hydrogels are used for water purification. Various metal ions and dyes can be removed from the waste or polluted water to recycle it, which can be an alternative to the wastewater treatment [148]. Magnetite/pectin nanoparticles remove the fluoroquinolones from the wastewater mainly ciprofloxacin and moxifloxacin. These molecules adsorb on the surface of the nanoparticles and photodegraded. The residues produced were also removed from the wastewater [149]. Pectin nanocomposite hydrogel or pectin (polyvinyl alcohol-*co*-polyacrylamide) hydrogel act as a catalyst to reduce the nitrophenols present in the polluted water. Some metals enhance the catalytic activity of the pectin nanocomposites [150]. Pectin stabilized magnetic graphene oxide prussian blue nanocomposites remove the cesium metallic ions from the polluted water [151,152]. A new magnetic gluten/pectin/Fe_3O_4 nano-hydrogel was prepared and used to remove the pollutants present in Lake Urmia sediments. More than 50% of the total heavy metals and 42% of the total organic content present in the wastewater was removed, showing it a promising tool for better wastewater treatment [153].

Future prospective and conclusion

Pectin-based nanomaterials can find applications in delivery of drug to any part of human body due to their good stability in diverse body fluids, ease of dissolution in basic environment and ability to form gels in acidic environment. In addition, mucoadhesive nature of pectin nanomaterials makes them good candidate for mucosal drug delivery addressing both local and systemic diseases. Pectin nanoparticles can be easily modified with various functional groups to make them suitable for the controlled delivery of both hydrophilic and hydrophobic drugs. The ability to form covalent bonding with drug molecules also makes pectin-based nanoparticles useful for future *in vivo* applications. Pectin nanoparticles has the potential to become an ideal drug delivering agent due to their high drug loading capacity and controlled sustained release. However, in-depth toxicity assessment of pectin-based nanomaterials of different size and chemical composition needs to be rigorously done prior to their common industrial uses.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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