A Methodical Study to Unravel the Potential of using Polysaccharides based Organic Nanoparticles Versus Hybrid Nanoparticles for Pesticide Delivery

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ABSTRACT: Conventional pesticide release pollutes the atmosphere and root healthiness threats. To daze its limitations, nanotechnology mediated pesticide delivery using various natural polymers have been actively investigated. However, the lack of information on what are the beneficial/non-beneficial aspects of using hybrid- and organic- nanoparticles (NP) and among the polysaccharides which are better suited concerning pesticide loading efficiency (PLE), entrapment efficiency (E.E), and sustained-pesticide-release (SPR) has prompted us to investigate this study. In this report, we systematically investigate a series of polysaccharides such as starch (S), cellulose (C), aminocellulose (AC) and sodium carboxymethylcellulose (NaCMC) coated on magnetite NP (MNP, Fe_3O_4) and complete organic nanocarrier systems (starch and cellulose) that have no MNP part were compared for the PLE and SPR efficiencies for chlorpyrifos (ChP) insecticide. Overall, all nanocarriers (NCs) have shown good to excellent PLE due to the smaller sized NP obtained through optimal conditions. However, among the hybrid polysaccharides studied, starch MNP (S-MNP) has shown a maximum PLE of 111 wt% in comparison with other polysaccharides (80 – 94 wt%) as well as with organic- NCs (81 – 87 wt%). The use of inorganic support does improve the PLE greatly for starch but

not for cellulose derivatives. Similarly, the SPR results of S-NP showed remarkably better sustained-release-profile for ChP of 88 % in 14 days, whereas other unfunctionalized and functionalized celluloses exhibited poor release profiles of 60 – 20 % for the same period. These results indicate that the superior performance of starch might be due to the β -1,4- & 1,6-linkages of sugar moieties leading to the branched polymers which bring more room for the pesticide to be entrapped and allow them to release in a sustainable manner. We believe that this study may help the researchers to choose the right system for designing and achieving enhanced pesticide efficiency.

KEYWORDS: Pesticide; Polysaccharides; nanoencapsulation; iron oxide nanoparticles; controlled release; chlorpyrifos.

1. INTRODUCTION

To serve food for an increasing population over the world, there is a tremendous need to ensure the sustainability of food.¹ Pesticides play an inextricable role in improving crop protection thereby securing food security for the global population.^{2,3} Meticulous pesticide release schemes are cast-off on farmlands by picking an appropriate and judicious administration course to accurately control the target pest.^{4,5} In the last decade, the application of nanomaterials in the arena of pesticides has made significant strides.⁶⁻¹² This knowledge aims to lessen the unperceptive usage of conventional pesticides and safeguard their innocuous submission.¹³ In precise, targeted and controlled release property of nanomaterials can expand the pesticide application and lessen residue and contamination.^{10,14-19} The prime benefit of measured-release preparation is that they let considerably fewer pesticides to be used for the same period of action. Furthermore, unlike conventional pesticide delivery, the use of nanocarrier can enhance the efficacy and protect the pesticide which is beneficial especially when pesticide with short-lifetime is to be used.²⁰

Diverse materials such as metal oxides,²¹⁻²³ SiO₂,²⁴⁻²⁸ graphene derivatives,²⁹⁻³¹ polymers,³²⁻³⁵ polysaccharides,³⁶⁻³⁸ nanocomposites,³⁹ etc. have been cast-off for the controlled release of pesticides. Among these systems, natural biodegradable polymers have been extensively studied for agricultural applications^{20,40} besides drug delivery,^{34,38,41-43} tissue engineering,^{34,43-45} cosmetics,⁴⁶ and food,^{20,37,47-51} etc. In particular, polysaccharides and its nanocomposites with metal oxides are considered as a good nanocarrier for pesticide delivery due to their characteristic features such as natural abundance, biocompatibility, easy functionalization etc

(Figure 1).^{4,5,22,36,37} Unlike drug therapy, agriculture sector demands sustainable drug release over extended period, which is a critical parameter apart from PLE. So far the polysaccharides namely alginate/starch/clay,⁵² alginate/bentonite,⁵³⁻⁵⁵ alginate/chitosan,⁵⁶ hydrogels of calcium and nickel alginates,⁵⁷ starch/gaur-gum,⁵⁸ ethylcellulose,⁵⁹⁻⁶¹ ethylcellulose-lignin,⁶² and polysaccharides-clay nanocomposite,⁶³⁻⁶⁴ with various cross-linking agents⁶⁵⁻⁶⁶ to obtain macro to micro-sized spheres and beads have been majorly used as insecticide carrier. Though a large number of reports were dealt with the macro- to micro-particles,^{21,47} it has been shown that particles size reduction to nano size exhibited pronounced E.E and SPR values due to more rooms (surface area) for insecticide molecules to be entrapped. However, in general, the existing polysaccharides based nanocarriers have shown fast pesticide release (8 h to 6 days) presumably due to the sub-micron size of the particles (100–800 nm) (Table S4, Supplementary Information (SI)).

Figure 1. Types of systems evaluated for pesticide loading and release.

Nevertheless, the above examples infer that carbohydrates are promising candidates and still offer more rooms to improve the PLE and SPR properties in combination with nanotechnology. Thus, in order to achieve upright sustained pesticide release and enhanced PLE, we synthesized a series of even smaller sized NP of polysaccharides (cellulose, functionalized cellulose, and starch) without and in combination with iron oxide NP (MNP, Fe₂O₃) as hybrid particles by tweaking the nanoprecipitation method and coprecipitation method, respectively (Scheme 1). Another major objective of this study is to find that which polysaccharide is the better suited for organic vs hybrid pesticide nanocarrier. This is the first systematic relative account of E.E

%, PLE wt% and aqueous release behavior of chlorpyrifos (ChP) from organic versus hybrid nanomaterials.

2. EXPERIMENTAL SECTION

2.1 Materials and Reagents. Iron (III) chloride hexahydrate ($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$); iron (II) chloride tetrahydrate ($\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$); microcrystalline cellulose ($\text{C}_6\text{H}_{10}\text{O}_5$)_n, urea, chlorpyrifos, and ethylenediamine were obtained from Sigma-Aldrich. Sodium carboxymethylcellulose, starch, hydrochloric acid (HCl), dimethyl sulfoxide (DMSO), sulphuric acid (H_2SO_4), sodium hydroxide (NaOH), perchloric acid (HClO_4), isopropanol (iPrOH), methanol (MeOH), and acetone (Me_2CO) were obtained from Rankem. Dialysis tubes (MWCO 1KDa) were procured from G-Biosciences. Aminocellulose was synthesized from microcrystalline cellulose as per literature procedure.⁶⁷

2.2 Analytical methods. X-ray Diffraction (XRD) was performed using Bruker D-8 advanced diffractometer in the 2θ range of 10 to 90 degree. The average crystalline size of NPs with and without surface coating was estimated using the Scherrer equation. Fourier transform infrared (FT-IR) spectra were recorded on Agilent Cary 660 spectrometer using the KBr pellet technique in a range of 4000–400 cm^{-1} . Thermogravimetric analysis (TGA) was performed to determine the degradation/decomposition behavior of samples using thermogravimetric (TG) analyzer-(Perkin Elmer STA 8000) at a N_2 flow rate of 10 mL/min and heating rate of 10 $^\circ\text{C}/\text{min}$. Magnetic measurements of MNP, C-MNP, NaCMC-MNP, AC-MNP, and S-MNP were performed using Dynacool, 14 T physical property measurement system (PPMS) at room temperature, with a magnetic field in the range of –15000 to 15000 Oe, and parameters such as saturation magnetization (M_{sat}), and coercive field (H_c) were evaluated. Atomic force microscopy (AFM) images were acquired using NanoScope 9.1, Bruker Multimode 8 in a tapping mode. The samples were deposited on silicon wafers and analysis was performed at different sections at room temperature and ambient atmosphere. Transmission electron microscopy (TEM) images were acquired on a JEOL-JSM2100 HR operating at 200 kV. Samples were prepared by depositing a drop of diluted NP suspension on 300 mesh TEM grid followed by dried under vacuum for 2 h. Inductively coupled plasma-mass spectrometer (ICP-MS, Model: Agilent 7700 Series provided by Punjab Biotechnology Incubator, Mohali, India), the analysis was performed to estimate the percentage of iron oxide content in the hybrid-NCs. The GC-MS analysis was performed to determine the EE and PLE using a Shimadzu GC coupled with a GCMS-QP 2010 plus mass detector and a single-quadrupole mass spectrometer Quantum (Shimadzu) with 100% dimethyl polysiloxane (Restek Rxi-1ms; 30 m $\times$ 0.25 mmID.,

0.25 μm film thickness) column. GC-MS operating conditions: The initial oven temperature was 60 $^{\circ}\text{C}$, maintained for 1 min and then ramped to 270 $^{\circ}\text{C}$ at a rate of 10 $^{\circ}\text{C}/\text{min}$ followed by holding for 5 min at 270 $^{\circ}\text{C}$. The initial temperature of the injector was 63 $^{\circ}\text{C}$ and then programmed at the same rate as the oven. Helium was used as carrier gas with primary pressure of 570 KPa. The split injection mode was used with a split ratio of 10.0. The injection volume of each sample was 1 μL and the total time for one GC-MS run was 27 min. Mass spectrometer settings: electron impact ionization mode with an electron energy of 70 eV, ion source and interface temperatures were set at 200 and 270 $^{\circ}\text{C}$, respectively and scan mass range m/z 50–500. Shimadzu 2600 UV-Vis spectrophotometer was used to estimate the amount of entrapped pesticide at 290 nm during the aqueous release study after every 12 h. The calibration curve of ChP was prepared in MeOH.

2.3 Synthesis of hybrid- and organic-nanoparticles as pesticide nanocarriers (NCs). In this study, two types of nanocarriers i.e. hybrid and organic have been designed and synthesized (Scheme 1). Hybrid-NCs such as C-MNP, AC-MNP,⁶⁷ NaCMC-MNP and S-MNP comprising of magnetite nanoparticles (MNP) coated with various polysaccharides such as cellulose (C), aminocellulose (AC), sodium carboxymethylcellulose (NaCMC) and starch (S) were synthesized (Scheme 1a). These polysaccharides have been used as stabilizer or capping agents for the *in situ* prepared smaller sized superparamagnetic iron oxide nanoparticles (SPIONS).

Scheme 1. Synthesis of a) hybrid-NCs based on polysaccharide coated magnetite NP b) organic-NCs based on polysaccharide NP.

2.3.1 General procedure for hybrid-NCs (*S-MNP*, *C-MNP*, *AC-MNP*, *NaCMC-MNP*). The procedure for the synthesis of hybrid-NCs was adopted from the literature procedure with slight modification.²² Magnetite NP (Fe_3O_4 , MNP) were prepared by the co-precipitation method. Iron dichloride tetrahydrate ($\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$, 7.3 g, 0.037 mol) and iron trichloride hexahydrate ($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 5 g, 0.0185 mol) were mixed in 100 mL of 2 M HCl at 40 °C. The blend was released into polysaccharides (5 g in 60 mL of water) and 100 mL of 2M NaOH solution under vigorous stirring for about 30 min. The resulting solution was stirred (200 rotations per minute (rpm)) and heated at 90 °C for 1 h. The 5 M NaOH was added dropwise to obtain a pH of 11. The precipitate was centrifuged and treated repeatedly with 3 M HClO_4 solution to obtain a pH of 3. After the last separation by centrifugation, the particles were dispersed into polysaccharide (5 g in 60 mL of water). The polysaccharide-coated iron oxide nanocomposites were obtained by centrifugation followed by drying the material at 40 °C to give the corresponding hybrid-NCs (Scheme 1a).

2.3.2 Synthesis of organic-NCs (*C-NP*, *S-NP*). In the case of organic-NCs, the cellulose- and starch-nanoparticles were prepared by the nanoprecipitation method in the absence of MNP.

(i) Preparation of cellulose nanoparticles (*C-NP*). The procedure for the synthesis of C-NP was adopted from the literature with slight modification (Scheme 1b).⁶⁸ Microcrystalline cellulose (5 g) was dispersed into 40 mL of the alkaline solution (5 M NaOH) made with cold deionized (DI) water and heated to 80 °C for 3 h. Then the slurry was filtered and thoroughly washed with DI water until the wash water is neutral pH. The resulting residue was air-dried and then transferred into DMSO (40 mL) followed by heated to 80 °C for 3 h. The solution was then filtered and washed with DI water (3×20 mL). The pretreated fibers were transferred into 170 mL of an aqueous acidic solution (made of 120 mL DI water, 20 mL 12.1 N HCl and 60 mL 36 N H_2SO_4). This suspension was sonicated at 80 °C for 8 h. In this hydrolysis process, the fiber slurry solution has turned in to milky colloid suspension. This suspension was then centrifuged at 2000 rpm and washed continuously with the addition of DI water (3×20 mL). After washing, 2 N NaOH was added to adjust the solution to pH 7. The neutralized products were further washed with 3×20 mL DI water. The residue obtained after the dialysis was freeze-dried and stored at 5 °C for further process.

(ii) Preparation of starch nanoparticles (*S-NP*). The procedure for the synthesis of S-NP was adopted from the literature with slight modification (Scheme 1b).⁶⁹ Starch (5 g) was dispersed in 50 mL of the alkaline/urea solution (NaOH (0.8 wt%, 200 mg in 25 mL) and urea (1 wt%, 250 mg in 25 mL) were dissolved in cold deionized water) and heated to 68 °C for 15 h. Then the solution was cooled to 25 °C and filtered. The filtered starch solution was added dropwise

at a rate of 1 mL/min with a syringe into 200 mL of ethanol stirring at 350 rpm. The starch nanoparticles suspension was centrifuged at 8000 rpm for 10 min and washed twice with ethanol (3×20 mL). Then the obtained starch nanoparticles (S-NP) were re-dispersed into DI water to obtain the dispersed solution and for dry powder, the solution was frozen at -80 °C and freeze-dried for various measurements.

2.3.3 General procedure for loading of ChP into hybrid and organic-NCs (C-MNP/AC-MNP/NaCMC-MNP/S-MNP) and organic-NCs (C-NP/S-NP). A methanolic (2 mL) solution of ChP (20 mg) was added dropwise to a suspension of hybrid-NC (S-MNP/C-MNP/AC-MNP/NaCMC-MNP, 90 mg) or organic-NC (S-NP/C-NP, 90 mg) in MeOH (10 mL), and stirred at 500 rpm for 3 h at 25 °C (Figure 2). The ChP loaded nanocarriers (ChP-NCs) were collected with the help of an external magnet, washed with methanol and vacuum dried at 37 °C for 1 h. The supernatant was collected to estimate EE and PLE.

Figure 2. Synthesis of ChP loaded NCs.

2.4 Quantification of pesticide loading efficiency (PLE) and entrapment efficiency (E.E).

The amount of free pesticide present in the supernatant was calculated by using gas chromatography–mass spectrometry (GC–MS) analysis with the retention time 19.9 min (Section B in the SI). The calibration curve of ChP was prepared in MeOH (Figure S3, SI). PLE (wt%) and E.E% were calculated using the following equations and results are provided in the Tables S2 and S3, SI.

$$E.E\% = \frac{\text{Amount of pesticide} - \text{Amount of free pesticide}}{\text{Total amount of particles}} \times 100 \quad (1)$$

$$PLE\% = \frac{\text{Amount of pesticide} - \text{Amount of free pesticide}}{\text{Total amount of pesticide}} \times 100 \quad (2)$$

2.4.1 The PLE and E.E values correction by ICP-MS for hybrid-NCs. Since the pesticide loading and entrapment occurs only in the organic part that is polysaccharide layer, for a fair comparison the PLE and E.E should be compared with a similar amount of organic content present in the NCs. The results were corrected by substituting the percentage of inorganic content present in the hybrid-NCs as pesticide loading study was carried out with the same amount (90 mg) for both the NCs. The percentage of iron oxide content present in the hybrid-NCs such as C-MNP, AC-MNP, NaCMC-MNP, and S-MNP was estimated as 12.27, 8.04, 19.06, and 15.73% respectively by using the ICP-MS (GC-MS/ ICP-MS data available in the Section B, SI).

2.5 Aqueous release behavior of ChP from hybrid- and organic-NCs. *In vitro* aqueous release profiles of the ChP in various NCs were carried out by adding 110 mg of the dried ChP loaded NCs of each formulation in water (10 mL) and stirred at 25 °C. The UV-Vis spectrophotometer was used to analyze the time-dependent release of the ChP from their nanoformulations in water after every 12 h upto 18 days. All the experiments were carried out in triplicate.

3. RESULTS AND DISCUSSION

3.1. Synthesis of hybrid- and organic-nanoparticles as pesticide nanocarriers (NC). In this study, we have chosen polysaccharides such as cellulose (C), aminocellulose (AC), sodium carboxymethylcellulose (NaCMC) and starch (S) because cellulose and starch are the least studied polysaccharides in the field of pesticide delivery in comparison with chitosan, alginate and CMC (Table S4, SI).^{14,37,47} In addition, cellulose and starch are the most abundant natural polymers (biomass) on earth, which is complimentary for the agricultural applications. For inorganic part, we chose SPIONS of magnetite nanoparticle (MNP) (iron oxide, Fe₃O₄) because it has been widely used for pesticide delivery application due to its characteristic features like low-cost with the superparamagnetic property.

3.1.1 Synthesis of hybrid-nanoparticles. As shown in Figure 1, the polysaccharides (C/AC/NaCMC, and S) required for the synthesis of hybrid-NCs such as C-MNP, AC-MNP, NaCMC-MNP, and S-MNP were purchased commercially, except aminocellulose⁶⁷ whose synthesis and characterization has been recently reported by our group. In-situ generation of

MNP and stabilization by corresponding polysaccharides lead to the isolation of hybrid-NCs C-MNP, AC-MNP, NaCMC-MNP, and S-MNP in substantial conversion. Due to the presence of poly hydroxyl groups the polysaccharides act as templates for the development of nanosized Fe_3O_4 as they impart dynamic supramolecular associations facilitated by inter- and intramolecular hydrogen bonding interactions. All the synthesized nanocomposites were dense with a smooth surface and they were easy to handle when dried off (Scheme 1).

3.1.2 Synthesis of organic-nanoparticles. In order to understand the importance of having SPIONS in the hybrid-NCs, we have synthesized organic-NCs from cellulose and starch independently to provide C-NP⁶⁸ and S-NP⁶⁹, respectively. The syntheses of these organic NP were achieved using weak-acid sonication and nanoprecipitation methods, respectively as reported with slight modifications.

3.2 Characterization of hybrid- and organic-nanoparticles. Characterization of organic-NCs (C-NP and S-NP) and hybrid nanocomposites (C-MNP, AC-MNP, NaCMC-MNP, and S-MNP) were investigated by FT-IR, PXRD, TEM, AFM, and TGA analysis. The ICP-MS and magnetometry analysis was also carried out on hybrid nanocomposites in order to quantify the iron oxide content and magnetization property, respectively. The details are discussed below.

3.2.1 FT-IR analysis. Comparative FT-IR spectra of hybrid- and organic-NCs were shown in Figure 3a and 3b, respectively. The bare MNP has shown the characteristic stretching frequencies peak at 605 cm^{-1} for the Fe-O bonds.⁶⁷ All nanocomposites have shown peak at 605 cm^{-1} as well as characteristic peaks of C-H and O-H stretching vibrations at 2900 and 3424 cm^{-1} , respectively suggesting iron oxide has been synthesized with polysaccharide-coated NCs. However, NaCMC has shown a slight shift in the peak probably due to COO^- binding on the iron oxide surface unlike OH binding on the other polysaccharides. The peaks in the spectral range of $900\text{--}1500\text{ cm}^{-1}$ were due to $\nu(\text{C-C})$ and $\nu(\text{C-O})$ stretching vibration with contributions from $\delta(\text{C-O-H})$ motion.²² These results clearly indicate that polysaccharides have clearly attached on the surface of the MNPs. Similarly, Figure 3b shows the characteristic peaks for starch and cellulose stretching frequencies between $4000\text{--}500\text{ cm}^{-1}$.

Figure 3. FT-IR spectra of the synthesized nanocomposites: (a) Hybrid-NCs, (b) organic-NCs.

3.2.2 PXRD analysis. Powder XRD (PXRD) pattern of MNP (Fe_3O_4 NPs), hybrid- and organic-NCs are shown in Figures 4 (a,b). The PXRD pattern of MNP showed the diffraction peaks at 30.0° , 35.6° , 43.3° , 53.3° , 57.3° and 62.8° corresponds to (111), (220), (311), (400), (422) and (511) planes of magnetite that matches with the JCPDS no. 03–0863.^{67,68,71} Comparative PXRD pattern analysis of S-MNP, and C-MNP showed the presence of characteristic peaks of MNP, which suggests the binding of magnetite NP, while the AC-MNP and NaCMC-MNP has not show sharp peaks indicating amorphous in nature.⁶⁷⁻⁷² The crystallite size of the pure MNP sample and the MNP nanocomposites was determined on the based on the Scherrer equation using the main characteristic peaks position at $2\theta = 35.6^\circ$. Accordingly, the average crystallite sizes of various samples viz., MNP, S-MNP and C-MNP were 9.80, 10.87, and 11 nm, respectively as calculated by Debye-Scherrer equation. Organic NCs S-NP showed clear peaks due to the presence of more ordered amylopectin while the C-NP has shown amorphous nature.

Figure 4. PXRD pattern for a) hybrid nanocarriers, b) organic nanocarriers.

3.2.3 *Particles size analysis by TEM & AFM studies.* The control of the monodispersed smaller sized NP is very important because the properties of nanocrystal strongly depend upon the surface area of the NP. The TEM images of NCs are provided in Figure 5 and all of them exhibited very low size of <50 nm. To the best of our knowledge, such a smaller size NP for the pesticide delivery application have not been reported (Table S4, SI). More accurately, the hybrid NCs such as S-MNP, C-MNP, AC-MNP, and NaCMC-MNP have exhibited an average diameter of 6, 8, 33, and 8 nm, respectively. The morphology of hybrid-NCs revealed that the samples composed of highly distributed NPs with a spherical shape except for the AC-MNP, which showed the clusters of aminocellulose coated MNPs with the mean size of 33 nm (Figure 5c). The presence of polysaccharide prevents the agglomeration of the MNP and this stability remains even after 6 months. This means that starch chains wrapping around the MNP *via* the interaction between the hydroxyl group and iron provide high colloidal stability. HR-TEM images of all hybrid NCs have shown an individual MNP with a lattice spacing of 0.3 nm corresponds to the *d* spacing of the cubic plane of MNP (Figure S1, SI).

Figure 5. TEM images for (a) S-MNP (b) C-MNP (c) AC-MNP (d) NaCMC-MNP (e) S-NP (f) C-NP.

The particles size on TEM micrographs of organic NCs viz., S-NP and C-NP was calculated to be of ~ 20 and 18 nm, respectively (Figures 5e and 5f). Starch has shown spherical, monodisperse NP with no aggregation, while cellulose showed irregular spheres aggregated nanoparticles probably due to strong hydrogen bonding established between the cellulose NP.

To shed more lights about the surface morphology and to corroborate the TEM results the AFM images of the hybrid- and organic-NCs are recorded and presented in the Figure 6. The AFM image of S-MNP image revealed that the highly dispersed spherical MNP were formed (Figure 6a). In the case of C-MNP (Figure 6b) again we observed irregular spheres dispersed in the cellulose matrix as in the TEM. In Figure 6c, the AC-MNP showed the incorporation of MNP in the aminocellulose matrix. It is also possible to note a significant level of agglomeration. NaCMC-MNP particles has been found to be homogeneously dispersed. S-NP and C-NP showed the relevant smooth and good structural integrity (Figures 6e,f).

Figure 6. AFM images for (a) S-MNP (b) C-MNP (c) AC-MNP (d) NaCMC-MNP (e) S-NP (f) C- NP.

3.2.4 Vibrating sample magnetometer (VSM). The magnetic characteristics of the prepared hybrid MNP NCs were measured using VSM in the presence of a magnetic field. The magnetic stability of hybrid MNP comparing hysteresis loops at 5 K and 300 K is given in Figure 7.

Figure 7. Magnetic hysteresis curves for the as-synthesized: a) S-MNP b) C-MNP c) AC-MNP d) NaCMC-MNP.

The VSM comparison study of hybrid MNP results illustrated that the magnetic moment of S-MNP and NaCMC-MNP composites appears maximum while C-MNP and AC-MNP could not achieve its saturation magnetization (Figure 7). While all hybrid MNPs found to show ferromagnetic character, C-MNP and AC-MNP could not achieve their saturation magnetization (Figure 7b,c). The VSM results affirm that S-MNP has reasonable magnetic properties, as well as magnetic stability. This suggests that S-MNP may be useful in the recovery of the used NCs using an external magnet and can be considered as one of the potential biomaterials in field applications.

3.2.5 TGA Analysis. TGA analysis was performed to determine the organic content of the hydrophilic polymer attached to MNP (Figure 8). The measurement was carried out under N_2 atmosphere from 30 °C to 1000 °C, with a heating rate of 10 °C/min. In Figure 8a, all hybrid NCs have shown a small weight loss of 8–11% till 210 °C, which is assigned to the release of moisture from the samples. Hybrid-NCs such as C-MNP, AC-MNP and NaCMC-MNP have

shown single exothermic peaks from 210 to ~600 °C with weight losses of 8, 46 and 38%, respectively except in S-MNP. In case of starch, two exothermic peaks appear i.e., one at 283 °C followed by 619 °C with weight loss up to 17% at 960 °C indicating more stable nanocarrier than cellulose. The later has shown complete degradation with the lowest temperature of 490 °C. We infer that the two-stage degradation of starch may correspond to the presence of amylopectin and amylose structures in starch.

Figure 8. TGA profiles for (a) hybrid- and (b) organic-nanocarriers.

The TGA profiles of organic NCs S-NP and C-NP are shown in Figure 8b. Similar to hybrid NCs, here too the starch has shown two exothermic peaks at 360 and 415 °C corroborating the presence of amylopectin and amylose degradation in starch. Whereas unlike in MNPs, the cellulose has shown two steps degradations, one at 181 °C to about 64% and complete degradation at 489 °C. Interestingly, the comparative evaluation of the thermal profiles of S-MNP and S-NP showed that the temperature for onset of thermal degradation was much lower (~490 °C) in the nanocomposite than that of S-NP indicating the hybrid NCs exhibit great thermal stability over organic NCs.

3.3 Comparison of PLE and E.E for organic- and hybrid-NCs.

Pesticide loading efficiency (PLE, wt%) and encapsulation efficiency (E.E %) were quantified using gas chromatography–mass spectrometry (GC-MS) analysis after the successful loading of chlorpyrifos (ChP) pesticide onto the hybrid- and organic-NCs (Table 1, Tables S2 and S3 in SI). However, the pesticide is expected to be entrapped within pores of the cavities generated due to entanglement of polysaccharide chains. For a fair comparison, it is imperative to quantify and adjust the inorganic content in to organic using ICP-MS, since the hybrid-NCs

contain significant amount of MNP (for details see Section B, SI). The corrected E.E and PLE values were listed in Table 1.

Table 1. Comparison of E.E% and PLE% of hybrid- and organic-NCs

Types of NC	NC	E.E (%) ^a	PLE (%) ^a	Corrected E.E (%) ^b	Corrected PLE (wt %) ^b	Relative PLE ^c
Hybrid	S-MNP	20.7	93.3	24.6	111	100
	C-MNP	16.7	75.2	19.0	86	77
	AC-MNP	16.4	73.8	17.8	80	73
	NaCMC-MNP	16.9	76.0	20.9	94	85
organic	S-NP	19.3	87.0	19.3	87	79
	C-NP	18.0	81.0	18.0	81	73

^a E.E and PLE obtained from GC-MS (Table S1) including MNP part, ^b in case of hybrid-NCs correction was applied by replacing the inorganic content to organic using ICP-MS (the calculation is provided in Section B3, ESI. ^c Relative PLE with respect to S-MNP = corrected PLE of (other MNP / S-MNP)*100.

Overall, almost all the NCs have shown efficient entrapment of ChP into polysaccharide NP with the corrected E.E and PLE values ranging between 17.8–24.6% and 81–111 wt%, respectively. Comparison of corrected PLE values have revealed couple of observations, i) hybrid-NCs S-MNP (111 wt%) and C-MNP (86 wt%) showed significantly better performance than corresponding organic-NCs S-NP (87wt%) and C-NP (81 wt%), respectively. This is particularly true for S-MNP which shown remarkably high PLE. ii) Among the cellulose-based NCs, amine-functionalized AC-MNP exhibited less PLE of 80 wt% than the COONa functionalization, which showed ~94 wt% while unfunctionalized cellulose showed in between 86%. These results indicate that though slight alternation was found in terms of PLE, functionalization did not greatly improve the PLE value. iii) Among the hybrid-NCs, S-MNP has outperformed over cellulose derivatives. Based on these results, we infer that the high performance of starch over cellulose derivatives may be attributed to the branching nature of starch due to β -1,4- & 1,6-linkages of glucose unit upon binding on the MNP, can generate more rooms for the loading of the pesticide.

3.4 In-vitro aqueous release behaviour of nanocarriers. Time-dependent pesticide release behaviour was determined based on the absorbance of ChP monitored using UV–Vis spectroscopy. Figures 9a and 9b show the release profiles of hybrid- and organic-NCs, respectively. Among the hybrid-NCs, the AC-MNP and NaCMC-MNP has showed inferior

release profiles of 24 and 20 %, respectively in 4 days which did not improve even up to 17 days. Then, C-MNP has shown initial burst release of 49 % in two days followed by a sustained release up to 61 % in 13 days, which did not improve even up to 17 days. Interestingly, S-MNP has shown better release profile with initial burst release of 44 % in one day followed by a remarkable steady release of 89 % for up to 10 days which did not improve up to 17 days. These results imply that overall, the cellulose-based polysaccharides have shown inferior release profiles than starch presumably due to branched nature which creates bigger rooms while holding on the MNP support. This is also supported by the better C-NP vs C-MNP. Further comparison of release profiles within the cellulose based-NCs, suggest that chemical modification does not give healthier aqueous release results. However, in contrast to C-MNP, organic C-NP has shown better and steady release profile having an initial burst release of 52 % in two days followed by a steady release of 76 % for up to 8 days. However, S-NP has shown a comparable release profile to hybrid S-MNP, having initial burst release of 42 % in one day followed by a steady release of 82 % in 8 days. After 8 days, no significant increase was observed for up to 17 days. These results suggest that starch is outperforming in both organic and hybrid systems with respect to loading as well as SPR. The observation of initial burst followed by steady release has been considered advantageous as it will be readily available to kill the existing pest and subsequently kill and inhibit new infestation.

Figure 9. Aqueous release behaviour of ChP for a) hybrid- and b) organic-NCs.

Release kinetics. The pesticide release rates were analysed by applying different models such as Korsmeyer–Peppas, Makoid–Banakar and Peppas–Sahlin with DDSolver software, which is the Excel-plugin module to understand the release kinetics mechanism of the entrapped ChP molecules from the NCs.⁷³ Only Makoid–Banakar Model^{74,75} to the following empirical

equation 3 showed goodness of fit based on Figure 9, the correlation coefficient (R^2), the adjusted coefficient of determination (R^2_{adj}), the sum of squares of residues (SSR), the mean square error (MSE), the Akaike Information Criterion (AIC), and MSC values (Table S5).

$$F = M_t/M_0 = kMB t^n \exp^{-ct} \quad (3)$$

where M_t/M_0 is the percentage of ChP released at time t , and kMB , n , and c are empirical parameters (kMB , n , $c > 0$). F-ratio probability commonly used as a pesticide-release model selection criterion. The R^2 adjusted value was used as the model selection criterion with the best fit model showing in Table S5. the R^2 adjusted value closest to 1.⁷⁶

Table 2. Best-fit values and secondary parameter from the fitting Makoid-Banakar model.

Type of NCs	NCs	Parameter			
		kMB	n	k	T25
Hybrid-NCs	S-MNP	58.487	0.267	0.023	1.622
	C-MNP	46.609	0.008	0.017	1.722
	AC-MNP	22.091	0.005	0.014	7.235
	NaCMC-MNP	16.557	0.152	0.013	-
Organic-NCs	S-NP	55.638	0.286	0.026	1.698
	C-NP	50.841	0.286	0.026	1.721

The parameter k of the Makoid–Banakar model did not equal to zero for all the NCs. Further, the T25 value increase from C-MNP to NaCMC-MNP as given in Table 2, which indicates the pesticide release deceleration from C-MNP to NaCMC-MNP. In the Table 2, the parameter of n values from the Makoid–Banakar model were not close to ~ 0.43 , Thus the mechanism of pesticide release from the both hybrid and organic NCs is an insignificant effect of diffusion principle.^{76,77} The formation of a porous structure in the S-MNP on swelling in water is expected to enhance the release. Water uptake and swelling of the polysaccharides were shown to be fast compared to the rate of release of ChP from the NCs. These results in the release of

ChP being controlled by diffusion through the polysaccharides rather than by the swelling of polysaccharides.

4. CONCLUSIONS

We systematically designed, synthesized and characterized the hybrid- and organic-NCs having various polysaccharides in order to discern the role of inorganic support used in the hybrid-NCs and the type of nanomaterials synthesis such as hybrid vs organic systems being adopted for pesticide delivery. Further, to understand the beneficial effect of functionalization of natural polysaccharide (cellulose), this study has unravelled the answers for these questions. Though MNP support does not exhibit much benefit for the cellulose derivatives (PLE: 80 – 94 wt%, SPR: 60-20 %), the starch has shown outstanding PLE (111 wt%) and SPR (87 % in 10 in days) results. The superior performance (SPR) of starch might be due to the β -1,4- and 1,6-linkages of sugar moieties which are absent in cellulose derivatives leading to the branched polymers onto the MNP support. This brings more rooms for the pesticides to be entrapped and allow them to release in a sustainable manner. Further, the results infer that functionalization of cellulose derivatives is not beneficial. Though S-MNP showed better PLE and similar SPR profile in comparison with organic S-NC, by keeping the cost and benefits balance, the organic-NCs are better for practical use as pesticide delivery agent. It is noteworthy that unlike previously reported polysaccharide nanocomposites based NCs, the present NCs have shown good to excellent PLE (81-111 wt%) owing to their smaller sized particles. We believe that the lessons learned in this study would help researchers working in the pesticide delivery for designing and improving the NCs to achieve practical agricultural applications.

ASSOCIATED CONTENTS

Supplementary Information.

The Supplementary Information (SI) is available free of charge at . Elemental composition study by TEM–EDX, calculations details of PLE and EE estimation and comparison table with literature NC system.

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463 authors. All authors have given approval to the final version of the manuscript.

464

465 **Notes**

466 The authors declare no competing financial interest.

467

468 **ACKNOWLEDGMENTS**

469 This work was supported by the SERB, Department of Science and Technology (DST), Grant
470 Nos. SB/S2/RJN-047/2015 and SR/WOS-B/818/2016 (G) and Department of Biotechnology
471 (DBT), Grant No BT/CIAB-Flagship/2018. GJ and RM thank for Ramanujan and WOS-B
472 Fellowships, respectively. The authors thank Panjab University (SAIF facility) for NMR and
473 Punjab Biotechnology Incubator for ICP-MS measurements.

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Table of Contents

A Methodical Study to Unravel the Potential of using Polysaccharides based Organic Nanoparticles Versus Hybrid Nanoparticles for Pesticide Delivery

Hybrid vs organic nanocarriers were compared for pesticide encapsulation and release behaviour. Among the polysaccharides, the MNP support was beneficial for starch. In general, the present NCs have shown good results owing to their smaller sized particles.

Supplementary Information

A Methodical Study to Unravel the Potential of using Polysaccharides based Organic Nanoparticles Versus Hybrid Nanoparticles for Pesticide Delivery

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Section A. HR-TEM and Elemental composition by TEM-EDX studies

Figure S1. HR-TEM images of a) S-MNP, b) C-MNP, c) NaCMC-MNP, and d) AC-MNP.

Energy dispersive X-ray (EDX) spectra were measured using Transmission Electron Microscope equipped with EDX facility. The elemental composition and relative abundances are given in Table S1. EDX measurements showed the presence of iron (Fe) and oxygen (O) in addition to carbon (C) and nitrogen (N) peaks for hybrid NCs suggesting successful capping of polymers such as S, C, AC, NaCMC on MNP besides Carbon (C) and nitrogen (O) peaks were observed for S and C in organic NCs.

Table S1. TEM-EDX spectra measurement of S-MNP, C-MNP, AC-MNP, NaCMC-MNP, S-NP and C-NP.

Elements	Weight (%)					
	S-MNP	C-MNP	AC-MNP	NaCMC-MNP	S-NP	C-NP
Iron (Fe)	3.71	3.84	16.93	12.47	-	-
Oxygen (O)	13.66	12.93	14.11	8.01	11.15	10.98
Carbon (C)	82.63	83.23	59.88	57.33	89.85	89.02
Nitrogen (N)	-	-	9.08	-	-	-
Sodium (Na)	-	-	-	22.19	-	-

Figure S2. Energy dispersive X-ray (EDX) spectrum of (a) C-MNP (b) S-MNP (c) AC-MNP (d) NaCMC-MNP (e) S-NP and (f) C-NP.

Section B. Estimation of the Pesticide Loading Efficiency (PLE, wt%) and Entrapment Efficiency (E.E%)

B1. General procedure for loading of ChP into hybrid NC (S-MNP/C-MNP/AC-MNP/NaCMC-MNP) and organic NC (S-NP/C-NP). A methanolic (2 mL) solution of ChP (20 mg) was added dropwise to a suspension of hybrid-NC (S-MNP/C-MNP/AC-MNP/NaCMC-MNP, 90 mg) or organic-NC (S-NP/C-NP, 90 mg) in MeOH (10 mL), and stirred at 500 rpm for 3 h at 25 °C. The ChP loaded nanocarriers were collected with the help of an external magnet, washed with methanol and vacuum dried at 37 °C for 1 h. The amount of free pesticide present in the supernatant was calculated by using gas chromatography–mass spectrometry (GC–MS) analysis with the retention time 19.9 min. The calibration curve of ChP was prepared in MeOH (Figure S2). PLE (wt%) and E.E% were calculated using the following equations and results are provided in the Tables S2 and S3. However,

$$E.E\% = \frac{\text{Amount of pesticide} - \text{Amount of free pesticide}}{\text{Total amount of particles}} \times 100 \quad (1)$$

$$PLE (wt\%) = \frac{\text{Amount of pesticide} - \text{Amount of free pesticide}}{\text{Total amount of pesticide}} \times 100 \quad (2)$$

Figure S3. Calibration plots of free chlorpyrifos present in supernatant from GC-MS of (a) S-MNP (b) C-MNP (c) AC-MNP (d) NaCMC-MNP (e) S-NP (f) C-NP

B2. Estimation of the E.E and PLE of hybrid- and organic-NCs by GC–MS.

Table S2. E.E and PLE of hybrid- and organic-NCs by GC-MS.^a

NC	Free ChP ^b (mg)	E.E Formula (%)	E.E (%)	PLE Formula (wt %)	PLE (%)
S-MNP	1.34	(20–1.34)/90*100	20.7	(20–1.34)/20*100	93.3
C-MNP	4.97	(20–4.97)/90*100	16.7	(20–4.97)/20*100	75.2
AC-MNP	5.25	(20–5.25)/90*100	16.4	(20–5.25)/20*100	73.8
NaCMC-MNP	4.80	(20–4.80)/90*100	16.9	(20–4.80)/20*100	76.0
S-NP	2.60	(20–2.60)/90*100	19.3	(20–2.60)/20*100	87.0
C-NP	3.80	(20–3.80)/90*100	18.0	(20–3.80)/20*100	81.0

^a 20 mg of chlorpyrifos and 90 mg of NC were used for this study, ^b amount of untrapped ChP by GC-MS.

Table S3. Correction of E.E and PLE with equal ratio of organic content in the hybrid- and organic-NCs by ICP-MS analysis

NC Type	NC	E.E (%) ^a	PLE (%) ^a	Corrected E.E(%) ^b	Corrected PLE (wt%) ^b	Relative PLE to S-MNP (wt%) ^c
Hybrid	S-MNP	20.7	93.3	24.6	111	100.0
	C-MNP	16.7	75.2	19.0	86	77.4
	AC-MNP	16.4	73.8	17.8	80	72.5
	Na-CMC-MNP	16.9	76.0	20.9	94	84.7
organic	S-NP	19.3	87.0	19.3	87	78.6
	C-NP	18.0	81.0	18.0	81	73.2

^a E.E and PLE obtained from GC–MS (Table S2). ^b In case of hybrid NCs correction was applied by replacing the inorganic content to organic using ICP–MS (the calculation is provided in Section B3). ^c relative PLE corrected PLE of (other MNP / S-MNP)*100.

B3. Correction of PLE and E.E by ICP-MS analysis

Inductively coupled plasma mass spectrometry (ICP-MS) was performed to quantify the inorganic content in the hybrid NCs. The amount of iron oxide (MNP) content was subtracted and the efficiencies were extrapolated to keep the total organic content same as organic NCs. Since the room for the pesticide loading mainly provided by the organic content. The calculation are provided below. The corrected E.E% and PLE (wt%) with equal ratio of organic content in the hybrid- and organic-NCs by ICP-MS analysis is provided in the Table S3.

Estimation of the inorganic part in hybrid NCs from ICP-MS:

S-MNP

Estimation of inorganic content through ICP-MS

Sample weight used for ICP-MS analysis = 59.4 mg

Weight of (Fe₃) content determined from ICP-MS = 11.4%

= 11.4* 59.4/100 = 6.77 mg

Weight of oxide (O₄) = (iron mass/molar mass of Fe₃)*molar mass of oxide

= (6.77/168)*64 = 2.57 mg

Weight of inorganic (Fe₃O₄, MNP) content in S-MNP = 2.57 + 6.77 = 9.34 mg

Weight of organic (starch, S) content in S-MNP = S-MNP– MNP = 59.4 – 9.34 = 50.06 mg

The percentage of starch present in the S-MNP by ICP-MS = 50.66*100/59.4 = 84.27%

Estimation of PLE (wt%) for S in S-MNP

The 84.27% weight of starch in 90 mg of S-MNP = 75.84 mg and its corresponding PLE value obtained from GC-MS (see Table S2) = 93.3 wt%

Similarly, the estimated PLE value for 90 mg starch is = 93.3*90/75.84 = 110.7 wt%

Estimation of E.E (%) for S in S-MNP

The 84.27% weight of starch in 90 mg of S-MNP = 75.84 mg and its corresponding E.E value obtained from GC-MS (see Table S2) = 20.7%

Similarly, the estimated E.E value for 90 mg starch is = 20.7*90/75.84 = 24.6%

C-MNP

Estimation of inorganic content through ICP-MS

Sample weight used for ICP-MS analysis = 33.2 mg

$$\begin{aligned}\text{Weight of (Fe}_3\text{) content determined from ICP-MS} &= 8.9\% \\ &= 8.9 * 33.2/100 = 2.95 \text{ mg}\end{aligned}$$

$$\begin{aligned}\text{Weight of oxide (O}_4\text{)} &= (\text{iron mass/molar mass of Fe}_3\text{)} * \text{molar mass of oxide} \\ &= (2.95/168) * 64 = 1.123 \text{ mg}\end{aligned}$$

$$\text{Weight of inorganic (Fe}_3\text{O}_4, \text{MNP) content in C-MNP} = 2.95 + 1.123 = 4.073 \text{ mg}$$

$$\begin{aligned}\text{Weight of organic (cellulose, C) content in C-MNP} &= \text{C-MNP} - \text{MNP} = 33.2 - 4.073 = \\ &29.127 \text{ mg}\end{aligned}$$

$$\text{The percentage of cellulose present in the C-MNP by ICP-MS} = 29.127 * 100 / 33.2 = 87.73\%$$

Estimation of PLE (wt%) for C in C-MNP

The 87.73% weight of C in 90 mg of C-MNP = 79 mg and its corresponding PLE value obtained from GC-MS (see Table S2) = 75.2 wt%

Similarly, the estimated PLE value for 90 mg cellulose is = $75.2 * 90 / 79 = 85.7 \text{ wt}\%$

Estimation of E.E (%) for C in C-MNP

The 87.73% weight of C in 90 mg of C-MNP = 79 mg and its corresponding E.E value obtained from GC-MS (see Table S2) = 16.7%

Similarly, the estimated E.E value for 90 mg cellulose is = $16.7 * 90 / 79 = 19.0\%$

AC-MNP

Estimation of inorganic content through ICP-MS

$$\begin{aligned}\text{Sample weight used for ICP-MS analysis} &= 33.7 \text{ mg} \\ \text{Weight of (Fe}_3\text{) content determined from ICP-MS} &= 6\% \\ &= 6 * 33.7/100 = 1.962 \text{ mg}\end{aligned}$$

$$\begin{aligned}\text{Weight of oxide (O}_4\text{)} &= (\text{iron mass/molar mass of Fe}_3\text{)} * \text{molar mass of oxide} \\ &= (1.962/168) * 64 = 0.747 \text{ mg}\end{aligned}$$

$$\text{Weight of inorganic (Fe}_3\text{O}_4, \text{MNP) content in AC-MNP} = 0.747 + 1.962 = 2.709 \text{ mg}$$

$$\begin{aligned}\text{Weight of organic (aminocellulose, AC) content in AC-MNP} &= \text{AC-MNP} - \text{MNP} = 33.7 - \\ &2.709 = 30.991 \text{ mg}\end{aligned}$$

$$\text{The percentage of aminocellulose present in the AC-MNP by ICP-MS} = 30.991 * 100 / 33.7 = 91.96\%$$

Estimation of PLE (wt%) for AC in AC-MNP

The 91.96% weight of AC in 90 mg of AC-MNP = 82.77 mg and its corresponding PLE value obtained from GC-MS (see Table S2) = 73.8 wt%

Similarly, the estimated PLE value for 90 mg aminocellulose is = $73.8 \times 90 / 82.77 = 80.3$ wt%

Estimation of E.E (%) for AC in AC-MNP

The 91.96% weight of AC in 90 mg of AC-MNP = 82.77 mg and its corresponding E.E value obtained from GC-MS (see Table S2) = 16.4%

Similarly, the estimated E.E value for 90 mg aminocellulose is = $16.4 \times 90 / 82.77 = 17.8\%$

NaCMC-MNP

Estimation of inorganic content through ICP-MS

Sample weight used for ICP-MS analysis = 116.4 mg

Weight of (Fe₃) content determined from ICP-MS = 13.8%

$$= 13.8 \times 116.4 / 100 = 16.06 \text{ mg}$$

Weight of oxide (O₄) = (iron mass/molar mass of Fe₃)*molar mass of oxide

$$= 16.06 \times 64 / 168 = 6.119 \text{ mg}$$

Weight of inorganic (Fe₃O₄, MNP) content in NaCMC-MNP = $6.119 + 16.06 = 22.179$

mg

Weight of organic (sodium carboxymethylcellulose, NaCMC) content in NaCMC-MNP =

$$\text{NaCMC-MNP} - \text{MNP} = 116.4 - 22.179 = 94.22 \text{ mg}$$

The percentage of sodium carboxymethylcellulose present in the NaCMC-MNP by ICP-MS

$$= 94.22 \times 100 / 116.4 = 80.94\%$$

Estimation of PLE (wt%) for NaCMC in NaCMC-MNP

The 80.94% weight of NaCMC in 90 mg of NaCMC-MNP = 72.9 mg and its corresponding PLE value obtained from GC-MS (see Table S2) = 76.0 wt%

Similarly, the estimated PLE value for 90 mg sodium carboxymethylcellulose is =

$$76 \times 90 / 72.9 = 93.8 \text{ wt\%}$$

Estimation of E.E (%) for NaCMC in NaCMC-MNP

The 80.94% weight of NaCMC in 90 mg of NaCMC-MNP = 72.9 mg and its corresponding E.E value obtained from GC-MS (see Table S2) = 16.9%

Similarly, the estimated E.E value for 90 mg sodium carboxymethylcellulose is =

$$16.9 \times 90 / 72.9 = 20.9\%$$

Section C. Comparison with polysaccharide nanoparticles based nanocarriers reported in the literature.

Table S4.

S.N o.	Polysaccharides	Organic/hybrid	Size of NPs (nm)	Drug/pesticide	SPR	PLE (wt%)/EE (%)	references
1	Sodium alginate	organic	50–100	imidacloprid	N.M.	2.46 / 98.66	1
2	Alginate and Chitosan	organic	635	paraquat	100% in 8 h	NM/ 74.2	2
3	cyclodextrins	organic	<1	Bendiocarb and promecarb	N.M.	NM	3
4	chitosan and sodium tripolyphosphate	organic	420	Paraquat	60% in 6 h	NM/ 62.6	4
5	chitosan complexes and nanoparticles algae	organic	N.M.	dichlorprop	N.M.	NM	5
6	carboxymethyl chitosan with ricinoleic acid micelle	organic	200–500	azadirachtin	100% in 11 days	18/56	6
7	chitosan nanocapsules through ionotropic gelation method utilizing chitosan and tripolyphosphate	Organic	100	hexaconazole	N.M.	NM/73	7
8	azidobenzaldehyde (Az) and an aqueous solution of carboxymethyl chitosan (CMCS)	organic	153–254	methomyl	100% in 7 days	NM/90	8

9	Starch-xanthate	hybrid	NM	parathion	N.M.	NM	9
10	Starch	hybrid	20	Chlorpyrifos	88% in 10 days	111/ 24.6	This work
11	Starch	organic	25	Chlorpyrifos	83% in 10 days	87/19.3	This work

^a N.M. (not mentioned)

Section D. Release kinetics

We observed in Table S5. for the S-MNP, C-MNP, AC-MNP, NaCMC-MNP, S-NP & C- NP NCs the R^2_{adj} values were 0.9987, 0.9948, 0.9971, 0.9942, 0.9988 & 0.9988, AIC values were 51.6121, 59.8368, 17.9372, 25.5040, 47.1037 & 43.8599 and MSC values were 5.0109, 3.4243, 3.1591, 3.3991, 5.1603, & 5.1603 respectively. The R^2 adjusted value was used as the model selection criterion with the best model exhibiting the R^2 adjusted value closest to 1. The largest MSC value would be the most appropriate fit.

Table S5. The goodness of Fit Constant from fitting the empirical equation 3 (in the main text) to release date for ChP for ChP-loaded NCs.

Type of NCs	NCs	R^2	R^2_{adj}	MSC	MSC root	SS	WSS	AIC	MSC
Hybrid-NCs	S-MNP	0.9987	0.9984	0.8056	0.8976	11.2785	11.2785	51.6121	5.0109
	C-MNP	0.9948	0.9937	1.2722	1.1279	17.8111	17.8111	59.8368	3.4243
	AC-MNP	0.9971	0.9965	0.1241	0.3522	1.7368	1.7368	17.9372	3.1591
	NaCMC-MNP	0.9942	0.9929	0.1829	0.4346	2.6446	2.6446	25.5040	3.3991
Organic-NCs	S-NP	0.9988	0.9986	0.6271	0.7919	8.7796	8.7796	47.1037	5.1603
	C-NP	0.9988	0.9986	0.5236	0.7236	7.3311	7.3311	43.8599	5.1603

Figure S4. Pesticide release kinetics Makoid–Banakar Model for S-MNP, C-MNP, AC-MNP NaCMC-MNP, S-NP and C- NP.

Section E. References

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