Sodium Triphosphate Effect on Encapsulation of Vitamin B_6 into Chitosan-Alginate Nanoparticles and Its *In Vitro* Drug Release Study

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Received: March 25, 2023
Accepted: June 26, 2024

DOI: 10.22146/ijc.83380

Abstract: *The* in-vitro *drug release study of vitamin B_6 encapsulated into sodium tripolyphosphate crosslinked chitosan-alginate (B_6-TCA) nanoparticles aims to determine the effect of sodium tripolyphosphate on the encapsulation efficiency of vitamin B_6 and effectiveness of the nanoparticles to release vitamin B_6. The focus of this research is synthesizing and characterizing TCA nanoparticles to encapsulate vitamin B_6 as an effective delivery system by studying the kinetics release of vitamin B_6. The research resulted in the formation of coarse solid powder nanoparticles in yellowish-white color with a nanoparticle size of 22.55 nm. Sodium tripolyphosphate decreased the percentage of encapsulation efficiency in the B_6-TCA nanoparticles as its concentration increased. However, the increasing sodium tripolyphosphate causes a slower release of vitamin B_6 from nanoparticles. The encapsulation efficiency of vitamin B_6 is 82.04%. The optimum composition of B_6-TCA nanoparticles ratio is 2:1:1.5:2, where Korsmeyer-Peppas kinetics model suited its better with the Fickian diffusion mechanism of 0.989 and has the smallest reaction rate constant of 0.039 occurred within 6 h.*

Keywords: *alginate; chitosan; nanoparticles; vitamin B_6; sodium tripolyphosphate*

■ INTRODUCTION

Vitamins are needed by the human body, and play a significant role in the growth and maintenance of the body. Vitamins are defined as organic compounds needed by the body in tiny amounts for growth and maintaining the body's metabolism [1]. There are “fat-soluble” and “water-soluble” vitamins based on how they are absorbed, stored, and removed from the body [2]. Fat-soluble vitamins have a broader range of physiological functions than water-soluble vitamins [3]. They play a crucial role in the muscles and heart function, immune system, easy flow and clotting of blood, and eye health [2-3]. The human body cannot produce vitamins except vitamins D and B_3. This means that most vitamins must be obtained from outside the human body [1].

Vitamin B_6 is a water-soluble vitamin. In the body, this vitamin plays a role in the amino acids, carbohydrates and fats metabolism. Apart from that, vitamin B_6 is also responsible for synthesizing neurotransmitters in brain cells and helps the production of serotonin and norepinephrine hormones, which influence mood. Vitamin B_6, along with vitamin B_{12} and folic acid, help to control homocysteine levels in the blood [4]. Vitamin B_6 takes a part as a coenzyme in over 150 biochemical reactions and makes it a vital molecule in most changes in the human body. It is active in the metabolic processes of carbohydrates, lipids, amino acids, and nucleic acids, and participates in cellular signaling. Vitamin B_6 is an antioxidant with the ability to reduce the advanced glycation end product (AGE) levels which is associated with diabetes, heart disease, cancer, or the prognosis of COVID-19 [5], anemia, skin rashes, depression, and weak immune system. Vitamin B_6 is often combined with vitamins B_1 and B_{12} as neurotrophic vitamins. The combination of vitamins B_1 and B_{12} will improve the nervous system. This illustrates the importance of obtaining enough vitamin B_6 in the human body.

Vitamins have important physiological functions, including being anti-inflammatory, immunoregulatory, antioxidative, etc. Unfortunately, the chemical

structures of vitamins are extremely sensitive to light exposure, high temperatures, oxygen, and extreme pH levels [6]. The crucial role of vitamin B_6 in maintaining body health based on scientific literature led to the conclusion that vitamin B_6 is a vital molecule, and its role cannot be overestimated. Therefore, it is necessary to find a way to load vitamin B_6 and make it more stable and controlled during its delivery in the human body. One of the ways is to load vitamin B_6 into nanoparticles.

The choice of material as a polymer matrix must be considered because the material must have biodegradable, edible, and non-toxic properties. Alginates consist of (1,4) connected β-d-mannuronic and α-l-guluronic acids, each in pyranose conformation, organized in homogeneous (MM or GG) and heterogeneous (MG or GM) blocks [7-8]. The COO^- groups of guluronic acids from different chains strongly bind with divalent cations such as calcium. This interaction forms a water-insoluble and thermally reversible three-dimensional lattice called "egg box" [9]. Alginate has the disadvantage that it easily releases active compounds which makes it unsuitable for active compound release purposes [10].

One of the biopolymers suitable for alginate coatings is chitosan. Chitosan consists of D-glucosamine and *N*-acetyl-D-glucosamine copolymer [11] and includes a positive ionic charge. These properties allow chitosan to interact with negatively charged substances such as lipids, cholesterol, fat, proteins, ions, etc. Moreover, chitosan stands out for its biodegradability, bioavailability, adsorption properties, and non-toxicity. These properties make it valuable in various package applications in multiple fields, including pharmaceutical and biomaterial purposes, drug carriers, wound treatment, chelating agents, meal packaging, nutritional supplements, etc. [10,12]. When the amino group of chitosan interacts with the carboxylate group of alginates, a complex chitosan-alginate will be formed with strong electrostatic interaction. This interaction enhances the ability to maintain microcapsules during encapsulation and control the compound release. This positive charge of chitosan is important in drug delivery systems because it plays a role in the interaction with the drug it delivers [13].

The use of chitosan as an oral drug delivery material needs to be modified due to its unstable nature in acidic media. Chitosan can be modified by combining it with certain polymers or cross-linking agents to make it more inert and resistant in acidic media [14]. Sodium tripolyphosphate is a cross-linking agent that forms electrostatic bonds with polycationic polymers, such as chitosan, by a technique called ionic gelation. Sodium tripolyphosphate is physiologically nontoxic when it is compared with glyoxal, glutaraldehyde, and other chemical cross-linkers. Additionally, it offers the advantage of being water-soluble and requires only a single-step reaction for ionic gelation. Sodium tripolyphosphate with its high charge density (six ionic groups), guarantees high cross-linking density with chitosan amine groups through ionic gelation. The use of chitosan-sodium tripolyphosphate as a nanocarrier enabled the encapsulation of drugs, which included risperidone [15], influenza vaccines [16-17] and gene delivery [18].

Considering the importance of vitamin B_6 in human life, it is necessary to study the process of vitamin B_6 encapsulation in TCA nanoparticles. The effectiveness of B_6-TCA nanoparticles when applied to the delivery system will be conducted by studying the kinetics release of vitamin B_6. The stability of vitamin B_6 and a higher percentage of encapsulation efficiency on B_6-TCA nanoparticles are expected to be achieved. Furthermore, B_6-TCA nanoparticles are expected to control the release of vitamin B_6 under certain conditions, allowing side effects on the body to be minimized.

■ EXPERIMENTAL SECTION

Materials

Sodium alginate, chitosan, sodium tripolyphosphate, pyridoxine (vitamin B_6), $CaCl_2$, sodium hydroxide (NaOH), hydrochloric acid (HCl), 1% (v/v) acetic acid solution, aquabidest, and phosphate buffered saline (PBS) with a pH of 7.2 were obtained from Merck and Sigma Aldrich with pro analytical quality.

Instrumentation

The instruments used include laboratory glassware, pH meter, analytical balance, centrifugation (Sorvall Biofuge Primo), magnetic stirrer, UV-vis spectrophotometer (GENESYS 50 Thermo Scientific), scanning electron microscope (SEM-EDX, JSM-6510 JEOL/EO), transmission electron microscopy (TEM, JEM-1400 JEOL/EO), and Fourier transform infrared spectrophotometer (FTIR, Shimadzu Prestige-21).

Procedure

Preparation of B_6-TCA nanoparticles

Preparation of chitosan-alginate nanoparticles is primarily based on ionic interactions between the negative charge of the alginate solution and the positive charge of the chitosan solution. Chitosan was dissolved in 1% acetic acid solution with numerous concentrations (0.5, 1.0, 1.5 and 2.0%), alginate was dissolved in aquabidest with numerous concentrations (1.0, 1.5, 2.0 and 2.5%) while vitamin B_6 is dissolved in aquabidest. Rajaonarivony's method is used to synthesize sodium tripolyphosphate crosslinked chitosan-alginate (TCA) nanoparticles with modifications.

An amount of 5 mL of alginate solution is mixed with 10 mL of vitamin B_6 solution. The mixed solution was added to 10 mL of chitosan solution drop by drop while stirring with a magnetic stirrer (1,000 rpm). Then sodium tripolyphosphate was added with various concentrations (0.5, 1.0, 1.5 and 2.0%) while stirring at constant speed at room temperature. B_6-TCA nanoparticles are formed instantly. The suspension of B_6-TCA nanoparticles was maintained with stirring for 240 min for further crosslinking of the nanoparticles. B_6-TCA nanoparticles were collected by centrifugation (5,000 rpm) for 30 min, followed by further filtration using filter papers and then dried.

Characterization of B_6-TCA nanoparticles

B_6-TCA nanoparticles were characterized using a FTIR. The powder state of the sample was prepared and formed with KBr, pressed to form pellets. FTIR spectra are decided in the wavenumber region between 400–4000 cm^{-1}. The size of B_6-TCA nanoparticles was characterized using TEM with a scale of 20–500 nm. B_6-TCA nanoparticle morphology was characterized by SEM.

Encapsulation efficiency (EE) of B_6-TCA nanoparticles

An amount of vitamin B_6 (5 mg) encapsulated nanoparticles in dry conditions were put into 100 mL of aquabidest, then shaken until the vitamin B_6 was perfectly extracted from the nanoparticles. The UV-vis spectrophotometer was used to analyze the extracted vitamin B_6 at its maximum wavelength (λ_{max}), with aquabidest as a blank solution. Encapsulation efficiency was calculated in Eq. (1):

$$\%EE = \frac{\text{Vitamin } B_6 \text{ concentration in nanoparticle}}{\text{Vitamin } B_6 \text{ concentration}} \times 100\% \quad (1)$$

Evaluation of in vitro *release of B_6-TCA nanoparticles*

The release of vitamin B_6 in B_6-TCA nanoparticles was determined *in vitro*, where 20 mg of nanoparticles were put into a vial containing 20 mL of PBS solution (pH 7.2 and 25 °C) and incubated in an incubator shaker at 80 rpm at 25 °C. The release study was conducted by taking 5 mL of sample to analyze the concentration of vitamin B_6. The release study was evaluated at 30 min time intervals for 6 h. The amount of vitamin B_6 released was calculated using UV-vis spectrophotometer at λ_{max} of vitamin B_6. The concentration of vitamin B_6 released from the nanoparticles was calculated using the linear regression equation (y = a + bx) of the standard curve of vitamin B_6. The concentrations of vitamin B_6 data at each observed time were converted into a C_t vs t for the zero-order, ln C_t vs t for the first order, $\%C_t$ vs $t^{1/2}$ for Higuchi model kinetics and log $\%C_t$ vs log t for the kinetics of the Korsmeyer-Peppas model. The release constant (k) of vitamin B_6 was determined from the data obtained.

■ RESULTS AND DISCUSSION

The research resulted in coarse solid powder nanoparticles with yellowish-white color. One of the factors that influence the efficiency of encapsulation and efficiency of drug release from the matrix is the addition of crosslinker agents in the matrix. Therefore, the effect of adding sodium tripolyphosphate was studied.

FTIR Characterization

The FTIR spectra of chitosan, alginate, sodium tripolyphosphate, vitamin B_6 and B_6-TCA nanoparticle

are represented in Fig. 1(a–e). The characteristic peak of chitosan (Fig. 1(a)) showed the amine group and the hydroxyl group at 3449 cm^{-1}. The carbonyl stretching (C=O) of the secondary amide (amide I band) is found at 1651 cm^{-1}. The peaks in wavenumbers 1419 and 1381 cm^{-1} stood for the N–H stretching of the amide and ether bonds (amide III band) and the N–H stretching (amide III band). The wavenumbers of 1080 and 1026 cm^{-1} are secondary hydroxyl groups and primary hydroxyl groups [19-21].

Chitosan's FTIR spectrum is different from alginate's (Fig. 1(b)) because it has NH_2 groups while alginate has carboxylic groups. The NH_2 group in chitosan was shown by wavenumbers of 3449 and 1651 cm^{-1}, while the carboxylic group in alginate was shown by wavenumbers of 1620 and 1420 cm^{-1} [1,22-24]. Sodium tripolyphosphate (Fig. 1(c)) has a peak of 800 (antisymmetric stretching of the P–O–P bridge), 1093 (symmetric and antisymmetric stretching vibrations in PO_3 group), 1150 (symmetric and antisymmetric stretching vibrations in PO_2 group), and 1211 cm^{-1} (P=O stretching) [25]. Vitamin B_6 (Fig. 1(d)) also showed a characteristic peak at 1281, 1543 and 1620 cm^{-1} indicating the presence of C–O, aromatic C=C and C=O stretching vibration.

From Fig. 1, there has been a shift in the characteristic spectra of chitosan from wavenumber 1597 to 1528 cm^{-1}. This happens due to the interaction $–NH_3^+$ from chitosan with $–COO^-$ from alginate. Interaction occurs in an electrical interaction, which causes the–NH group bending frequency on the amino to decrease. The frequency drop can be related to the amount of energy dropped during the interaction process, and this bond can strengthen the matrix of the nanoparticles. In addition, the wavenumbers 1026 cm^{-1} in chitosan and 1033 cm^{-1} in alginate had a change in wavenumber to 1103 cm^{-1}, which indicates the stretching vibrations of C–O–C. Sodium tripolyphosphate's wavenumber at 1150 cm^{-1} shifted to 1172 cm^{-1}, indicating the presence of P=O group in sodium tripolyphosphate [26]. The interaction between tripolyphosphate ions in sodium tripolyphosphate and ammonium ions in chitosan with the shifted wave number indicates that chitosan and sodium tripolyphosphate were successfully crosslinked during the synthesis of nanoparticles.

SEM-EDX Characterization

B_6-TCA nanoparticle's surface morphology and elemental composition before and after the release of

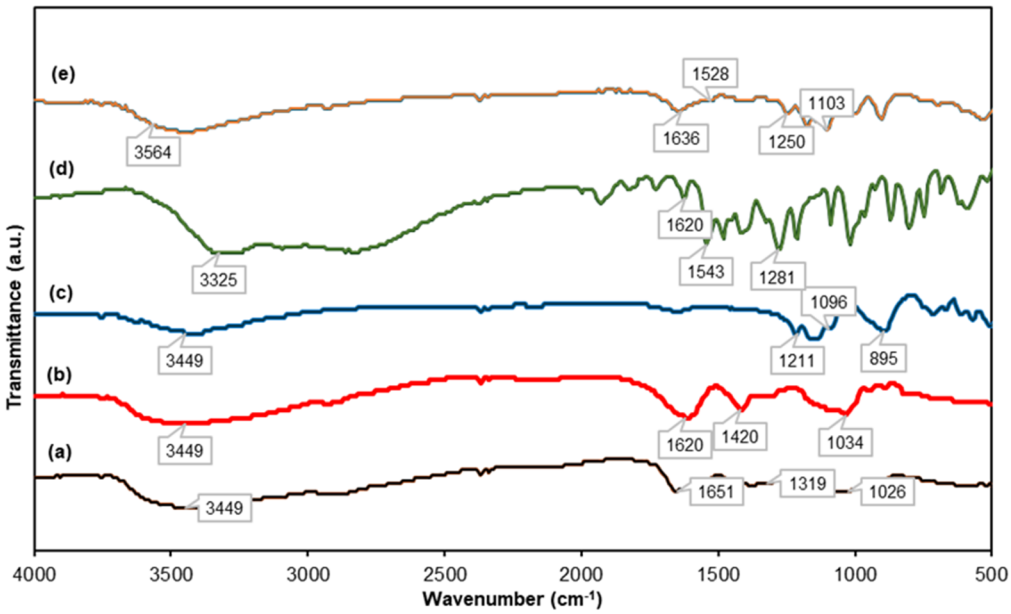


Fig 1. FTIR spectra of (a) chitosan, (b) alginate, (c) sodium tripolyphosphate, (d) vitamin B_6 and (e) B_6-TCA nanoparticles

vitamin B_6 was figured out with SEM-EDX. SEM images taken with a magnification of 200 times on nanoparticles before and after the release of vitamin B_6 are represented in Fig. 2. Before vitamin B_6 is released, nanoparticles exhibit a rough, irregular, and slightly porous surface that can form aggregates, as shown in Fig. 2(a). There is a distinction between the nanoparticles before and after release in Fig. 2(b). In the SEM image of B_6-TCA nanoparticle, before vitamin B_6 is released, the loss of the porous structure in the nanoparticles is feasible because the surface of the nanoparticle has been covered by vitamin B_6, which may have filled the pores. Table 1 provides information on the elemental composition of B_6-TCA nanoparticles before and after release.

The release process in B_6-TCA nanoparticles can be understood by analyzing the composition changes of the nanoparticle constituent elements before and after the release process. In Table 1, there was a composition decrease in C and N elements of the nanoparticles. Before the release process, the C element had a weight percentage of 38.23% and decreased to 35.46% after the release process. As for N element, the weight and atomic percentages were 19.86%, then decreased to 15.69%. There was an increase in the composition of O element from 27.05 to 46.95%. The percentage of elements in the nanoparticle product decreased after the release of vitamin B_6, except O element. This is possible due to the oxidation process of certain groups, such as hydroxyl, aldehyde and other groups, which causes the increase in elemental. The decrease in these elements, which was not too significant, indicated that there was no damage (erosion) to the polymer carriers during the release process.

TEM Characterization

The inner morphology and average size of the B_6-TCA nanoparticles were studied using TEM and represented in Fig. 3(a and b) with a magnification scale of 100 and 50 nm. The TEM images of the B_6-TCA nanoparticles have a spherical but relatively irregular shape with some darker parts than the others. This characteristic indicates the tendency of B_6-TCA nanoparticles to form aggregates. B_6-TCA nanoparticles have an average particle size of 22.55 nm based on the size distribution graph in Fig. 4. The result suggests that the ionic gelation method yields smaller particle sizes.

Encapsulation Efficiency (EE) of Vitamin B_6

Drug encapsulations enhance the therapeutic effect of compounds that are difficult to dissolve, fragile or aggressive along with minimising the side effects. On the other hand, formulating bioactive compounds with high encapsulation efficiencies remains a big challenge during pharmaceutical development [27]. Encapsulation enhances the delivery of drugs to targeted

Table 1. Elemental composition of B_6-TCA nanoparticles before and after vitamin B_6 released

Element	Weight (%)	
	Before release	After release
C	38.23	35.46
N	19.86	15.69
O	27.05	46.95
Na	0.25	1.48
P	7.27	-
Cl	0.30	0.14
Ca	7.04	0.27

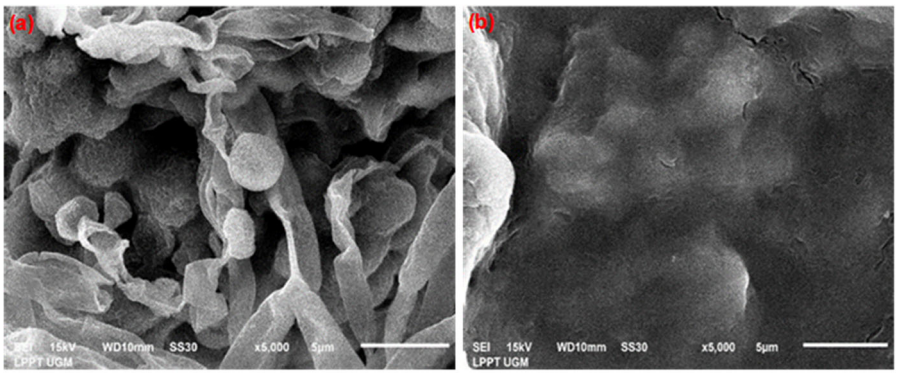


Fig 2. SEM image of B_6-TCA nanoparticles (a) before and (b) after vitamin B_6 release

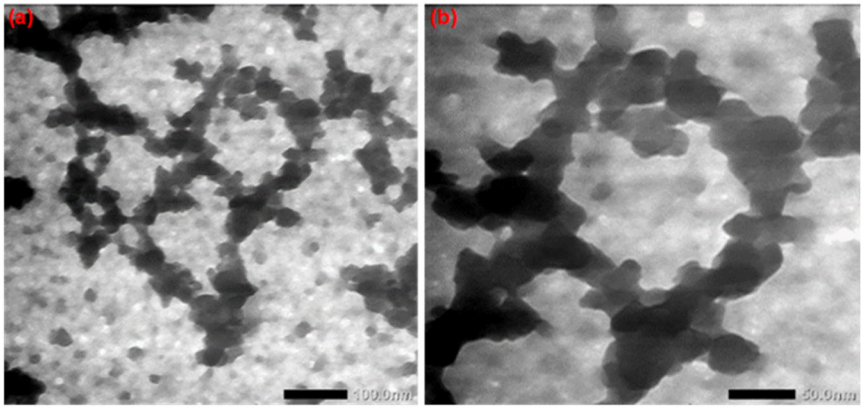
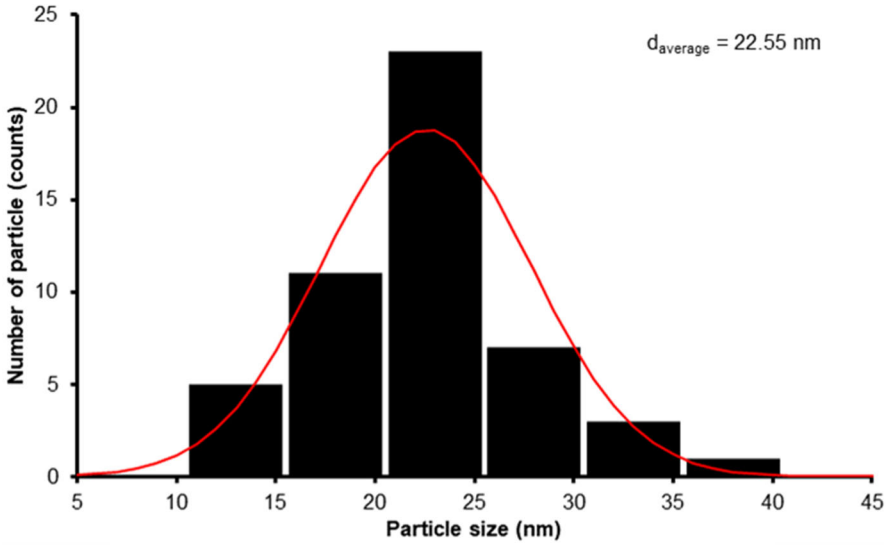


Fig 3. TEM image of B_6-TCA nanoparticles: (a) 100 nm and (b) 50 nm scale



Model	Gaussian
Equation	y = y0 + A/ (w*sqrt (pi/ (4*ln (2)))) * exp (-4*ln (2) *(x-xc) ^2/w^2)
Plot	Counts
y0	1.94979 ± 1.08905
xc	21.83848 ± 0.45565
A	181.74817 ± 27.17664
w	8.03857 ± 1.00814
Reduced Chi-Sqr	4.10006
R-Square (COD)	0.96736
Adj. R-Square	0.93472

Fig 4. Particle size distribution of B_6-TCA nanoparticles

sites, increases drug stability, prolongs pharmacological activity by continuously releasing the active molecules locally and reduces side effects, thereby enhancing the efficacy and safety of therapies [28].

The technique of encapsulation involves packaging, adsorption, or coating active substances in solid, liquid, or gas forms in a matrix. Encapsulation techniques have the advantage of protecting and controlling the release of active ingredients under specific conditions to minimize the potential side effects [29]. The preservation of bioactive properties can be effectively improved by encapsulation, which enables the administration of sensitive vitamins and their metabolization [27]. The encapsulation efficiency parameter is used to determine how much vitamin B_6 is packed into the matrix. The alginate-chitosan polymer was evaluated for its ability to bind vitamin B_6 and form nanoparticle complexes by conducting encapsulation efficiency testing. The test was

conducted by measuring the amount of vitamin B_6 in the matrix and compared with the total vitamin B_6 used in the preparation.

The results of calculations for the encapsulation efficiency of vitamin B_6 with variations in vitamin B_6, chitosan, alginate, and sodium tripolyphosphate concentration are displayed in Tables 2 and 3. In the various concentrations of sodium tripolyphosphate, the optimum encapsulation efficiency value in the ratio of vitamin B_6:chitosan:alginate:sodium tripolyphosphate is 2.0:1.0:1.5:0.5 of 95.91%. As the concentration of sodium tripolyphosphate increased, the percentage of encapsulation efficiency decreased. This is because chitosan-tripolyphosphate crosslinks increase with sodium tripolyphosphate concentration, making the bond network tighter and the free space in the nanoparticle system reduced so that the vitamin B_6 encapsulated by the matrix also decreases.

Evaluation of *In Vitro* Release of B_6-TCA Nanoparticles

Phosphate buffer saline (PBS) solution with a pH value of 7.2 was used to release vitamin B_6 from nanoparticles using aquabidest at 25 °C. Samples were taken and analyzed using UV-vis spectrophotometer to study the kinetics release. The effect of sodium tripolyphosphate concentrations on nanoparticle preparations was studied by varying the concentrations of vitamin-chitosan-alginate-sodium tripolyphosphate, namely with a composition ratio of 2.0:1.0:1.5:0.5; 2.0:1.0:1.5:1.0; 2.0:1.0:1.5:1.5 and 2.0:1.0:1.5:2.0 (Tables 2 and 3). The effect of varying sodium tripolyphosphate concentrations on the synthesis of B_6-TCA nanoparticles is depicted in Fig. 5.

From Fig. 5, it is known the addition of sodium tripolyphosphate causes a slower release of vitamin B_6 from nanoparticles. An increase in the concentration of

Table 2. Influence of vitamin B_6, chitosan, and alginate concentrations on encapsulation efficiency (%EE) of vitamin B_6 in B_6-TCA nanoparticles

Influence of composition	Nanoparticle products vitamin B_6-chitosan-alginate-sodium tripolyphosphate	%EE
Variation concentrations of vitamin B_6	**0.5**:1.0:1.0:2.0	77.37
	1.0:1.0:1.0:2.0	90.49
	1.5:1.0:1.0:2.0	96.35
	2.0:1.0:1.0:2.0	97.65
Variation concentrations of chitosan	2.0:**0.5**:1.0:2.0	83.69
	2.0:**1.0**:1.0:2.0	89.84
	2.0:**1.5**:1.0:2.0	88.08
	2.0:**2.0**:1.0:2.0	82.16
Variation concentrations of alginate	2.0:1.0:**1.0**:2.0	94.34
	2.0:1.0:**1.5**:2.0	96.42
	2.0:1.0:**2.0**:2.0	95.95
	2.0:1.0:**2.5**:2.0	89.41

Table 3. Encapsulation efficiency of vitamin B_6 in various concentrations of sodium tripolyphosphate

Nanoparticle products vitamin B_6-chitosan-alginate-sodium tripolyphosphate	%EE
2:1:1.5:0.5	95.91
2:1:1.5:1.0	92.57
2:1:1.5:1.5	85.01
2:1:1.5:2.0	82.04

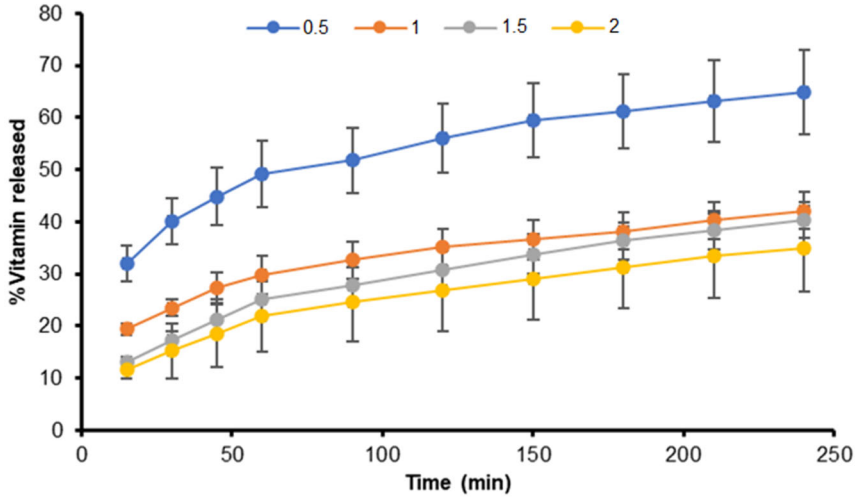


Fig 5. Effect of variations of sodium tripolyphosphate concentrations on the release of vitamin B_6

sodium tripolyphosphate will result in higher cross-links with chitosan so that the path of diffusion becomes obstructed [30]. Sodium tripolyphosphate can be used as a medium to control the slow release of vitamin B_6, because the slower the release of vitamin B_6 from the nanoparticles, the lower the dose of the drug required. Using zero order, first order, Higuchi and Korsmeyer-Peppas models, the kinetics of vitamin B_6 release from B_6-TCA nanoparticles was investigated. Table 4 summarizes the results of calculating the *in vitro* release parameters of vitamin B_6 from B_6-TCA nanoparticles.

According to the data in Table 4, the ratio of 2.0:1.0:1.5:2.0 in the composition has the highest linearity value (R^2), which is the closest to 1 in the Korsmeyer-Peppas kinetics model, amounting to 0.989 and has the lowest reaction rate constant, which is equal to 0.039. The small reaction rate indicates that the process of releasing vitamin B_6 is slow. In addition, the n value for the product composition ratio of 2.0:1.0:1.5:2.0 is less than 0.45. This indicates that the release of vitamin B_6 from the TCA nanoparticles occurred through a Fickian diffusion process without being followed by erosion of the carrier polymer. The composition ratio of 2.0:1.0:1.5:2.0 resulted in a vitamin B_6 %EE of 82.04%. The %EE obtained in this study is above the average of other vitamins encapsulated in other polymers (nano)microparticles, where the previous research resulted in an average of %EE in the range of 27–45% [31].

Table 4. Parameter calculation results for *in vitro* release of vitamin B_6 on B_6-TCA nanoparticles

Model and Parameter	Score
Zero-order	
R^2	0.926
K_0 (min^{-1})	9.660×10^{-4}
First-order	
R^2	0.946
K_1 (min^{-1})	2.605×10^{-4}
Higuchi	
R^2	0.984
K_H ($min^{-1/2}$)	1.970×10^{-2}
Korsmeyer-Peppas	
R^2	0.989
K_{KP} (min^{-n})	0.039
N	0.400

Possible interactions between vitamin B_6 and TCA nanoparticles could involve the interaction between alginate and chitosan which is shown in Fig. 6. This interaction entails the negatively charged carboxyl group in alginate and the positively charged amino group in chitosan. The interaction between chitosan and sodium tripolyphosphate occurred between the negative group of polyanions in sodium tripolyphosphate and amine groups in chitosan. Fig. 7 shows the possible interaction between vitamin B_6 with TCA nanoparticles due to the interaction between hydrogen bonds between hydroxyl groups from vitamin B_6 and chitosan.

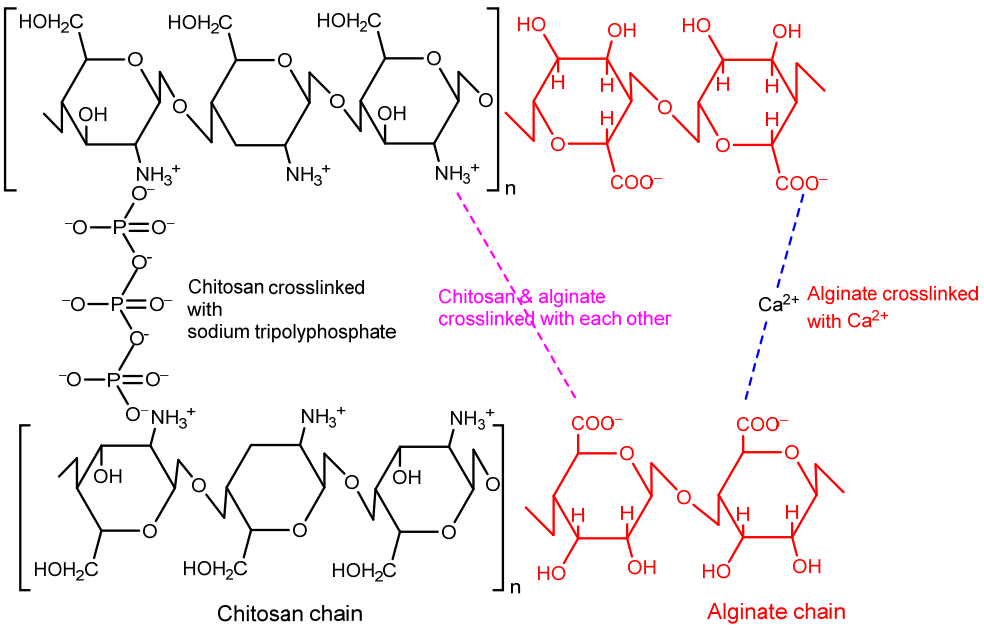


Fig 6. Structure of TCA nanoparticles

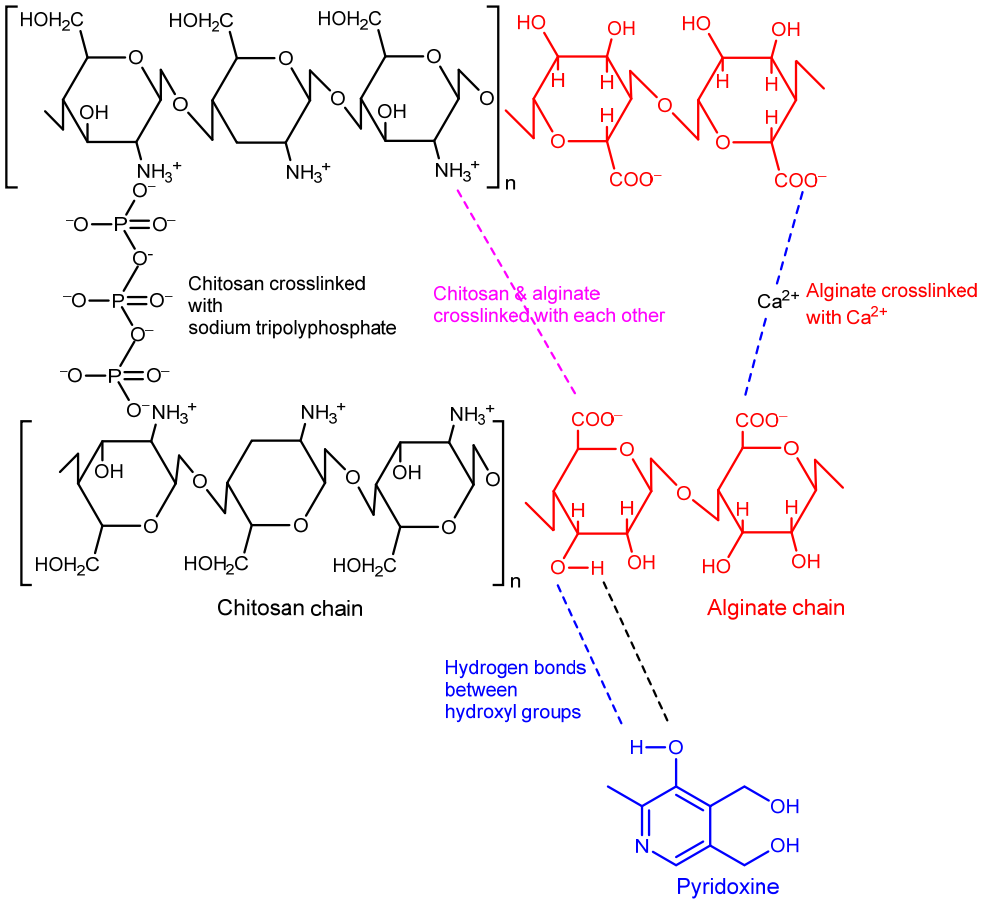


Fig 7. Possible interactions between vitamin B_6 and TCA nanoparticles

■ CONCLUSION

B_6-TCA nanoparticles were successfully synthesized, and the resulting nanoparticles had an average particle size of 22.55 nm. The optimum composition of B_6-TCA nanoparticles ratio is 2.0:1.0:1.5:2.0 followed by Korsmeyer-Peppas kinetics as its best-fitted model with the Fickian diffusion mechanism, amounting to 0.989 and has the smallest reaction rate constant, which is equal to 0.039 occurred within 6 h. The results show that the encapsulation efficiency of vitamin B_6 in this study reaches 82.04% and is above the average encapsulation efficiency of other vitamins in polymers.

■ ACKNOWLEDGMENTS

The authors would like to sincerely thank the Department of Chemistry, Universitas Gadjah Mada for providing the necessary support and infrastructural facilities.

■ CONFLICT OF INTEREST

The authors declare no conflict of interest.

■ AUTHOR CONTRIBUTIONS

Aulia Rahman: investigation, formal analysis, writing – review & editing. Suherman: validation and review. Adhitasari Suratman: supervision, conceptualization, review.

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