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The Effect of Using Chitosan and Nano-chitosan Synthesized from Blue Carb in the Treatment of Hyperglycemia and Glomerulus of Diabetic Guinea Pigs

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Abstract

Chitin, the most presence of biopolymer after cellulose, it consisting the major compound of crustacean shell. Chitosan is biopolymer derived by deacetylation of chitin. Diabetes Mellitus (DM) is a collection of metabolic diseases characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both leading to metabolic abnormalities in carbohydrates, lipids, and proteins. Increasing the ROS level as complication of hyperglycemia during diabetes, damage the cell membrane lipid and proteins that change in cell metabolism thereby defect in function of tissue and organ. The aim of current study was to evaluate the effect of chitosan and nano-chitosan on guinea pigs with hyperglycemia. Diabetes induced by injection of 3mg/kg of dexamethasone for 5 weeks. FBS significantly decrease in treatment groups (168.2±24.38 and 156.4±53.71). Also, blood urea and creatinine levels reduced in treatments groups (38.1±7.81, 36.7±5.41), (1.38±0.087, 1.27±0.038). Chitosan and nano-chitosan reduced FBS significantly when injection in guinea pigs and improve the function of kidney.

Keyword: Diabetes, Blood urea, Serum creatinine, Chitosan, Fasting blood sugar.

1. Introduction

Chitin, the most presence of biopolymer after cellulose, is the major compound of crustacean shell such as shrimp, prawn, crab and crawfish. Chitosan (CS) is a biopolymer derived by deacetylation of chitin (1). It is a bi-product extracted from chitin by using alkali treatment which involves three main steps. Chitosan is non- toxic, antimicrobial, and biodegradable material which has many applications such as food industry, water treatment, manufacturing of membranes, cosmetics, antifungal and antibacterial products (2).

Diabetes mellitus (DM) is chronic disease that has a significant influence on human health and the quality of life of millions of peoples. Prevalence is rapidly increasing on a global scale with an expected increase to 600 million by 2035 (3). Diabetes Mellitus is a collection of metabolic diseases characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both leading to metabolic abnormalities in carbohydrates, lipids, and proteins (4).The symptoms of diabetes include high blood sugar, frequent urination, thirst, and weight loss without diet (5, 6). Determining the suitable strategy for therapy need diagnosis the type of diabetes that's plays a key role in treatment. The classification of diabetes according to American diabetes association (ADA) is type I diabetes, also called insulin-dependent diabetes, type II diabetes, which is called insulin-independent diabetes, gestational diabetes, and specific type of diabetes (7). Type II diabetes is a major cause of chronic disease and death worldwide. It accounts for more than 90% of diabetic patients. Poor control and untreated diabetes leads to serious complications, such as cardiovascular disease, retinopathy, chronic kidney disease, and hypertension (8). Oxidative stress has a main role in the progress of complications that related to diabetes especially in type II diabetes. Oxidative stress is generated by enzymatic and non-enzymatic activity formation of advanced glycation products (AGEs) (9, 10) which affect the cellular metabolism and proteins cell membrane caused production of free radical. Increase the ROS results in cell membrane, lipid and proteins damage

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furthermore its change the activity of antioxidant. Defect in antioxidant activity results in further damage include tissue and/or organs that's affect the functions of organ (11, 12). Oxidative stress contribute in kidney damage by increasing the generation of oxidants due to decrease in antioxidant production. Type II diabetes is one of the main risk factors that play a role in development of kidney disease, about 30%–50% of diabetes patients (13). The aim of current study was to evaluate the effect of chitosan and nano-chitosan on guinea pigs with hyperglycemia.

2. Experimental

The materials were used in present study purchased as following,acetic acid and chloroform (BDH), formalin (Romil), glucose kit (Randox) blood urea and creatinine kit (Linear), hematoxylin and eosin (Biopharm). The blue crabs were purchased from (Alwarda) local market. Chitosan and nano-chitosan were synthesized by method (14) with modification from blue crab shell. 24 male guinea pigs 36 weeks old with average weight (0.485±0.054 g) provided by Iraqi national center for drug control and research. The animals were housed in poly vinyl cage with conditions (12 h/12 h light/dark), 24 °C, and free access to food and water for 2 weeks. Diabetes induced by daily injection of 3mg/kg of dexamethasone followed by orally 5 ml of 50% sugar solution for 5 weeks. The animals were divided into four group as negative control, positive control (diabetes), treated with 2% of chitosan (B-CS), and treated with 2% of nano-chitosan (Np-CS). The B-CS and Np-CS were dissolved in 1% acetic acid solution. The animals were injected for 21 days with chitosan and nano-chitosan. The animals pass through using over dose of chloroformfollowed by collection of blood sample and clear serum was separated into eppendorf tube for time assay. The pancreas and kidney were harvested and incubated in 10% formalin. The SPSS version 24.0 was used for t-test statistical analyses to obtaining the results. Also, mean and standard devotion (mean±SD)utilized to explain the results.

3. Results and discussion

The level of FBG determined and compared in positive control (204.6±37.01) with chitosan and nano-chitosan treatment groups with mean ± SD (168.2±24.38 and 156.4±53.71) respectively. The results indicate that serum sugar reduced significantly ($p < 0.001$) decrease in groups that treated with chitosan and nano-chitosan Figure 1.

To our knowledge this is the first time to study the nano-chitosan biopolymer effect on diabetes but there are related studies show that other biopolymers reduce the serum postprandial sugar. Albert Bär and his coworkers, showed that α-cyclodextrin biopolymer reduce the postprandial sugar from 157 to 111 mg/dl of volunteer intake only 50 g starch compared with who intake 50g starch with 10 mg of α-cyclodextrin (15). Other study also mentions the lowering of postprandial sugar when use 50 mg ϒ-cyclodextrin and maltodextrin in separated volunteer group compare with who non-intake of this biopolymers (16).

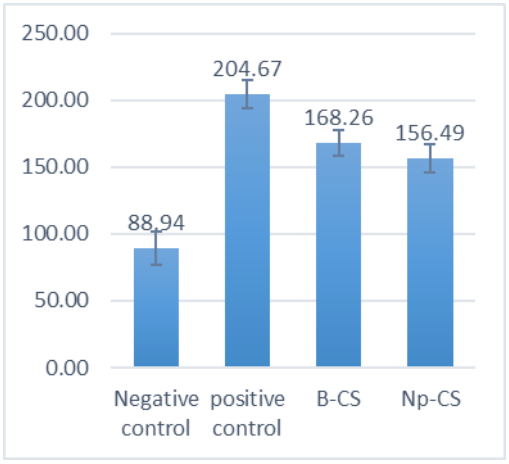

Fig 1. Level of fasting blood glucose in Negative control, Positive control (diabetes), chitosan (B-CS) and nano-chitosan (Np-CS) treated groups

The level of blood urea reduced significantly $p>0.000$ in both groups after injection of 20 mg of chitosan and nano-chitosan (38.1±7.81, 36.7±5.41) compared with positive control (66.66±10.0) group Figure 2.Also, the level of serum creatinine decreases significantly $p>0.000$ in both treatment groups (B-CS and Np-CS) (1.38±0.087, 1.27±0.038) compared with positive control (2.34±0.21) group Figure 3.

These results are agree with Andrea Z. and his collagenous, they reported improvement of renal function (b.urea and s.creatinine) in dog with chronic kidney disease (CKD) when orally administrated with chitosan for 8 weeks (17).They proposed two possible explanations for the lowering serum concentrations of urea and creatinine, including increased clearance due to compensatory hypertrophy of the remaining nephrons, and enhanced excretion

bound to chitosan in the digestive tract. Three other study report improvement of renal function after using of chitosan orally in human with CKD (18, 19).

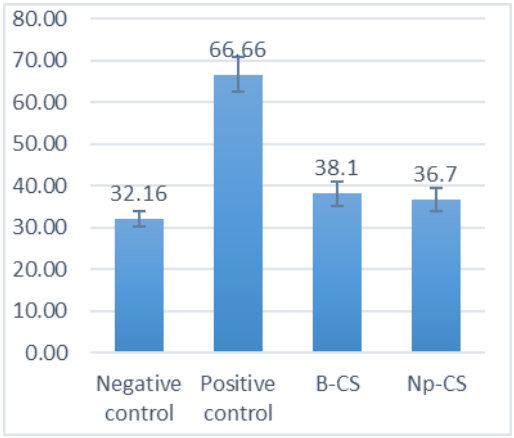

Fig 2. Level of urea in Negative control, Positive control (diabetes), chitosan (B-CS) and nano-chitosan (Np-CS) treated groups.

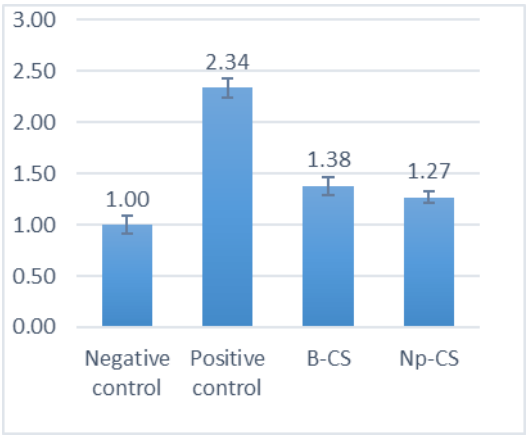

Fig 3. Level of serum creatinine in Negative control, Positive control (diabetes), chitosan (B-CS) and nano-chitosan (Np-CS) treated groups.

Histopathology study of pancreas section of A, B, D and E groups Figure (4).Also, histopathology study of kidney section of four study groups were investigated Figure 5. It is clearly appeared that the glomeruli capsule (like sac) is thick, that maybe due to retention of fluid (urine) in group (B) due to defect of glomeruli to clearance while other treatment groups (C) and (D) show normal sac like of negative control group. These micrographs may describe the lowering of blood urea and serum creatinine in (C) and (D) group.

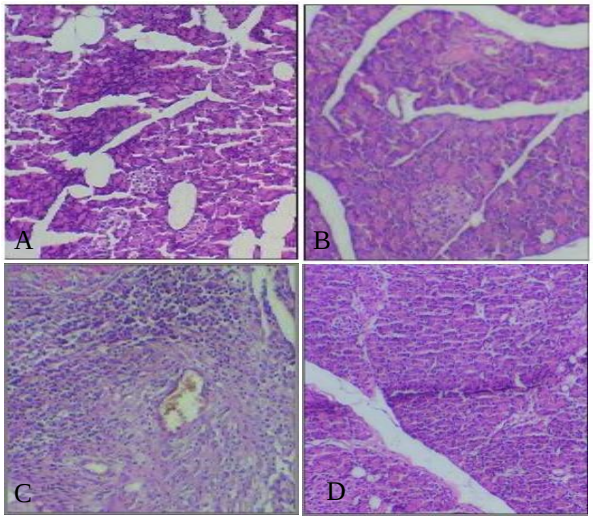

Fig 4. H and E micrograph of pancreas section 10x, of Negative control (A), Positive control (B), treated with chitosan (C) treated with nano-chitosan (D)

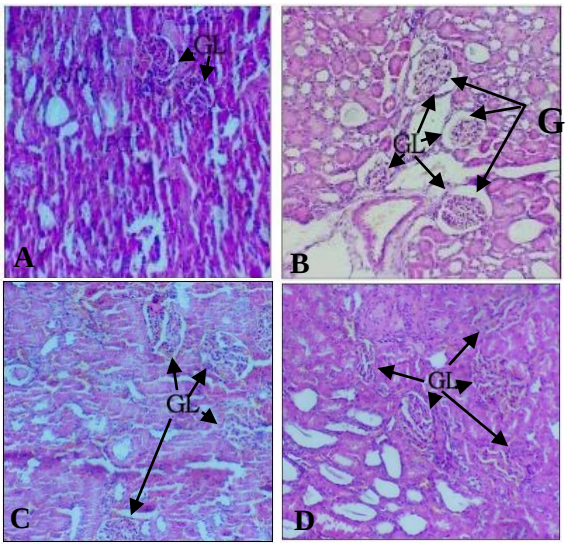

Fig 5. H and E micrograph of pancreas section 10x, of Negative control (A), Positive control (B), treated with chitosan (C) treated with nano-chitosan (D). Glomeruli (GL), glomeruli capsule or glomeruli space (GS).

Conclusions

1- Fasting blood glucose reduced significantly when injection of 20mg/kg of chitosan and nan-chitosan and nano-chitosan have better effect more than bulk chitosan to lowering sugar.

2- Chitosan and nano-chitosan injection improve the function of kidney (urea and creatinine) in diabetes nephropathy and again nano-chitosan give better results.

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