WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 7, Issue 2, 91-97. Research Article ISSN 2277– 7105

CHARACTERIZATION OF THE COMBINATION OF CHONDROTIN SULFATE, CHITOSAN AND KAPPA CARERGEENAN USING THE IONIC GELATION METHOD FOR PAINFUL KNEE OSTEOARTHRITIS

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Article Received on
27 Nov. 2017,
Revised on 17 Dec. 2017,
Accepted on 07 Jan. 2018
DOI: 10.20959/wjpr20182-10713

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ABSTRACT

Objective: Application of the use of chondroitin sulfate as an alternative medicine in addition to nonsteroidal antiinflammatory drugs has the ability to inhibit the development of osteoarthritis. The use of chondroitin sulfate in the form of nanoparticles can increase the bioavailability of the drug. This study aims to characterize the combination formula of condroitin sulfate, chitosan and kappa carrageenan. **Methods:** Preparation of formula consisting of 0.1% chitosan, 0.1% chondroitin sulfate and 0.05% kappa carrageenan at volume ratio of 10: 1: 1 were prepared by using ionic gelation method This method was based on the electrostatic interaction between opposite charges. Characterization of nanoparticles were performed by measuring pH, particle size, polydispersity index, zeta potential and examination of infrared spectrum. **Results:** The results showed that pH 3.1, an average particle size 582.9 nm, polydispersity index value of 0.324 and zeta potential value as much as -0.47 mV.

KEYWORDS: Chondroitin sulfate, chitosan, kappa carrageenan, anoparticles, Ionic gelation, characterization.

INTRODUCTION

In recent years, many studies have been conducted to determine the efficacy of glucosamine, a condrotin in the treatment of osteoarthritis of the knee (OA). Osteoarthritis is a degenerative joint condition causing pain, loss of function and often some degree of disability.[1] The

results of clinical trials show that chondroitin sulfate can reduce the process of osteoarthritis.[2]

The development of nanoparticle technology in drug delivery systems, has an advantage in increasing the bioavailability of drugs.[3] The application of chitosan and carrageenan as a natural polymer in the manufacture of nanoparticles has advantages such as: safe, biodegradable, biocompatible, mucoadhesive and hydrophilic.[4] Other studies have shown that the combination of chitosan and carrageenan has excellent potential in drug delivery systems. Carrageenan types used in these studies is kappa carrageenan.[5] The method of making nanoparticles from chondrotin sulfate, chitosan and kappa karegenan with is the ionic gelation method. The formula to be characterized has a composition 0.1% chitosan, 0.1% chondroitin sulfate and 0.05% kappa carrageenan at volume ratio of 10: 1: 1.

MATERIAL AND METHOD

Materials

Materials used in this study include Chondroitin sulfate (Bioiberica), Chitosan (Biotech Surindo), Kappa carrageenan (PT. Quadrant), Acetic acid and potassium bromide (merck), and aqua destilled (Brataco).

Methods

Characterization of nanoparticles

1. pH measurement.

pH measurement of chondroitin sulfate nanoparticles using a pH meter.

2. Measurement of particle size and polydispersity index

The particle size and polydispersity index of nanoparticles was measured by Particle Size Analyzer (PSA). The resulting dispersion system was taken about 3 mL inserted into the cuvette and analyzed by means of Particle Size Analyzer. The principle of measuring particle size were visible light scattering.[6]

3. Zeta potential measurement

Zeta potential of the sample was measured with Laser Droppler Electrophoresis (LDE) method using a Zetasizer. Zeta potential was measured to determine the nature of the particle surface charge and determine the stability of colloidal.[7]

4. Determination of nanoparticles with FTIR

Chondroitin sulfate nanoparticles was determined by FTIR, samples placed in a special cuvette is then measured.

RESULTS AND DISCUSSIONS

Characterization of nanoparticles

1. pH measurement

pH measurement chondroitin sulfate nanoparticles in three formulas showed that all three had an acidic pH. This is because the environment of the nanoparticles that wass a solution of acetic acid used as a solvent chitosan. The pH value of the formula is 3.1.

2. Particle size

Determination of particle size is a primary characteristic in the manufacture of nanoparticles. The particle size was used to look at the success of the manufacture of nanoparticles, in general, the nanoparticle size range of 1-1000 nm.[8] Particle size was determinated by Particle Size Analyzer (PSA) with the diluent water. Aside from the three formulas, particle size measurement performed also on nanocarrier that only contains the polymer and crosslinker. The aim of the nanocarrier particle size measurement was to determine the particle size of the resulting dispersion system before adding the active ingredient. The particle size of chondroitin sulfat nanoparticle is shown in table 1.

Table 1: Particle size of chondroitin sulfate nanoparticles.

Sample	Particle size (nm)			
	Mean	D10	D50	D90
Formula	582,9	79,7	112,8	236,9
Nanocarrier	637,2	96,3	136,7	284,7

Based on the parameters of the average diameter (mean), the particle size of the Formula tend to be large at more than 500 nm. The particle size distribution can be described from three points, namely D10, D50 and D90. D10 illustrates that there are 10% of the dispersion system which has a smaller particle size, while the remaining 90% has a particle size that is larger than the value stated, contrary D90 illustrates that 90% smaller particle size and 10% particle size larger. D50 or median illustrate that there are 50% of the dispersion system that has a smaller size and 50% have a particle size that is larger than the value stated.[9] The definition when applied to the measurement results of the formula which has a D10 79.7 nm, meaning that 10% of the particles have a particle size smaller than 79.7 nm and 90% of the particles

have a larger particle size of 79.7 nm. The results of research conducted in accordance with Grenha et al (5) which showed that the particle size of the nanocarrier chitosan-kappa carrageenan is in the range 350-650 nm.

3. Polydispersity index

Measurement of particles using Particle Size Analyzer (PSA) may also be obtained polydispersity index value. Measurement of the value of polydispersity index aims to determine the particle size distribution which indicates the level of uniformity of size of nanoparticles produced. The polidispersity index of chondroitin sulfate nanoparticle is 0.324.

Polydispersity index value measured from the formula indicates a value below 0.5, which means that a homogenous dispersion system formed is monodisperse. Polydispersity index value for monodisperse systems starting from 0.01 up to the value of 0.5-0.7. While the value of polydispersity index of more than 0.7 shows a very wide size distribution and may contain large particles or aggregates.[10] The smaller the value of polydispersity index showed that the narrower the particle size distribution, which means the more homogeneous particle size diameter.[11]

4. Zeta potential

Zeta potential is one of the most important nanoparticle characterization. Zeta potential measurements were conducted to determine the surface charge and give an idea repulsive force among particles of the resulting nanoparticle dispersion system. The interaction between particles had an important role in the stability of the colloidal solution. In general, a dispersion system declared stable if the value of the zeta potential was more positive than +30 mV or more negative than -30 mV were determined based on electrostatic repulsion.[12]

The formula containing chitosan 0.1%, chondroitin sulfate 0,1%, kappa carrageenan 0.05% with a volume ratio of 10: 1: 1 had a zeta potential value -0.47. This is influenced by the presence of a free amino group that can cause increased surface charge and zeta potential value generated.[13]

5. Determination of nanoparticles with FTIR

Spectrum of Chondroitin sulfate nanoparticles was determined by Fourier Transform Infra Red (FTIR) aims to see whether or not a shift in absorption area that appears.

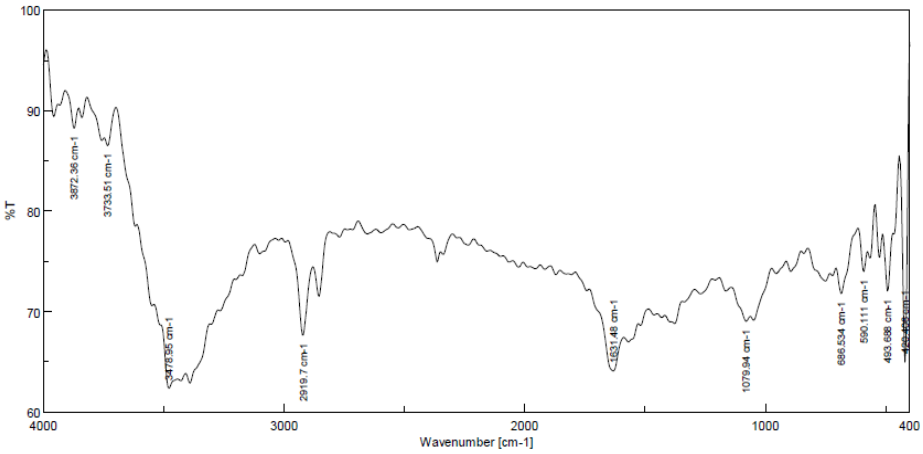

Figure 1: FTIR spectrum of chondroitin sulfate nanoparticles.

Infra-red spectrum of chondroitin sulfate nanoparticles Figure 1 compared to the infra-red spectrum of chondroitin sulfate. The results showed that the spectrum of chondroitin sulfate nanoparticles they are symmetric stretching of the hydroxyl group (O-H) and NH_2 which generates vibration at 3478.95 cm^{-1}, C-H aliphatic shown at 2919.7 cm^{-1} and the carbonyl group is shown in 1631.48 cm^{-1}. C-O group at 1079.94 cm^{-1}.

Absorption area of functional groups contained in chondroitin sulfate nanoparticles experienced a slight shift compared with the absorption area chondroitin sulfate raw materials. Shifting catchment area occurs because the bonds that are formed between chondroitin sulfate with the polymer and crosslinker used. Some peaks of chondroitin sulfate that was at wavenumber 1565.31 cm^{-1} and 1244.06 cm^{-1} disappeared after being made nanoparticles, this could be caused due to the resulting dispersion system is not homogeneous.

CONCLUSION

Nanoparticles best chondroitin sulfate based on the results of characterization that has been done is to use the composition of formula 1 containing chitosan 0.1%, 0.1% chondroitin sulfate, kappa carrageenan 0.05% with a volume ratio of 10: 1: 1 had a pH value of 3.1 (acid), an average particle size (mean) 582.9 nm, 236.9 nm D90 value, 0.324 polydispersity index and zeta potential -0.47 mV. Chondroitin sulfate nanoparticles formed from the formula was not stable so it has a tendency to form aggregates.

ACKNOWLEDGMENTS.

The author would like to thank Richie A.I. Chandra, M.S.c., Apt for his cooperation in this study.

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