Industry Pharmaceuticals: Chitosan as an Alternative Replacement Gelatin Capsules on Shell

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Abstract*—Chitosan is a biopolymer derived from the deacetylation of chitin. Chitosan is composed of poly (2-deoxy-2- asetilamin-2-glucose) and poly (2-deoksi-2-aminoglukosa) that binds (1-4) β-glycosidic. Chitosan character is non-toxic, biodegradable and biocompatible. Chitosan also has a very much usefulness in everyday life such as adsorbent of heavy metal waste and dye, preservatives, antifungal, cosmetics, pharmaceuticals, flocculants, anticancer and antibacterial. The pharmaceutical industry is now preoccupied with issues about capsule shell. The main ingredient of making current commercial capsule shell is gelatin derived from cow bones and pork skin. The weakness shell gelatin capsules of pig skin makes this product can't be consumed by the majority of society, while gelatin made from cow bones makes people worried about contracting mad cow disease. from the cow. Standard shell capsules for pharmaceutical purposes must have the specifications for water content is 12,5% to 15%. Gel strength in the range of 240 bloom to 140 bloom. Viscosity in the range of 4,7 cps to 3,2 cps. Ash content does not outtop 5%. The degree of acidity (pH) in the range of 5,5 to 5,7. The results of several studies on samples of shrimp chitosan obtained result is 5,56% water content, ash content is 0,8%, and the viscosity was 120,5 cps. Manufacture of chitosan capsule shell is intended to substitute shell gelatin capsules made from pork or cow bones. Increase the value of the capsule shell because chitosan character as antibacterial, antiradiasi, as a preservative of food products, and can absorb heavy metals.

***Index Terms*—chitosan, chitin, capsule shell, pharmaceutical**

I. Introduction

Shrimp is a member of the phylum Arthropoda, sub-phylum Mandibulata and belonging to the class Crustacea. The whole body is composed of segments segments wrapped by outer skeleton or exoskeleton of substance horn or chitin and reinforced by calcium carbonate lime. Shrimp waste generated by shrimp processing business such head, skin and tail. Shrimp shell contains protein (25% - 40%), chitin (15% -20%) and calcium carbonate (45% -50%). Currently shrimp farming has grown rapidly so that the shrimp used as a reliable export commodities and the marine life of high economic value (BSI 2104).

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Shrimp are generally used as a food ingredient because it has a high nutritional value. Indonesian shrimp exported in frozen form that has throw the head, tail and skin. Utilization of waste is now being carried out in several places for preserve the environment as well as to generate added value. Shrimp body part that is not utilized now now processed into chitin and chitosan. Chitin and chitosan are carbohydrate compounds that can be produced from waste water results mainly crabs, shrimp, and scallops. Chitin and chitosan have very many benefits for human, one of which can be used as an ingredient absorption of heavy metals, as antibacterial, antiradiasi, as a preservative for food products and many other benefits.

The pharmaceutical industry is currently busy with a variety of problems, one of which is about the capsule shell. The main ingredient of making current commercial capsule shell is gelatin. Gelatin is used in general obtained from cow bones and pork skin. Weakness shell gelatin capsules of pork skin makes this product can not be consumed by the majority of society, while gelatin made from bovine bones makes people worried about contracting mad cow disease from the cow. Therefore, needed an alternative that can be used as the manufacture of gelatin capsule shell apart from pig skin or cow bone. In this research, we tried to make a new discovery by using chitin chitosan is processed into a capsule shell.

II. Review of Literature

A. Chitin and Chitosan

Chitosan is a natural product of biopolymer chitin distilled the which is the second highest in nature after cellulose, the which is found in many insects, crustaceans, and fungi (Sanford 1987). Chitosan is a biopolymer derived from the deacetylation of chitin. Chitosan is composed of poly (2-deoxy-2- asetilamin-2-glucose) and poly (2-deoksi- 2-aminoglukosa) that binds (1-4) β-glycosidic (Tolaimatea et al 2003). Chitosan character non-toxic, biodegradable and biocompatible character. Chitosan also has a very wide usefulness in everyday life such as adsorbent of heavy metal waste and dye, preservatives, antifungal, cosmetics, pharmaceuticals, flocculants, anticancer and antibacterial. Chitosan can be active and interact with cells, enzymes or negatively charged polymer matrix.

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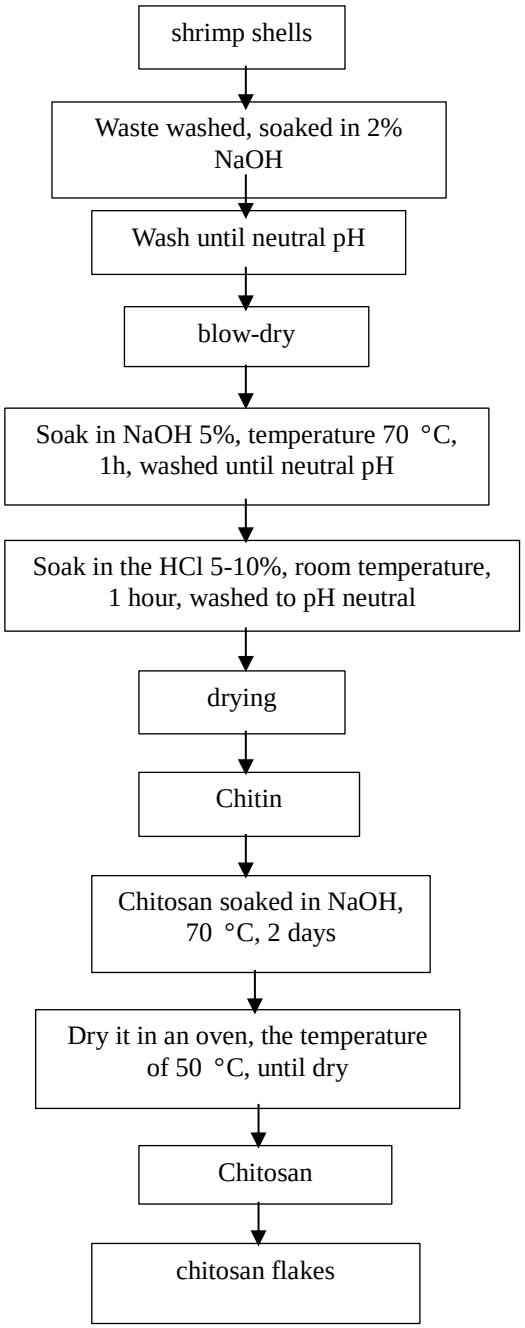
Ingredients to make shrimp shell chitosan is NaOH 2% and 60%, HCl 10%, while the tools used are stainless steel pan, pH meters, loft, oven. Application of chitosan on fishery products using chitosan, acetic acid, aqudes, while the tools used are glass beaker, measuring cups, blender. In addition, TPC test to determine the number of bacteria associated with the effectiveness of chitosan in inhibiting bacterial work performed laboratory tests based on the ISO method.



B. Source: Swastawati 2008

1) Analysis results chitin

- Water content

According to Proton Laboratories chitin on the market is not expected to have a water content greater than 10%, it is given the physical properties of chitin are hygroscopic.

- Ash content

Ash content of chitin note that both sodium hydroxide and potassium hydroxide are used in the process of deproteinization (removal of protein) does not give a real difference to the ash content of chitin.

2) Analysis results chitosan

- Water content

The water content is one of the most important things on Chitosan Quality Standards. Chitosan on sale to the water content of not more than 10% (Chitosan Quality Standards), due to the higher water content, the greater the likelihood the perishability of the product. The average water content of chitosan is higher than the average water content of chitin that is, 5.22% to 6.25% for the chitin and chitosan. While the water content is not influenced by the treatment given. This is mainly influenced by humidity resulting in the absorption of water content from the surrounding environment during storage chitosan (Tsigos 2000).

- Ash content

Ash is left behind when the mineral elements contained in the material, in which the ashing process, the elements that form oxides, or join a negative radical such as phosphate, sulfate, nitrate or chloride. While organic materials that would otherwise be burned (Permadi 1999). Chitosan ash content is not influenced by the type of base on deproteinization process and by comparison of the number of bases in the process of deacetylation. Actually, that play a role in determining the ash content of chitosan is performed demineralization (Bastaman 1990). Ash content of chitosan is mainly caused by $Ca_3(PO_4)_2$ and $CaCO_3$. If the demineralization process is only done once only, the possibility of loss of minerals was not as good as the demineralization process is done twice. To that end, the ash content of chitosan on the market is not expected to be greater than 2% (*Proton Laboratories*).

- The yield of chitosan

The yield is the percentage of chitosan produced from the main raw material, which in this study in the form of dried shrimp shell. Percentage calculation based on a comparison of the levels of chitin. The yield of chitosan is not influenced by the type of base on deproteinization process and comparison of the bases in the process of deacetylation.

- Viscosity analysis of chitosan

Viscosity is measured based on chitosan dissolved in 2% acetic acid, in order to obtain a solution with a concentration of 1%. The viscosity of chitosan is affected by the type of shrimp shell. The viscosity of chitosan is one important factor in determining the quality of chitosan. It matters that affect the viscosity of chitosan, such as the choice of shrimp and alkali concentration, as well as the comparison with the base volume used in the process of chitin deacetylation, HCl concentration and duration of the process demineralisai (Tsigos 2000).

- Results Analysis of degree of deacetylation chitosan

Degree of deacetylation of chitosan is the percentage of acetyl groups of chitin are successfully removed in order to obtain chitosan deacetylation process.

Difficulties that arise to achieve the degree of deacetylation of more than 90% is due to the example in the form of flakes with a size of 3 mm, do not undergo a process of deacetylation homogeneously in every part. Some parts of the bulk sample undergo deacetylation process that is less perfect than the other parts of the same bulk. This is what causes the flakes are not soluble in acetic acid solution (Natsir 2000). Fragments of insoluble chitosan this will disturb the analysis infrared spectrophotometry.

TABEL I. RESULTS OF ANALYSIS OF CHITOSAN FROM SHRIMP SHELLS

Parameters	Research conducted	Standards (BRKP, 2006)
water content	5,56%	10%
ash	0.8%	0,2%
viscosity	120,5 cps	200 cps
Degree of deacetylation	90%	>70%
The yield	15%	

C. The Shell Capsules

Standard gelatin capsules for pharmaceutical purposes must have the specifications for water content is 14%. Gel strength in the range of 240 to 140 bloom bloom. Viscosity in the range of 4.7 cps to 3.2 cps. Ash content in the range of 1% to 2%. The degree of acidity (pH) in the range of 5.5 to 5.7 (Paranginangin et al. 2005).

1) Weight capsule shell

Testing the weight of the capsule shell aims to determine the thickness of the capsule shell. The thicker the shell of the capsule, the weight is increased. The weight of the capsule shell is one of the standards that must be met for commercial capsule shell. Commercial standard capsule shell weight is set at 69-83 mg / 100 shell capsules (Kapsulindo 2007).

2) Water content capsule shell

The water content of the capsule shell is very important to determine its value because it is associated with resistance to microbial activity capsule shell mainly bacteria. Products made from organic materials will generally be invaded by fungi and molds if the water content is more than 20% to 60%, and if more than 60% will be easily covered by bacteria. The water content is a parameter that must be met for commercial capsule shell.

Commercial capsule shell must have a water content content of 12.5% to 15% (Kapsulindo 2007). The water content of the capsule shell such as organic products other drying results greatly influenced by several things including temperature, humidity, and drying time and the physical properties of viscosity.

3) Ash content of the capsule shell

Ash in the capsule shell are inorganic materials such as minerals. The existence of minerals in the capsule shell should not exceed 5% (Ministry of Health 1995).

2.2.4 The degree of acidity (pH) Capsule Shell

One of the parameters for the provision of commercial capsule shell is the degree of acidity of pH (Kapsulindo 2007). The degree of acidity of the capsule shell that must be met to be in the range of 5 to 7 (Department of Health 1995).

4) Endurance capsule shell in water

Capsule shell serves as a wrapper dosage form of powder. The purpose is to reduce the bitter taste, therefore the capsule shell must have a maximum resistance in the water. Capsule shell are easily broken or easily penetrated by water can lead to dissolution of drug dosage in it so that the bitter taste of the drug will be felt. Resilience in the water for commercial capsule shell is predetermined minimum of 15 minutes (Kapsulindo 2007).

D. Chitin and Chitosan Benefits as Capsule Shell

Chitosan in modern industry is very widely used for industries such as food, detergents, textiles, leather, paper, pharmaceuticals, and cosmetics. Among the many greatest use in the food industry, namely 45% and 34% of industrial detergents. These days many countries use the product of chitin and chitosan are Japan, about 700 tons/ year and the United States about 500 tons/ year.

The magnitude of the benefits of chitin and chitosan as well as the availability of raw materials abundant shrimp shell, even a waste that can pollute the environment and damage the aesthetic environment, then these compounds need to get the most attention, especially in terms of efforts to use, research processes and products, as well as pollution prevention . Useful shrimp waste to produce chitosan products of high economic value as raw materials pharmaceutical industry, such as antihiperkolesterol, and minimize pollution by industrial waste processing and utilizing frozen shrimp industry in order to create a clean and friendly environment (Sanusi 2004).

Chitosan is a cationic polymer that is nontoxic, biodegradable and biocompatible character. Chitosan also has a very wide usefulness in everyday life such as adsorbent of heavy metal waste and dye, preservatives, antifungal, cosmetics, pharmaceuticals, flocculants, anticancer and antibacterial. Chitosan can be active and Interact with cells, enzymes or negatively charged polymer matrix as well as an antibacterial ingredient (Lim et al. 2002; No. et al. 2002).

According to Fernández et al. (2006) chitosan provide antibacterial activity (E. coli, S. aureus, Pseudomonas aeruginosa and Salmonella paratyphi B). The ability of chitosan coagulating and form complexes with DNA, causing mechanism between cells and cationic groups on the chitosan polymer still needs to be studied further (Dunn et al. 1992). Performance properties of chitosan is strongly influenced by two important parameters, namely: the degree of deacetylation (DD) and molecular weight (MW). The amount of DD and BM is strongly influenced by the base concentration, temperature, time and repetition of the process for the formation of chitosan.

III. METHODOLOGY

The collection of data is the most important thing that must be done in a study, so that the data is concerned with the study strongly support the completion of this study. The data collection in this study is Literature form formulas and theoretical concepts from the literature

studied and understood in order to be met in developing the theoretical foundation of the concept of research studies in the pharmaceutical industry as the main ingredient replacing gelantin capsule shell with chitin and chitosan. Literature study involves the collection of data and information from books and journals that have relevant, as well as input from various parties.

IV. Discussion

Standard shell capsules for pharmaceutical purposes must have the specifications for water content is 12.5% to 15%. Gel strength in the range of 240 bloom to 140 bloom. Viscosity in the range of 4.7 to 3.2 cps cps. Ash content does not exceed 5%. The degree of acidity (pH) in the range of 5.5 to 5.7. The results of several studies showed that chitosan on shrimp samples generally obtained result is 5.56% water content, ash content is 0.8%, and the viscosity was 120.5 cps.

The water content of the resulting chitosan is not the same as the standard capsule shell water content. High water content can rapidly damaged chitosan or degraded by fungi. Standard shell capsules with a water content of 12.5% to 15% should be met with a water content of chitosan which has a value of 5.56%. Water content has associated with levels of viscosity. Viscosity is a decisive factor for the manufacture of the capsule shell. The technology can be used to reduce levels of viscosity is to use lecithin.

Lecithin is a popular name for a mixed of commercial and phospholipid. Lecithin is used to stabilize the emulsion and reduce the viscosity also facilitate the spread of the particles so that a homogeneous material. Naturally found in peanut soybean lecithin 1.48% - 3.08%, 1.11% peanuts, 0.85% calf liver, wheat 0.65%, 0.39% and eggs. Effective ingredient for lowering the viscosity of chitosan to 4.7 cps and 3.2 cps is soybeans. Decreased levels initially watery viscosity will cause the viscosity becomes much thickened and reduced moisture content. The decreasing water content in chitosan standard will affect water levels capsule shell.

The water content of the capsule shell which has a value of less than 10% will tend to become brittle, and otherwise moisture content of more than 18% will cause the capsule shell becomes soft. The addition of lactose or starch (neutral inert material) will inhibit the fragility of the capsule shell. Lactose has adsorbent properties that are intended to protect the active substance or substances efficacious than the effect of moisture, helping to improve the homogeneity of the mixture, and avoid moisture due to the reaction between the ingredients in the tablet.

V. Conclusion

Chitosan is derived chitin from shrimp shell waste. Chitosan is a cationic polymer that is nontoxic, biodegradable and biocompatible character. Chitosan also has a very extensive benefits in daily life such as adsorbent of heavy metal waste and dye, preservatives, antifungal, cosmetics, pharmaceuticals, flocculants, anticancer and antibacterial. One use that can be produced from chitosan is the pharmaceutical industry in the manufacture of gelatin capsule shell replacement.

Ash content of chitosan eligible to serve as shell capsule while water content and viscosity do not meet the standards. High viscosity levels in chitosan can be reduced with the addition of lecithin. Decreased levels of viscosity causes the water content decreases and substandard water content capsule shell. Moisture content below 10% will result in brittleness of the capsule shell. Lactose or starch needed to resolve the issue so that the capsule shell of chitosan can meet the standard of the water content in order not to fragility.

Chitosan can be used as a substitute for gelatin in the manufacture of commercial capsule shell. Capsule shell made of chitosan have added value because of its antibacterial and anticancer. The content of chitosan as an antibacterial and anticancer make diseases such as cancer than those focused preventable. Moreover, the abundance of shrimp waste makes the availability of such materials can be met for the needs of the pharmaceutical industry.

VI. Advice

This paper discusses all aspects of the manufacture of chitosan capsule shell covering, the definition of chitosan, the benefits of chitosan, how to make chitosan and capsule shell, and the recommended amount. And this paper is suitable for the pharmaceutical industry who want to implement innovation capsule shell from chitosan material. And can be used as a medium for giving insight into the processing and biotechnology chitosan. This paper can be used as a reference for manufacture of the capsule shell made of chitosan to replace the before capsule shell material is made from gelatin of skin pig and cow bones which has caused concern in the community because of the negative effects of both the material.

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