CHAPTER 3

PREPARATION AND CHARACTERIZATION OF RADIOPAQUE CHITOSAN MICROSPHERES

3.1 INTRODUCTION

Polymeric beads with diameter in the micrometer range find use in various medical applications, such as bone cements\(^1\), in local delivery of drugs\(^2\) and in treatment of female stress urinary incontinence.\(^3,4\) Medical microspheres usually consists of poly (methyl methacrylate), poly (lactic acid-co-glycolic acid), poly (tetra fluoroethylene) or silicone rubbers. A particularly important application of microspheres relates to their use as so-called bulking agents; microspheres are injected via a syringe, usually as a suspension. The practical utility of microspheres with X-ray visibility lies in the fact that the clinician can assess possible migration in a direct manner. Polymers encapsulated with radiopacifying agents have recently been proposed as particulate emboli in endovascular embolization and for investigation of a variety of gastrointestinal disorders. Radiopaque hydrogel microspheres derived from many natural and synthetic
polymers such as collagen, gelatin, cellulose, silicones and acrylates have been used as embolization agents. Non-biodegradable hydrogel microspheres, which possess high hydrophilicity, compressibility, swelling ability and biocompatibility have recently been shown to perform better in vascular occlusion. Radiopaque hydrogel microspheres were commonly prepared by the encapsulation of barium sulphate. Barium sulphate encapsulated poly vinyl alcohol, poly (methyl methacrylate), poly (hydroxyethyl methacrylate) and poly (ethylene) were reported.

During the past few decades, there has been a significant increase of interest in using natural polymers for various medical applications. Different types of polysaccharides such as agar, alginate, carrageenan, chitin and chitosan have been used in different fields of medicine. Chitin is the second most abundant natural polymer and is found as a structural component of crustacean shells and fungal cell walls. Chitosan is derived from chitin via deacetylation with an alkali. Chitosan has been reported as a rather imperative matrix in a variety of pharmaceutical, environmental and biotechnological applications due to its excellent properties like biocompatibility, low toxicity, and chemical inertness, good film forming properties, high mechanical strength and hydrophilicity. Chitosan is a copolymer of linked β (1-4), 2-amino-2-deoxy-D-glucan and 2-acetamidodeoxy-D-glucan. Chitosan has been extensively examined for its potential in the development of controlled release drug delivery systems in the form of chitosan gels, tablets, capsules, microcapsules and microspheres.

In this chapter the studies on the preparation, characterization and radiopacity of chitosan microspheres are reported. The chitosan microspheres are prepared using different emulsion systems and are converted into radiopaque by the incorporation of barium sulphate. The synthesis and radiopacity of chitosan derivatives and chitosan / PVA blends are also reported.
3.2 STUDIES ON RADIOPAQUE CHITOSAN MICROSPHERES

3.2.1 INTRODUCTION

Microcapsule is defined as a spherical particle with size varying from 50 nm to 2 nm, containing a core substance. Microspheres are in a strict sense, spherical empty particles. However, the terms microcapsules and microspheres are often used synonymously. In addition, some related terms like microbeads and beads are used alternatively. Recently Yao et al. highlighted the preparation and properties of chitosan microspheres and microcapsules. Chitosan microspheres have been prepared by chemical denaturtion, ion-induced coagulation spray drying methods and multiple emulsion techniques.

Spray drying includes four sequential stages: atomization through a spray nozzle, contact of sprayed feed with warm air, drying of the droplets and collection of the solid chitosan. In drug delivery, chitosan solutions with drug can fed to a spray drier at a slightly acidic pH. The size of the particle is influenced by various process parameters such as size of the nozzle, rate of feeding and inlet air temperature. The inlet air temperature is measured prior to flowing into the drying chamber and may be set at 160°C or higher; however the gradient between the wet surface and unsaturated gas actually leads to evaporation at much lower temperatures. The spray drying technique has been applied to chitosan suspensions, chitosan salts, chitosan (gelatin–ethylene oxide) and chitosan-ethyl cellulose mixture. These microspheres are most suitable as a drug carrier.

The multiple emulsion techniques include three steps: Preparation of primary oil/water emulsion in which the oil dispersed phase is constituted of CH₂Cl₂ and
the aqueous continuous phase is a mixture of 2 % v/v acetic acid solution: methanol (4/1) containing Chitosan (1.6 %) and tween (1.6 w/v); (2) Multiple emulsion formation with mineral oil (oil outer phase) containing span 20 (2 % w/v); (3) Evaporation of aqueous solvents under reduced pressure. Chemical cross linking is an option of this method if the cross linking agent is added just after the emulsion formation; enzymatic cross linking can also be performed. Physical cross linking may take place to a certain extent if chitosan is exposed to high temperature. The emulsion technique is convenient when the drug is particularly sensitive to certain parameters connected to the spray drying. The emulsion technique may associate to cross linking or other treatments of the microspheres.

Microspheres of chitosan, cross linked with glutaraldehyde, sulfuric acid or heat treatment, have been prepared to encapsulate diclofenac sodium by Kumbar et al. In many studies chitosan has been crosslinked with glutaraldehyde to make it a rigid polymer to be used as a core material in controlled drug delivery. Chitosan microspheres were produced in water-in-oil emulsion followed by cross linking in the water phase. The cross linking of Chitosan took place at the free amino groups in all cases and lead to the formation of imine groups or ionic bond. Polymer crystallinity also increases after cross linking. Microspheres have smooth surfaces with size in the range of 40-230 μm.

Of these methods the most common method used to prepare chitosan microspheres is the chemical denaturation method. Chemical denaturation involves denaturation of chitosan in the inner phase of water/oil (w/o) emulsion. Denaturation is usually carried out using glutaraldehyde with continues stirring. The chemical cross linking method for the preparation of chitosan microspheres involves emulsification followed by cross linking.
In this part, a method for the preparation of radiopaque chitosan micro spheres encapsulated with BaSO$_4$ is reported. An attempt is made to prepare radiopaque chitosan microspheres using different emulsion systems. Three emulsion systems, namely, silicone oil/ammonium oleate, naphthenic oil ammonium oleate and liquid paraffin/sorbitan sesqueoleate are used for the study. The micro spheres are characterized by SEM, XRD and IR spectroscopy. The radiopaque nature of the micro spheres is confirmed by their X-ray images.

3.2.2 EXPERIMENTAL

- **Materials Used**

1. Chitosan
2. Barium Sulphate
3. Silicone oil
4. Naphthenic oil
5. Liquid paraffin
6. Ammonium oleate
7. Sorbitan sesqueoleate
8. Glutaraldehyde

- **Preparation of Chitosan encapsulated Barium sulphate microspheres**

Chitosan solution in acetic acid was used for the preparation of chitosan microspheres. The cross linking reaction of chitosan with glutaraldehyde is an instantaneous one. 3 % solution chitosan having a viscosity of 55 cps is used for this study.
1. Using silicone oil/ammonium oleate and naphthenic oil/ammonium oleate systems

The dispersion medium was prepared by mixing 80 ml silicone oil, 20 ml water, 0.38g ammonia solution and oleic acid (3.2 g). The mixture was stirred for 30 minutes. A paste of chitosan containing barium sulphate was added. It was vigorously stirred for 2 min. Then glutaraldehyde saturated with toluene was added and vigorously stirred for another 2 min. Aqueous glutaraldehyde solution was added at every half an hour interval and the reaction was continued for a total of 3 h. After the reaction, it was filtered, washed with acetone, water and then dried in vacuum at room temperature.

Microspheres were also prepared in naphthenic oil using the same method.

2. Using liquid paraffin/sorbitan sesqueolate system

Equal volumes of heavy liquid paraffin and light liquid paraffin were mixed and the mixture was taken in a plastic beaker. 1 ml of sorbitan sesqueolate was added and stirred well. Then a free flowing paste of 3 % chitosan solution containing BaSO₄ was added while stirring. Glutaraldehyde saturated with toluene was added and the stirring was continued at the same speed for 5 min. After 5 min the stirring speed was reduced. Aqueous glutaraldehyde solution was then added at every 30 min intervals and the stirring was continued at room temperature for 3 h. After the reaction the spheres were filtered off, washed several times with hexane and water. The spheres were again washed with plenty of ice-cold water to remove excess acetic acid and glutaraldehyde. The microspheres were then dried in vacuum at room temperature.
3. Radiopaque microspheres from the blend of Poly vinyl alcohol (PVA) and Chitosan

A 4 % solution of 55cps chitosan in acetic acid was blended with 4 % solution of Poly vinyl alcohol (PVA). A paste of barium sulphate and this blend was added to liquid paraffin/sorbitan sesqueoleate system. It was then cross linked with glutaraldehyde. The reaction was continued for 3 h. The microspheres obtained were washed several times with hexane and with plenty of ice-cold water to remove excess acetic acid and glutaraldehyde. The spheres were then dried in an air oven at 50° C.

3.2.3 RESULTS AND DISCUSSION

3.2.3.1 Studies on Chitosan microspheres prepared in Silicone oil/ ammonium oleate and Naphthenic oil/ammonium oleate emulsion system

The SEM photographs of microspheres prepared from silicone oil/ammonium oleate emulsion systems, washed with diethyl ether and acetone are shown in figures 3.1 and 3.2 respectively. It is clear from the photographs that the microspheres prepared from naphthenic oil/ammonium oleate emulsion system do not possess good spherical geometry and surface smoothness. It may be due to the instantaneous cross linking reaction. It is also clear from the figure 3.1 that the diethyl ether washing give only irregular micro particles.
Radiopaque chitosan microspheres

Figure 3.1: SEM photograph of microspheres prepared from Silicone oil/ammonium oleate system with diethyl ether washing (Sil/DEE)

Figure 3.2: SEM photograph of microspheres prepared from Silicone oil/ammonium oleate system with acetone washing (Sil/ACT)
In acetone washing the particles formed are found to be non-spherical. They are of non-uniform size and are not smooth as evident from the figure 3.2. Large clumping is observed in these spheres.

Figures 3.3 and 3.4 shows the SEM micrographs of microspheres obtained from Naphthenic oil/ammonium oleate system with diethyl ether washing and acetone washing respectively. In Naphthenic oil/Ammonium oleate system after washing in diethyl ether, the particles lost their spherical shape as shown in figure 3.3. Perfectly spherical microspheres are obtained after acetone washing, but large clumping is observed in these spheres as in the case of silicone oil/water emulsion system.

Figure 3.3: SEM photograph of microspheres obtained from naphthenic oil/ammonium oleate system with diethyl ether washing (NO/DEE)
Since the naphthenic oil/ammonium oleate and silicone oil/ammonium oleate systems does not give smooth spherical microspheres of chitosan, these microspheres are not taken for further detailed studies.

3.2.3.2 Studies on Chitosan microspheres prepared in liquid paraffin oil/sorbitan sesquioleate system

a. Characterization

- SEM Analysis

The SEM micrographs of chitosan microspheres prepared from liquid paraffin / sorbiton sesquioleate system is shown in figure 3.5 (a and b). The microspheres
formed have smooth surfaces, with sizes in the range of 30-240 \( \mu m \). In liquid paraffin/sorbitan sesquioleate system cross linking reaction takes place in a slow and uniform manner in order to generate microspheres of good spherical geometry and non-agglomeratory in nature. The degree of stirring (i.e., time and speed of stirring during emulsification) affects the size of dispersed droplets. The particle size depends on the viscosity of the dispersant and the dispersion medium, concentration of the stabilizing agent and stirring speed. It is also observed that the barium sulphate is firmly trapped inside the microspheres, as it did not leach out on prolonged standing in water on sonication. Chitosan microspheres obtained from liquid paraffin/sorbitan sesquioleate shows better surface morphology than other two systems. Hence for further detailed studies we have chosen microspheres prepared from liquid paraffin/sorbitan sesquioleate system.

![Figure 3.5a: SEM photograph of microspheres obtained from paraffin oil/sorbitan sesquioleate system](image)

Figure 3.5a: SEM photograph of microspheres obtained from paraffin oil/sorbitan sesquioleate system
Infrared Spectroscopy

Figures 3.6 and 3.7 show the IR spectra of chitosan microspheres and chitosan/barium sulphate microspheres respectively. In figure 3.6, a broad peak in the range 3350 to 3300 cm\(^{-1}\) is observed. The peaks are assigned to an -OH stretching, indicating inter molecular H-bonding. The spectra also overlapped in the same region of a -NH stretching\(^{19}\). Also a peak at 1647 cm\(^{-1}\) representing the stretching vibrations of C=\(N\) bond, confirms the formation of chitosan – glutaraldehyde crosslinks. The NH\(_2\) stretching peak at 1600 cm\(^{-1}\) indicates the presence of glucosamine functional group and the characteristic bands at 2879 cm\(^{-1}\) and 1300 cm\(^{-1}\) represents the protonated amine stretch and deformation vibrations.
Figure 3.7 shows a peak position of OH stretching at 3000 cm$^{-1}$. This low frequency shift is due to the interaction of barium sulphate and chitosan chain. The IR data suggested that there is an association between chitosan and barium sulphate ions and that may be link the chitosan chains.

![IR spectrum of chitosan microsphere alone](image)

**Figure 3.6: IR spectrum of chitosan microsphere alone**
From the IR spectra the cross linking reaction of chitosan-glutaraldehyde can be explained as follows.

Glutaraldehyde crosslinking occurs through a Schiff’s base reaction between aldehyde ends of the crosslinking agent and the amine moieties of chitosan to form imine functions as shown in figure 3.8. The crosslinking of chitosan took place at the free amino group in all cases and lead to the formation of imine groups or ionic bonds.
Figure 3.8: Crosslinked chitosan

- **X-ray Diffraction Studies (XRD)**

Figure 3.9 shows the XRD analysis of chitosan (CHN) and chitosan/barium sulphate (CHN/BS) microspheres. It is clear from the figure that the broad peak at $\theta = 20.03$ in chitosan is shifted to a sharp narrow peak at $\theta = 25.63$ in CHN/BS. Also the narrow peaks at $\theta = 28.65, 32.58$ and $42.41$ indicates the improvement of crystallinity due to the incorporation of barium sulphate inside chitosan microspheres.
Radiopaque chitosan microspheres

Figure 3.9: XRD patterns of chitosan and chitosan microspheres containing barium sulphate

- Radiopacity studies

X-ray photograph of the chitosan microspheres is shown in figure 3.10. Chitosan is radiolucent in nature. By the incorporation of barium sulphate, its electron density increases and it becomes radiopaque. The microspheres show intense radiopacity due to the presence of barium sulphate inside these spheres.
3.2.3.3 Studies on Chitosan / PVA blend microspheres prepared in Liquid paraffin/ Sorbitan sesqueoleate system

- **SEM analysis**

The surface morphology of the microspheres prepared from blend of Chitosan/PVA are studied using scanning electron microscopy and is shown in figure 3.11 (a and b). It is clear from the figure that the chitosan/ PVA blend gives smooth, spherical particles in liquid paraffin/ sorbitan sesqueoleate system.
Radiopaque chitosan microspheres

Figure 3.11 a: Scanning electron micrograph of radiopaque microspheres of chitosan/PVA blend

Figure 3.11 b: Scanning electron micrograph of single microspheres of chitosan/PVA blend
XRD analysis

Figure 3.12 shows the XRD analysis of chitosan/PVA and chitosan/PVA/barium sulphate microspheres.

![Graph showing XRD patterns of CHN/PVA and CHN/PVA-BS microspheres](image)

3.12: XRD patterns of blend of chitosan/PVA and chitosan/PVA microspheres containing barium sulphate

It is clear from the figure that the CHN/PVA microspheres give broad peak at 2θ in the range of 20° C to 50° C and it indicates that the blend is highly amorphous in nature. But when it is encapsulated with barium sulphate, it becomes more crystalline as evidenced by the sharp narrow peaks of CHN/PVA/BS microspheres.
Radiopaque chitosan microspheres

- Radiopacity studies

X-ray photograph of the blend of chitosan/PVA microspheres is shown in figure 3.13. The microspheres show intense radiopacity due to the presence of barium sulphate inside these spheres, as a result of increase in electron density.

![X-ray photograph of chitosan/PVA microspheres containing barium sulphate (filled in polyethylene tube)](image)

Figure 3.13: A X-ray photograph of chitosan/PVA microspheres containing barium sulphate (filled in polyethylene tube)

PART II

3.3 RADIOPAQUE MICROSPHERES FROM THE DERIVATIVES OF CHITOSAN

3.3.1 INTRODUCTION

Chitosan and its derivatives have been studied extensively for various biomedical applications. The poor intractability of chitin is due to the presence of strong inter and intra molecular hydrogen bonding. Chemical manipulation was seen as one
route to overcoming the intractability of chitin to make chitin more accessible. In chitin, the C-6, and C-3 positions of the monomer contain hydroxyl groups and in chitosan, there is an additional N-2 amino functionality that can participate in chemical reaction. All three sites are available for chemical reaction and therefore, the chemistry of chitin and chitosan has been principally one of chemical derivatization of the functional groups.

Historically, the intractability of chitin dictated heterogeneous chemical reactions as the starting point for scientists of the day to commence unraveling the chemistry of chitin. Concurrently, homogeneous reactions were conducted beginning with strong acids culminating in the introduction of homogeneous reactions with the chitin solvent 5% LiCl/dimethyl acetamide (DMAc). All this effort has led to a better understanding of the chemical modification reactions of chitin. Though chitosan is water insoluble, it is readily soluble in dilute organic acids such as acetic acid, citric acid, malic acid and hydrochloric acid. Many acids have been used to prepare chitosan base controlled release drug delivery systems. Chitosan was used as a vehicle for sustained release tablets, a direct compressible diluent, a tablet disintegrant and as a tablet binder. Chitosan derivative such as glutamate, aspirate and hydrochloride salts have been used for colon-specific drug delivery and to enhance the delivery of therapeutic peptide across intestinal epithelial. Spray dried chitosan microspheres using acetic acid as a solvent, loaded with insulin for protein delivery and chitosan microspheres loaded with dexamethasone as well as spray dried lactose composite particles containing an ion complex of alginate-chitosan were studied.

In this part, the preparation, characterization and radiopacity studies of chitosan derivatives are reported.
3.3.2 EXPERIMENTAL

1. Preparation of chitosan formate

Chitosan formate was prepared from chitosan of DA 86 % having viscosity of 330cps. Reaction was carried out at room temperature using formic acid in ethyl acetate. The product obtained was washed with ethanol and dried in an air oven at 50 °C.

2. Preparation of chitosan acetate

Chitosan acetate was prepared using glacial acetic acid in ethyl acetate. Chitosan having degree of deacetylation 86 % was used for the study. The product obtained was washed with ethanol and dried in an air oven at 50° C.

3. Preparation of O-Carboxy methyl chitosan (O-CMC).

Chitosan (15 g) and 9 g monochloroacetic acid were suspended in 150 ml sodium hydroxide solution (42 % by weight). The system was reacted at 0° C for 48 h and then the pH is adjusted to 1 with hydrochloric acid. After filtration, the solid product was washed with methanol for two times. The O-Carboxy methyl chitosan yielded was dried in an oven at 60° C.

4. Preparation of O-Carboxy methyl chitosan (O-CMC)/PVA blend

5 % solution of carboxymethyl chitosan was mixed with 5 % solution of PVA and this blend was used for the preparation of microspheres.

5. Preparation of microspheres from chitosan formate, chitosan acetate, carboxy methyl chitosan

Sorbitan sesqueoleate was mixed with paraffin oil. Then a free flowing paste of 3 % solution of derivative of chitosan containing BaSO₄ was added while stirring. Glutaraldehyde saturated with toluene was added and the stirring was continued at...
the same speed for 5 min. After 5 min the stirring speed was reduced. Aqueous glutaraldehyde solution was then added every 30 min intervals and the stirring was continued at room temperature for 3 h. After the reaction the spheres were filtered off, washed several times with hexane and water. The spheres were again washed with plenty of ice-cold water to remove acetic acid and glutaraldehyde. The spheres were then dried in an air oven at 50 °C.

3.3.3 RESULTS AND DISCUSSION

3.3.3.1 Studies on chitosan formate

- Infrared spectroscopy

Figure 3.14 shows the IR spectrum of chitosan formate. A broad peak in the range 3150 to 3600 cm\(^{-1}\) is assigned to an -OH stretching, indicating inter molecular hydrogen bonding. The peak at 1631 cm\(^{-1}\) representing the NH\(_3^+\) band and the peak at 1548 cm\(^{-1}\) represents the carboxylate band of –COO\(^-\). These characteristic peaks indicate the presence of electrostatic attractions between the chitosan and the formic acid. A formate ion stretching vibration is observed at 1413 cm\(^{-1}\), confirm the formation of chitosan formate.
- **SEM Analysis**

The microspheres prepared from chitosan formate with barium sulphate show good surface morphology, by cross linking with glutaraldehyde as shown in figure 3.15. Free flowing microspheres of different diameters are obtained.
**XRD studies**

The presence of barium sulphate inside the microspheres is confirmed by XRD patterns of these microspheres. The XRD patterns of chitosan formate with and without barium sulphate is shown in figure 3.16.
The polymer crystallinity increases after cross linking and after the incorporation of barium sulphate inside the chitosan microspheres. It is clear from the figure that the broad peak at $2\theta = 19.82$ in chitosan is shifted to a sharp narrow peak at $2\theta = 26.10$ in chitosan formate/barium sulphate. Also the narrow peaks at $2\theta = 28.93$, $33$ and $43.13$ in the case of chitosan formate/barium sulphate microspheres indicates the enhancement of crystallinity due to the incorporation of barium sulphate inside chitosan microspheres.
- Radiopacity studies

Figure 3.17 shows the X-ray photographs of chitosan formate microspheres containing barium sulphate. Due to the incorporation of barium sulphate the electron density of chitosan formate increases and it shows intense X-ray images as in the case of chitosan/barium sulphate microspheres.

![X-ray photograph of chitosan formate microspheres containing barium sulphate](image)

Figure 3.17: X-ray photograph of chitosan formate microspheres containing barium sulphate (filled in polyethylene tube)

3.3.3.2 Studies on chitosan acetate

- IR spectroscopy

Figure 3.18 shows the IR spectrum of chitosan acetate.
The spectrum exhibits characteristic peaks at 2970 cm\(^{-1}\) and 1380 cm\(^{-1}\) due to the protonated amine stretch and deformation vibrations. The peak at 1556 cm\(^{-1}\) indicates the presence of –COO\(^{-}\) due to the interaction between the chitosan chain and acetic acid. A peak at 1650 cm\(^{-1}\) indicates the presence of an amide band. The peak around 1400 cm\(^{-1}\) indicates that the symmetric stretching vibrations of carboxylate anion present and it confirms the formation of chitosan acetate.

- SEM Analysis

The SEM micrograph of the chitosan acetate microspheres are shown in figure 3.19. It is clear from the figure that the microspheres obtained from chitosan acetate do not exhibit good spherical geometry and surface smoothness. This may be due to the presence of bulky acetate group in chitosan, which will affects the
cross linking reaction. Hence further radiopacity studies are not carried in chitosan acetate.

Figure 3.19: SEM photograph of chitosan acetate/barium sulphate microspheres

3.3.3.3 Studies on carboxy methyl chitosan

- IR spectroscopy

The infrared spectroscopy of carboxy methyl chitosan is shown in figure 3.20. A broad peak in the range 3360 cm\(^{-1}\) is assigned to an -OH stretching, indicating inter molecular H-bonding. The spectrum also overlapped in the near by region of a -NH stretching (i.e at 2900 cm\(^{-1}\)). NH\(_2\) deformation peaks are observed at 1580 cm\(^{-1}\) and around 1300 cm\(^{-1}\). The peak at 1416 cm\(^{-1}\) indicates the symmetric
stretching vibrations of carboxylate anion, which confirms the formation of carboxy methyl chitosan.

![IR Spectrum of carboxy methyl chitosan](image)

Since the carboxy methyl chitosan does not give spherical microspheres, a blend of carboxy methyl chitosan/PVA is used for further studies.

### 3.3.3.4 Studies on CMC/PVA blend

- **SEM Analysis**

SEM micrographs of carboxy methyl chitosan/PVA blend microspheres with barium sulphate is shown in figure 3.18 (a and b). The figure shows that the blend gives free flowing, smooth spheres as in the case of chitosan.
Figure 3.21 a: Scanning electron micrographs of radiopaque microspheres of Carboxy methyl chitosan /PVA blend

Figure 3.21 b: Scanning electron micrographs of single microsphere of Carboxy methyl chitosan /PVA blend
• XRD studies

The polymer crystallinity increased after cross linking and due to the incorporation of barium sulphate inside the microspheres of CMC/PVA blend, as shown in the figure 3.22. The broad peak at $2\theta = 20^\circ$ obtained is changed to sharp narrow peaks in CMC/PVA/BS.

![XRD patterns of blend of CMC/PVA and BaSO₄](image)

**Figure 3.22** XRD patterns of blend of CMC/PVA and BaSO₄ encapsulated CMC/PVA microspheres

• Radiopacity studies

X-ray photographs of the blend of CMC/PVA microspheres is shown in figure 3.23. The blend of CMC/PVA contains carbon, hydrogen, oxygen and nitrogen
and is radiolucent in nature as in the case of chitosan. By the incorporation of barium sulphate its electron density increases and it becomes radiopaque. The microspheres show intense radiopacity due to the presence of barium sulphate inside these spheres.

Figure 3.23: X-ray photograph of CMC/PVA microspheres containing barium sulphate (filled in polyethylene tube)
3.4 CONCLUSIONS

- Chitosan microspheres can be prepared by the *in situ* cross linking reaction with glutaraldehyde.

- Liquid paraffin / sorbitan sesqueoleate emulsion system gives perfect spherical chitosan microspheres.

- Radiopacity is imparted on chitosan microspheres by the incorporation of barium sulphate.

- Excellent radiopaque microspheres of chitosan/PVA/BS blend is prepared using liquid paraffin/sorbitan sesqueoleate system.

- Chitosan derivatives like chitosan formate, chitosan acetate, carboxy methyl chitosan have been prepared.

- Chitosan formate and blend of CMC/PVA is found to give microspheres with perfect spherical geometry using liquid paraffin/sorbitan sesqueoleate system.

- Chitosan formate/BS, CMC/PVA/BS microspheres prepared from liquid paraffin/sorbitan sesqueoleate system show intense radiopacity.
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Radiopaque chitosan microspheres

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