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Nanosization of Drug Biomaterials and Its Solubility Enhancement by High Energy Ball Milling

S. Thamizharasan*, N. Anbu Saravanan

PG and Research Department of Zoology, Periyar E.V.R College (Affiliated with Bharathidasan University), Thiruchirappalli – 620 023, Tamilnadu, India.

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ABSTRACT

To evaluate the solubility enhancement of plant derived drugs in the form of nanosized biomaterials. Nanosization obtained from biomaterial sample of marine macro alga *Padina gymnosphora*, using high energy ball milling technique and structural characteristic studies of biomaterials were evaluated using FE-SEM microscope. Solubility enhancement study on both biomaterials were tested using deionized double distilled water. FE-SEM microscopic study showed the particle size differentiation in the ordinary crude biomaterial and nanosized biomaterial. Water solubility studies proved the quick soluble and polydispersibility behaviour of nanosized biomaterial. The solubility enhancement properties of nanosized biomaterials indicated that, when the grain or particle size is reduced, the solubility is enhanced.

1. Introduction

According to the World Health Organization, most populations still rely on traditional medicines for their psychological and physical health requirements. People living in rural areas from their personal experience know that these traditional remedies are valuable source of natural products to maintain human health, but they may not understand the science behind these medicines, but knew that some medicinal plants as herbal medicines are highly effective only when used at therapeutic doses [1-3]. Herbal medicines in the form of biomaterials are in great demand in both developed and developing countries. Plants produce a diverse range of biomaterials consists of potent bioactive molecules [4,5]. They making them rich source of different types of medicines. Most of the drugs today are obtained from natural sources or semi synthetic derivatives of natural products and used in the traditional systems of medicine [6-8]. Most of the herbal drug the challenging problems in formulating the drugs are mainly due to the poor solubility is associated to poor dissolution characteristics and thus to poor oral bioavailability [9,10]. It is because of the reason of bulk grain size of biomaterials. Due to the bigger grain size the biomaterial based pharmaceutical drugs could not well soluble [11, 12]. Most of the biomaterial incorporated drugs have the properties such as poor solubility, low dispersible nature and poor bioavailability [13]. Hence, the main aim of this study was to produce plant drugs in the form of nanosized biomaterials by a high energy ball milling technique. It is a novel technique for improving biomaterial based drug and enhancement of its solubility [14, 15].

2. Experimental Methods

2.1 Sample Biomaterial

Marine algae *Padina gymnosphora* are the excellent source of bioactive compounds such as carotenoids, dietary fiber, protein, essential fatty acids, vitamins and minerals. This algae have the antimicrobial, antiviral and antifungal activity. It is used in biopharmaceutical industries to produce antimicrobial drugs. In order to enhance the drug characteristics, formulation of bioactive materials of *Padina gymnosphora* in nanomaterial form using High Energy Ball Milling as a novel Nanocrystallization technology.

2.2 Sample Collection

Marine algae *Padina gymnosphora* sample was collected from the sea coast of Rameshwaram, Tamil Nadu, India. Samples were cleaned, epiphytes and necrotic parts were removed. Samples were rinsed with sterile water to remove any associated debris. Sample was kept under sunshade for 7 days. After drying the sample, it was ground thoroughly to powder form using manual mill Shimadzu Blender [16]. After the removal of fibrous and unwanted coarse particle, 100 g of crude biomaterial powder was taken for the nanosization of the biomaterial using high energy ball milling.

2.3 High Energy Ball Milling

The crude powder form of biomaterials (w/w) weighed 100 g was milled in steel cells (250 mL) using hardened steel balls (diameter 15 mm, weight 32 g) in ambient atmosphere for constant time of 15 hours (Retsch, PM 400). The milled materials were used directly without any added milling media. Five balls were kept in each cell along with 100 g of the sample powder. Two parallel cells were used in this experiment (the total weight of the sample powder was 20 g). The synthesized biomaterials were characterized and the morphology of the powders was analyzed using a field emission scanning electron microscope (FESEM), JSM-7500 F (JEOL-Japan) operated at 10 KV, in the Centre for Nanoscience and Technology, Bharathiar University, Coimbatore, Tamilnadu, India.

2.4 Experimental Design

To find out the highly potent water solubility of biomaterials (drugs), synthesized from the marine macro algae *Padina gymnosphora*, we have taken two types of algal biomaterial in the form of powder, 1. Crude biomaterial produced by manual mill Shimadzu Blender and 2. Nanosized biomaterial using high energy ball milling. Both the two powder samples were tested to observe the solubility.

3. Results and Discussion

3.1 Structural Studies

Fig. 1(A) shows FESEM micrograph image of the starting biomaterial sample before ball milling process. This sample contains particles covering the range 12–30 μm of different sizes/shapes. Around 70% of these particles are large and irregular shape. The ordinary powder form (crude biomaterial) produced by ordinary manual mill Shimadzu Blender may lead to formation of large irregular size and shape. Fig. 1(B) indicates FE-SEM micrograph image of the biomaterial sample milled for about 15 hours by High Energy Ball milling device. The images of the biomaterial

*Corresponding Author

Email Address: thamizhmsc25@gmail.com (S. Thamizharasan)

sample milled for 15 hours, show particles of nano size, almost all particles are semi spherical shaped nanoparticles. The particle size distributions for the sample with more collected particles have an average diameter of approximately 90 to 140 nm.

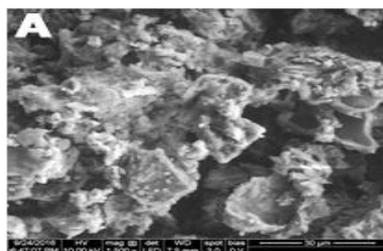


Fig. 1(A) FE-SEM image of the ordinary crude biomaterial prepared by manual mill Shimadzu Blender

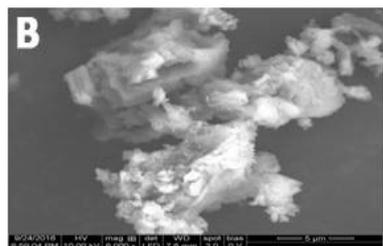


Fig. 1(B) FE-SEM image of the nanosized biomaterial prepared by High Energy Ball Milling

3.2 Solubility Enhancement Studies

The water solubility or aqueous solubility of crude algal biomaterial of the particles size (12–30 μm) and High energy ball milled algal biomaterial of the particle size (90 to 140 nm) shows differentiation. The crude biomaterial sample added into Deionized double distilled water partially soluble and partially dispersible and a lot of green depositions appeared in the solution. The solution shows acidic pH value 5.0.



Fig. 2(A) solubility of crude biomaterial (B) solubility of nanosized biomaterial

While in the nanosized sample, the particle solubility rate and dispersion efficiency is very high. The nanosized sample was quickly soluble in water and the pH value reached as 6.5 to 7.0. Further it was observed in the solution indicated mild brownish colour with uniform solubility and dispersibility properties.

High energy ball milling is a powerful non-equilibrium processing method capable of producing dispersion strengthened materials and alloys with fine microstructures as well as metastable nanostructured materials [17]. The milling process, which can be either mechanical milling or mechanical alloying, refines the grain size of all solid elements of materials into nanoscale [18].

During the ball milling process, algal biomaterials are repeatedly fractured, and nanosized. Fracture and nanosize are the two basic factors that produce a permanent ionic exchange between particles. Ball milling technology leads to an increase in dissolution rate depending on the increase in surface area obtained by reduction of the particle size of the active drug substance down to the nano size range preserving the crystal morphology of the drug biomaterial [19, 20]. A number of researchers have produced nanosized materials using the same technology [21, 22].

This technology leads to an increase in dissolution rate depending on the increase in surface area obtained by reduction of the particle size of the active drug substance down to the nano size range preserving the crystal morphology of the drug [23,24]. The milling process, which can be either mechanical milling or mechanical alloying, refines the grain size of all solid elements of materials into nanoscale [25, 26]. The minimum grain size can be obtained by a balance between the defect introduced by plastic deformation of milling and its recovery by thermal cases. The orientation

of the grain becomes random. The high angle grain boundaries replace the low angle grain boundaries by boundary rotation or sliding. Finally, the grain boundaries near the sample edge are broken and single crystals nanoparticles are peeled off the edge of the samples [27]. The main advantages of ball milling include large scale production of high purity nanoparticles with improved physical properties in a cost effective way [28, 29]. The ball milling treatments can also bring new properties to the matter depending on the grain size and materials composition [30]. In our investigation, the ball milling operation may lead to formation of nanosized particles. The ordinary blender produced microsized particles which is larger than the nano particle. This result clearly presents that the ball mills are more effective to reduce size, which ultimately increase the accessibility of particle size to biomaterials and easy solubility. Most differentiating features of drug nanocrystals are the increased saturation solubility and the accelerated dissolution velocity.

The main advantages of ball milling include large scale production of high purity nanoparticles with improved physical properties. In a cost effective way [31, 32]. The ball milling treatments can also bring new properties to the matter depending on the grain size and biomaterials composition including its solubility.

4. Conclusion

The present study proves remarkable experimental results on algal biomaterial using high energy ball milling processes for the controlled synthesis of drug nanoparticles found in the algal biomaterial were described. The ball milling process are successfully produced the nanoparticles in biomaterial with high solubilization capacity. The size reduction of algal biomaterial to nanometer levels (from 60–120 nm) has been achieved by this method on 15 hrs. This technology helpful to an increase in dissolution rate of drug biomaterial depending on the increase in surface area obtained by reduction of the particle size of the active drug substance down to the nanosize. Ball milling technology can be used to formulate and improve drugs and its compounds activity and enhance the solubility of the poorly water-soluble compounds.

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