Nanoencapsulation of ethylvanillin using Electrohydrodynamic technology

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Abstract. An electrohydrodynamic method for preparation of ethylvanillin-loaded polymer-lipid-based nanoparticles. Various parameters of electrohydrodynamic are optimized for generating ethylvanillin-loaded nanoparticles by controllable electrohydrodynamic parameters. Ethylvanillin-loaded polymer-lipid-based nanoparticles with mean diameters of around 64-90nm with encapsulation efficiency in the range 67-71% are generated with all the flow rate from 10 to 25µl/min, the stearic acid-ethylcellulose-ethylvanillin concentration ratio of 4:1:1.6 wt%, and ethylvanillin content of 0.16%. The size of the ethylvanillin-loaded polymer-lipid-based nanoparticles production is examined using scanning electron microscopy.

1. Introduction
Currently, the food industry is confronted with the challenges of developing and applying novel technology that can generate high-quality and healthy foods. Meeting these complex engineering and scientific challenges, novel technologies are instigated for developing new processes, products, and tools in this industry. Encapsulation of active ingredient (flavor) in different polymer compositions and sizes include in ranging from micro to nano-size is widely used in many industries like; pharmaceutical, food, and agriculture [1, 2]. The key benefit of encapsulation includes; coating, the barrier between the chemically, environmentally unstable active ingredient and environmental factors like light, O₂ and humidity, etc [3]. It also allows to control the release of active ingredients for delayed or prolong release [4-8]. Further, it can be used to convert liquid active ingredients into a solid (dry) system [9, 10]. The electrohydrodynamic study is a physical process result by the applied voltage force to the material solution or suspension, then the solution formed at the outlet of a tube, form a different mode of the jet (i.e. droplet, microdroplet, cone jet, multi con-jet) [11]. Electrohydrodynamic can be successfully used to produce solid lipid nanoparticles to encapsulate and deliver active compounds. The electrohydrodynamic spraying technique is inexpensive, flexible, simple, and single-step technology [12]. Therefore, it can encapsulate active ingredients in polymeric matrices. The work aimed to prepare solid lipid nanoparticles of ethyl vanillin using the single jet electrohydrodynamic technology. The polymers used to encapsulate ethylvanillin are ethylcellulose and stearic acid. Further optimization of ethylcellulose and stearic acid was also conducted to furnish minimum size particles with monodispersity and uniform size.
2. Materials and methods

2.1. Materials
All solvent and reagents were used as received without further purification. The reagents used are ethylvanillin, ethylcellulose, and stearic acid in powder form, and (95%) ethanol. All the tests were repeated five times.

2.2. Preparation and characterization of ethylvanillin-loaded polymer-lipid-based nanoparticles solution
Stearic acid and ethylcellulose were first dissolved in ethanol in different concentrations (10–50 mg/ml) and a magnetic stirrer was used to dissolve polymers until a clear solution was obtained. Ethylvanillin in various concentrations was also dispersed in the polymeric solution. The concentration of ethylvanillin was varied in the range of 0 to 5 mg/ml, to prepare particles with a maximum loading of ethylvanillin in terms of weight. The physical properties of the spraying solution were determined.

2.3. Preparation of ethylvanillin-loaded polymer-lipid based nanoparticle
Figure 1 Illustration of electrohydrodynamic spraying setup, used to prepare ethylvanillin-loaded polymer-lipid-based nanoparticle. Spraying solutions (ethylvanillin-loaded polymer-lipid-based nanoparticle) were pumped out, using a mechanical syringe pump from a metal needle (inner diameters of the needle were 450 μm). The spraying solution formed a compound drop under the exit of the needle. The products were collected on a petri-dish containing double distilled water. A camera was used to observed the behavior of spraying solution at the outlet of the needle.

3. Results and Discussion
Spraying is a widely applied encapsulation process in the food industry being flexible and involving less commercial operational cost. This study focuses on the preparation of polymer-lipid-based nanoparticles for the encapsulation of ethylvanillin using electrohydrodynamic technology. Electrohydrodynamic parameters can be controlled with optimization of applied voltage, flow rate. The electrohydrodynamic factors (i.e. applied voltage, flow rate) may influence the polymer-lipid-based nanoparticle encapsulation system and the study also discusses these factors. In this study, the nanoparticles were tremendously affected by varying the composition of ethylvanillin, stearic acid, and ethylcellulose. The effect of stearic acid and ethylcellulose ratio on the ethylvanillin-loaded polymer-lipid-based nanoparticle size was studied by changing the ratio of the stearic acid, and ethylcellulose ratio C from (0- 5% w/v). Figure 1 shows the electrohydrodynamic spraying setup, used to produce ethylvanillin-loaded polymer-lipid-based nanoparticles. Polymer-lipid-based nanoparticle solution with four different concentrations (stearic acid, and ethylcellulose w/w%), were sprayed using electrohydrodynamic spraying (Figure 1) technique. These particles produced by cone-jet are mono-dispersed.
The investigation of the relationship between electric voltage and polymeric concentration is shown in Figure 2. Initially, the voltage from 1 to 20kV was applied in small increments until a cone jet was shaped around (10 - 14kV) for concentrations C and D (i.e. 3:2 and 4:1). A stable cone jet can be obtained when the flow rate was 10µl/minute. The multi-jet mode was detected above 14kV for the entire concentrations and the dripping and micro dripping mode for less than 10kV. Ethyl vanillin concentrations (1.2, 1.6, 2.5, and 5 w/w%) were added to the selected spraying solution of stearic acid, and ethylcellulose (4:1 w/w%), which was optimized previously to furnish nano-size and uniform particles. Varying voltages (1-20kV) and varying flow rate (10 - 25µl/min) were applied to obtain the stable cone-jet particle [13]. It was found that ethanol was evaporated quickly during the spraying from the metal needle to the grounded collector. The ethylvanillin-loaded polymer-lipid-based nanoparticle acquired structure (Figure 4) is influenced by the evaporation of ethanol from the ethylvanillin-loaded polymer-lipid-based nanoparticle droplet [14].
Experimental results show that the applied electric voltage and flow rate of the sprayed solution can control the size of the produced ethylvanillin-loaded polymer-lipid-based nanoparticle using an electrohydrodynamic setup. Figure 4 shows that ethylvanillin-loaded polymer-lipid-based nanoparticles of various diameter sizes were produced at varying voltage. It is indicated from Figure 4 that different size particles were produced at a different flow rate. This indicates that flow rate has a tremendous effect not only in terms of generating cone-jet but also different size particles. It also confirms that at a lower flow rate small/nanoparticles were generated. However, at a high flow rate comparatively bigger sizes were obtained.

**Figure 4.** SEM images of ethylvanillin-loaded polymer-lipid-based nanoparticle prepared at 4:1:1.6 concentration of stearic acid, ethylcellulose, and ethyl vanillin, under varying flow rates (10, 15, and 20µl/min) and applied voltage set at cone-jet only (8 - 14kV), and multi cone-jet 16 and 19kV.

Ethanol evaporation rate from the formed ethylvanillin-loaded polymer-lipid-based nanoparticle droplet significantly affects the ethylvanillin-loaded polymer-lipid-based nanoparticle structures. Fast evaporation of the solvent causes cavities inside particles as seen in the ethylvanillin-loaded polymer-lipid-based nanoparticle. UV spectroscopic analysis of nanoparticles shown the entrapment efficiency of optimized ethylvanillin-loaded polymer-lipid-based nanoparticles was as high as possible. These values indicate that the electrohydrodynamic technique was able to generate ethylvanillin loaded into polymer-lipid-based nanoparticles with entrapment efficiencies range between 67 – 71%. The loss of ethylvanillin during the electrohydrodynamic technique was calculated with ethylvanillin-loaded polymer-lipid-based nanoparticles, being in total 30±3% losses. The loss was generally a result of scattering of the ethylvanillin-loaded polymer-lipid-based nanoparticle nanoparticles to the connection tube walls, collector, and during the electrospraying [15].

**4. Conclusions**

This study has demonstrated that solid lipid nanoparticles entrapping flavor can be generated by simple single needle electrohydrodynamic. Based on the findings of this study the diameter of the solid lipid nanoparticles could be controlled by adjusting the ethylvanillin-stearic acid-ethylcellulose concentration
and electrohydrodynamic processing parameters. The nanoparticles were found to have a homogenous structure, with the diameter being dependent upon electrohydrodynamic processing parameters and the concentration of ethylvanillin-stearic acid-ethylcellulose in the electrosprayed solution. The entrapment efficiency was similarly found to be dependent on the ethylvanillin-stearic acid-ethylcellulose concentration ratio. The entrapment efficiency of ethylvanillin into the nanoparticles in the range of 67-71%. The properties of the ethylvanillin remained physically unchanged during the process. The electrohydrodynamic process for the production of stearic acid-ethylcellulose nanoparticles may be a suitable form for the manufacture of stearic acid and ethylcellulose nanoparticles.

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