

# Production of Unsaturated Fatty Acids Concentrate Tablets from *Sardinella* sp. Oil

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**Abstract.** Tablets are medicinal ingredients in solid dosage forms which are usually prepared with suitable pharmaceutical ingredients. In this study, unsaturated fatty acids concentrate from *Sardinella* sp. oil was used as raw material and then it was microencapsulated. The microcapsule was formulated into a tablet with proportion of 250 mg concentrated unsaturated fatty acids for each 450 mg tablet. Tablet granules were analyzed for compressibility, flow rate, and fixed angle. While, the tablets were determined for weight uniformity, released time, hardness, and tablet size uniformity. The results showed that compressibility, flow rate and fixed angle of the tablet granules were 5.6%; 10.36 g/sec; and 32.4° respectively. Tablets had 447.85 mg weight uniformity; 48'12" released time; and 0.775 kg hardness. In addition, the tablet size uniformity with diameter 10 mm and thickness 4 mm was 2.5. Based on the pharmacopoeia, the tablets of unsaturated fatty acids concentrate from *Sardinella* sp. oil had met these requirements, but optimization was still needed for improving the released time and hardness of the tablet.

## 1 Introduction

Tablets are medicinal ingredients in solid dosage forms which are usually prepared by addition of suitable pharmaceutical additives. Tablets may vary in size, shape, weight, hardness, thickness, crushing, and other aspects depending on how tablets are used and what method is applied for manufacturing. Based on the method of manufacture, tablet can be classified into molding tablet and compressed tablet. Molding tablets are made by pressing the mass of damp powder with low pressure into the mold. Compression tablets are made by employing high pressure on the powder or granule using a steel mold (stainless) [1, 2].

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Keeping a healthy body, the tablets as a dietary supplement enriched with fish oil are currently being developed. Fish are especially rich in the beneficial oils known as the source of unsaturated fatty acids. Those fish include mackerel, herring, tuna, salmon, cod liver, whale blubber, and seal blubber. The most important of unsaturated fatty acids is omega-3 fatty acids ( $\alpha$ -linolenic, eicosapentaenoate/ EPA, and docosahexaenoate/ DHA) and omega-6 (linoleic acid) [1].

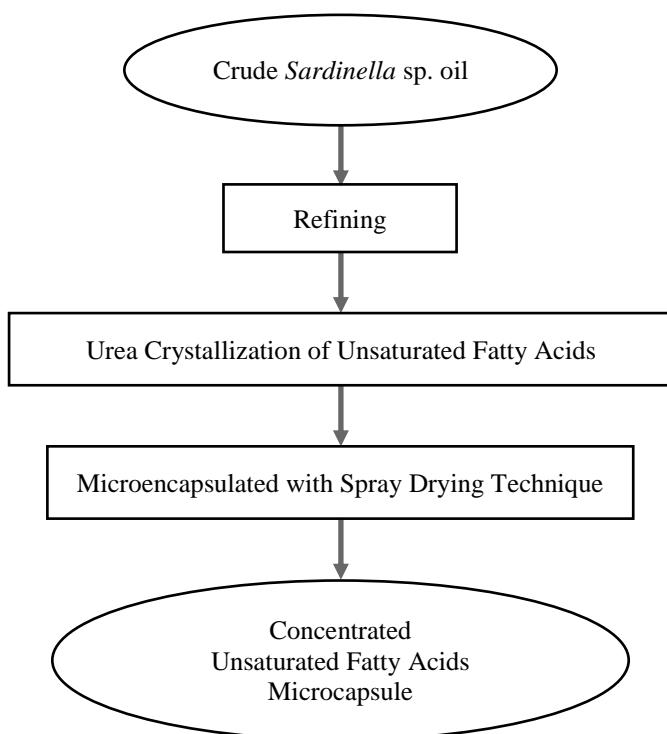
Fish oil is usually sold in soft capsules in the market. And in Indonesia there are only a few industries that produce them. Therefore many products in the market are imported directly from outside in ready-made soft capsules. This causes the label halal for using of soft shells is still often debated. Soft capsules are also usually used for liquid ingredients. If fish oil containing unsaturated fatty acids is marketed in liquid also has the problem of being easily oxidized thereby shortening the shelf life. This research was conducted with the aim of producing omega 3 concentrated tablets from fish oil *Sardinella* sp. to overcome the problems above [1].

## 2 Materials and methods

Raw material used in this study was the microcapsule of unsaturated fatty acids concentrate from *Sardinella* oil. Other ingredients were primojel (DFE Pharma) as disintegrant, Magnesium stearate (MgSt) (Sigma-Aldrich) as lubricant, polyvinyl pyrrolidone (PVP) (Merck Millipore) as binder, talc powder (Merck) as gelidant, aerosol as absorbent, butylated hydroxytoluene (BHT) (Sigma-Aldrich) as antioxidant, crystalline vanilla (Fluka), and lactose (Sigma-Aldrich) as filler.

Figure 1 shows the step for producing the concentrated unsaturated fatty acids into a microcapsule form. Crude fish oil was refined using the method of Hastarini [3], further processed into unsaturated fatty acid concentrated according to the method Hoiriyah et al. [4] with modification. The unsaturated fatty acid concentrated are microencapsulated using spray drying techniques with an inlet temperature of 180°C, an outlet temperature of 100°C, and a flow rate of 10 mL/ min [5] to obtain an unsaturated fatty acids concentrate microcapsule.

The concentrated unsaturated fatty acids in microcapsule was processed into a tablet with proportion of 250 mg concentrated unsaturated fatty acids microcapsule/ 450 mg capsule [2]. Tablets formulation was produced containing primojel, Mg stearat, PVP, talc powder, aerosol, BHT, crystalline vanila, and lactose [1, 2, 6]. Each concentration could be seen in Table 1. The tablet was prepared using tablet-making unit at *Lembaga Farmasi Angkatan Laut* (LAFIAL) Jakarta in October 2017. The tablets was made three replications and each as many as 25 tablets. The process involved in testing of the tablets such as compressibility, flow rate, fixed angle, weight uniformity, released time, hardness, and size uniformity [2]. Each test was carried out with three replications.



**Fig. 1.** Production of concentrated unsaturated fatty acids microcapsule form

**Table 1.** Formula of tablet made from unsaturated fatty acids concentrate 450 mg

No	Material	Concentration (%)
1	Concentrated unsaturated fatty acids	55.55
2	Primojel	2.00
3	Mg stearat	1.78
4	PVP	10.00
5	Talc powder	4.44
6	Aerosol	1.00
7	BHT	0.02
8	Crystalline vanilla	QS
9	Lactose	Ad to 450 mg

### 3 Results and discussion

Characteristics of tablet granules obtained in this study are exhibited in Table 2. The tablet granules had 5.6% compressibility, 10.36 g/s flow rate and 32.4° fixed angle. Comparing with Indonesian Pharmacopoeia [2], compressibility, and flow rate values of the tablet were classified as very good. In addition, the fixed angle value of the tablet granules produced in this study was categorized as good.

**Table 2.** Compressibility, flow rate, and fixed angle of tablet granules made of concentrated unsaturated fatty acids

Requirements [2]	Result	Information
Compressibility (5-15%)	5.6%	Very good
Flow rate (>10 g/s)	10.36 g/s	Very good
Fixed angle (Good: 31-36°)	32.4°	Good

Good compressibility is likely a consequence of lower bulk density and addition of filler increases density and decreases initial porosity/ volume of specific tablets [7]. Compressibility is influenced by flow rate of a tablet powder mixture. And one factor that affects compressibility is the use of filler-binders [8]. This research used two types of filler-binder such as PVP and lactose. PVP provides sufficient cohesive force on the powder between the excipient particles so as to create a compact and strong tablet structure after molding. PVP produces tablets that are not hard but slightly hygroscopic [8]. Whereas lactose has good flow and compressibility and low price [9] and it does not react with almost all medicinal ingredients [10].

Table 3 informs the result of the analyses of tablet for weight uniformity, released time, hardness, and size uniformity. The tablet was qualified for weight uniformity and size uniformity. The weight uniformity value was 447.85 mg. While the size uniformity of the tablet having 10 mm diameter and 4 mm thick was 2.5. However, other parameters, i.e. released time and hardness, were classified as not eligible, in which the values were 10.36 /s and 0.775 kg respectively.

**Table 3.** Weight uniformity, released time, hardness, and size uniformity of tablet made from concentrated unsaturated fatty acids

Requirements	Result	Information
Weight uniformity (427.5 – 472.5) mg	447.85 mg	Qualify
Released time (≤ 15 minutes)	48' 12"	Ineligible
Hardness (4 – 8) kg	0.775 kg	Ineligible
Tablet size uniformity: unless otherwise stated, diameter of tablets shouldn't be more than 3X and not less from 1 1/3 thick of tablet	Diameter (d) = 10 mm Thick (T) = 4 mm d/T = 2.5	Qualify



**Fig. 2.** Concentrated unsaturated fatty acids *Sardinella* sp. oil tablets

The weight uniformity can be determined to ensure an indication of dose uniformity of the active substance given and uniform distribution of active substances at the tablet time moulding so that it would have the same therapeutic effect [2]. The weight uniformity is influenced by the rate flow of powder/ granule used, the better of flow the powder properties then when filling the powder into the *hooper* on the tablet machine, it can flow constantly so that the weight is any uniform. Tablets are usually formulated with the ingredients that cause they dissolve easily [11].

Released time was important if the tablet was given by mouth, except tablets that had to be chewed before swallowing and some types of tablets are released slowly and delayed. The released time is closely related to bioavailability of the drug, the faster of tablet release time then the active substance will be easily released so that availability biological medicine will increase. Release time is in relation with the disintegrant material used in addition to the properties of other materials also greatly affect the results of release time [12]. This research used primojel as a disintegrant material with concentration 2%. Primojel could cause the tablet released time to be ineligible. A water soluble fillers in the tablet (lactose) will take longer to release and it reduces the effectiveness of primojel caused by increased viscosity of penetration fluid and expand the tablet pore [13].

The tablet hardness is influenced by several things, such as the compression pressure at the time moulding tablets, tablet material properties, the amount of mass that is loaded in the tablet moulding plat and density of the tablets mass while the diameter of tablet can be influenced by size tablet moulding plat. The greater the pressure given when press will increase tablet hardness. Hardness of tablet tightly relation to the process of disintegration and dissolution can affect the release of active substances and bioavailability of the active substance [14, 15]. Tablet must have enough hardness which is in accordance to the requirements, so therapeutic effects given by the drug preparation is as expected. The strength or certain hardness in order to survive in various mechanical shocks at the time manufacture, packing, and shipping. Sufficient hardness from a tablet was one of the important requirements of a tablet. Generally tablets are very good hardness, if it has between 4-8 kg [16].

Based on the above results, the concentrated omega 3 powder could actually be used as raw material for the production of tablet, even though not all quality parameters stated in Indonesia pharmacopoeia can be met. Mostly unsaturated fatty acids products found in the market were as soft capsule. Therefore, development of concentrated unsaturated fatty acids tablets as a new product should be continued until better quality tablet conforming to Indonesia pharmacopoeia for all parameters obtained [17].

## 4 Conclusion

The concentrated unsaturated fatty acids tablets obtained from this study has met the requirements. However, improvements are still needed, particularly to upgrade in terms of released time and hardness parameters.

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