Particle Size Distribution & Zeta Potential of Solid- Lipid Nanoparticles Emulsion

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Abstract- ***Solid lipid nanoparticles are at the forefront of the quickly expanding field of nanotechnology because of their numerous potentials uses in clinical treatment, research, drug delivery, and other diverse fields. The distinct size-dependent characteristics of solid-lipid nanoparticles present an opportunity to create novel therapies. This experiment was carried out to determine the particle size distribution and the zeta potential of two type of emulsion made using 1g of SLN particles (Ibuprofen/Tristearin/Poloxamer 40) at a ratio 10/20/70. The samples were made into an emulsion measuring 1g of SLN using Ibuprofen/ Tristearin/Poloxamer 407 in the ratio of 10/20/70 by homogenising using an Ultra Turraz K25 Homogeniser at 15,000rpm for 3mins and the other sample using an Ultrasonic Processor at 100% amplitude of 7watts for 1min. Emulsion made using the ultrasonic processor had a better zeta potential of -0.0036v, poly dispersity index of 28.5% and a hydrodynamic DM of 1.2600µm, which means a better stable emulsion as compared to sample made with ultra-homogeniser having a zeta potential of - 0.0008v, poly dispersity index (PDI) of 56% and a hydrodynamic DM of 22.996µm.***

Indexed Terms- ***Solid-lipid nanoparticles, Zeta-potentials, emulsions, Particle size distribution***

I. INTRODUCTION

Materials now range in particle size from the micro- to nano-scale due to technological advancements over the past 20 years. Materials' total surface area increases by several orders of magnitude when their particle size is reduced at the nanoscale. (1)

Nanoparticles are defined as colloidal particles that fall between 1nm to 1000nm in size. Nanoparticles have a lot of applications. (Figure 1) However, in biomedical applications, it is believed that the best drug delivery systems are made of nanomaterials with better biodegradability and biocompatibility. (1)
A successful strategy for treating chronic human diseases is the use of nanoparticular drug delivery systems, which also serve well in meeting pharmacological and biopharmaceutical requirements. As a result of the development of nanotechnology and the expanding capabilities of combinatorial chemistry, functional proteomics, genomics, and bioinformatics, scientists are now more eager to use their technical knowledge to find, develop, and investigate novel approaches for drug delivery systems using fresh methods. Since the therapeutic efficacy of medications is dependent on their pharmacokinetics and site of administration, novel drug delivery methods continue to be the cornerstone for delivering medications with difficulties that traditional drug delivery systems are unable to minimise. Physical-chemical characteristics like solubility, crystallinity, toxicity, and HLB value are also the foundation of pharmacokinetics.

All the aforementioned factors are significant obstacles since the formulation design significantly affects the active pharmaceutical ingredient's (API) efficient distribution. Hydrophilic and lipophilic molecules are the two kinds of drugs according to the HLB scale. (2)

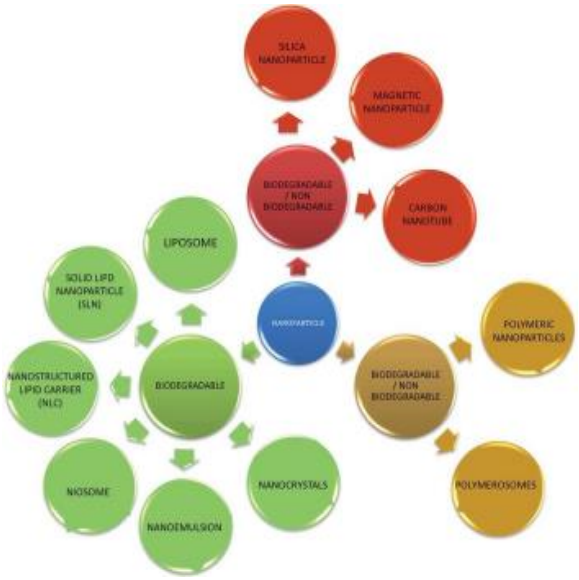

Figure 1: Different types of nanoparticles application (2)

Lipophilic molecule delivery has been the focus of novel medication delivery methods because they rely on lipids. However, lipid-based drug delivery systems have gained attention recently because of their intrinsic qualities, which include biocompatibility, self-assembly capabilities, particle size variability, blood-brain barrier bridging capability, and economic efficiency. Lipid based delivery systems are substantially more enticing because of these features. In Chart 1, lipid-based nanoparticles can also be divided into the following subcategories. (2)

A good nanoparticle drug delivery system should possess the following features:

- Targeting of tissues.
- Controlled release kinetics.
- Maximum drug bioavailability.
- Reduced immune response.
- Most be able to deliver traditional harsh medicines, including biomolecules, amphiphiles, and lipophiles.
- Sufficient ability for medication loading.
- Outstanding adherence from patients.

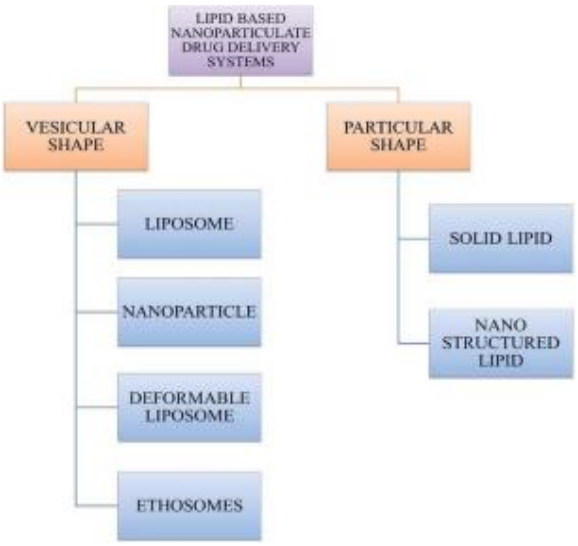

Chart 1: Classification of lipid-based nanoparticle drug delivery systems. (2)

Solid lipid nanoparticles are usually in sphere shapes and have a diameter of 50–1000 nm. Lipids (which are solid at room temperature), emulsifiers (or sometimes a combination of both), active pharmaceutical ingredients (APIs), and a suitable solvent system are the main components of SLN formulations.

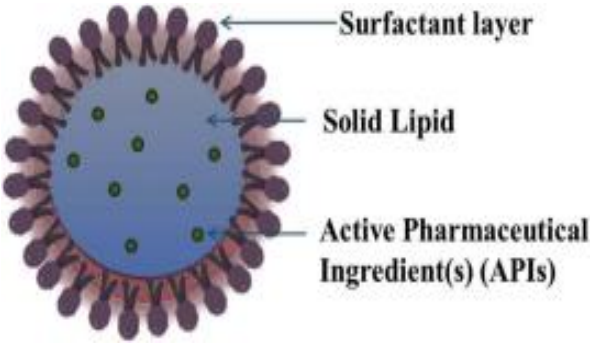

Figure 2: Solid lipid nanoparticle (SLN) structure (2)

Drug delivery has undergone a radical change thanks to solid lipid nanoparticles, which combine the greatest aspects of liposomes, polymeric nanoparticles, and microemulsion. Through surface modification, increased pharmacokinetic acceptability, formation of inclusion complexes, improved stability pattern, and integration of chemotherapeutic medications, solid-lipid nanoparticles have all their characteristics improved. (3).

Nanomaterials have become more popular as drugs in recent years. carriers. Liposomes are crucial biological components that have been in use for a long time, however there are now several different compounds. Niosomes are one of the promising cost-effective substitutes for liposomes.

By fusing the best features of liposomes, microemulsion, and polymeric nanoparticles, solid lipid nanoparticles have revolutionised medication delivery. (3)

SLN are safe nanotechnology-based drug delivery systems because they are made of physiologically biocompatible and biodegradable lipids and other generally recognised as safe (GRAS) materials. The drugs included in SLNs can be protected by the solid matrices, effectively enhancing the drug stability. SLNs have a higher entrapment efficiency than liposomes for both hydrophilic and hydrophobic drugs. (4)

This research was done to help understand how to evaluate the stability of a SLN based emulsion to ensure the stability of the drug actives embedded into the core structure of the SLN.

II. MATERIALS AND METHODS

Materials used: Measuring cylinder, 100ml beakers, 250ml beaker, hot plate, Ultra Turraz K25 Homogeniser, syringes, spatula, Ultrasonic Hielscher UP 200HT processor, Antor Paar Litesizer DLS 701.
Chemicals used: Poloxamer 407, Tristearin, Ibuprofen.

Method:
• A beaker containing 50 ml of water was heated to 70ºC on a hot plate.
• A beaker was filled with 1g of SLN components (Ibuprofen, Tristearin, and Poloxamer 407), measured at a ratio of 10/20/70. When the water heats up to 65ºC, the SLN components are heated to the point where the sample melts and achieves the lipid's melting point, which is 70ºC.
• The sample container with the molten lipid was poured into the hot water with the aid of a spatula with the hot water beaker still on the hot plate, and the sample was homogenised using a high-speed homogeniser at 15,000rpm for 3mins.
• The same procedure was repeated but the sample was homogenised using the Ultrasonic Hielscher processor at 100% amplitude at 7watts for 1min.
• A white, milky emulsion was created, and Antor Paar DLS (Dynamic Light Scattering) Litesizer DLS 701 was used to evaluate the zeta potential and particle size distribution of the emulsion to understand which is more stable to hold the (Active Pharmaceutical Ingredient) API intact throughout the lifespan of the product.

SLN Components	High Speed Homogeniser	Ultrasonic Hielscher Processor
Ibuprofen	0.1033g	0.1098
Poloxamer 407	0.7012g	0.2052
Tristearin	0.2080g	0.7029

Table 1: Samples with quantities measured.

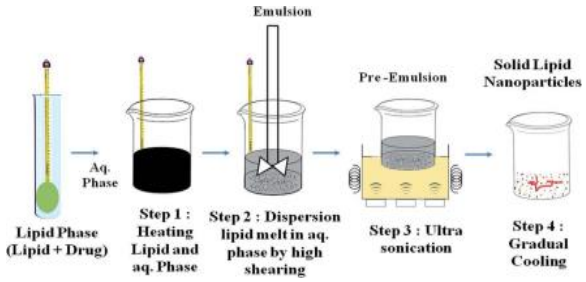

Figure 3: Solid lipid nanoparticle production using the ultrasonication process

III. RESULTS AND DISCUSSION

Parameters measured	High Speed Homogenizer	Ultrasonic Hielscher Processor
Hydrodynamic DN	22.966µm	1.260µm
Poly dispersity index [PDI]	56% [0.56nm]	28.4% [0.284nm}
Zeta potential mean	-0.0008v	-0.0036v

Table 2: Results obtained

The emulsion sample made with the ultrasonic processor had a higher zeta potential which is a function of how stable the emulsion system is. The higher the zeta potential, the more stable the emulsion. This means that the charged particle ions in the emulsion are wide apart hence, the emulsion remains stable. The PDI is used to calculate the average homogeneity of the sample, and a lower PDI indicates the SLN has a lower size distribution. The sample of emulsion made with the Ultrasonic processor had a lower PDI [0.284nm] as compared to the emulsion made with a high-speed homogenizer [0.56nm].

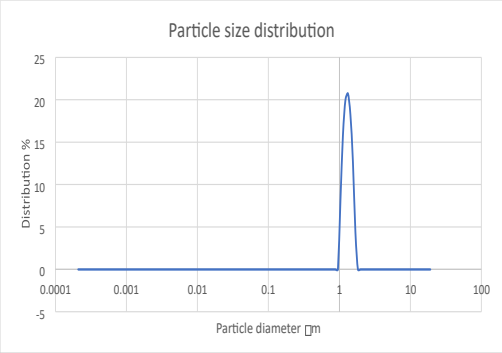

Figure 4: Particle size distribution of sample emulsion made with the homogeniser.

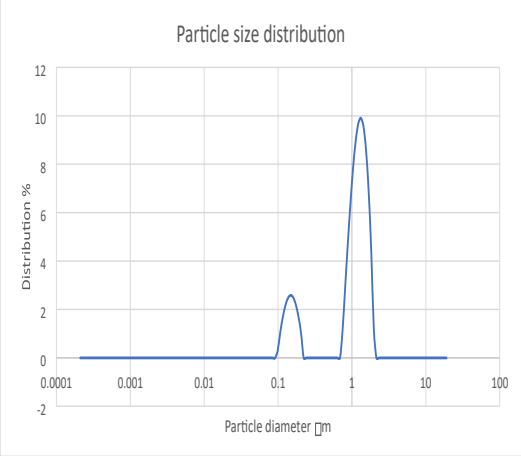

Figure 5: Particle size distribution of sample emulsion made with the ultrasonic processor.

For hydrophobic drug molecules like Ibuprofen the SLN preparation method is the solvent free high-pressure homogenization (HPH). SLNs and nano emulsions have all been prepared extensively via high-pressure homogenization (HPH). The reduction of particle and droplet size at extremely high pressure forms the basis of the approach. It provides a dependable and effective method for mass SLN preparation.

HPH is used to create SLNs two distinct processes: hot and cold homogenization. The drugs are either equally dispersed or dissolved in the molten lipid in hot HPH, where the temperature is usually between 5 and 10 °C above the melting point of solid lipids. To create a hot pre-emulsion, an aqueous phase containing surfactants is heated to attain the same temperature as the lipid melt and added while being constantly stirred. The homogenizer is used to homogenise the resulting pre-emulsion at the same temperature. After homogenization, lipid crystallisation and the creation of SLNs are brought about by cooling the nano emulsions. (5) A solution to some of the problems with hot HPH was the development of cool HPH. Drugs are dissolved or distributed across molten lipids, and mixtures are then rapidly chilled with dry ice for cold HPH or liquid nitrogen. Drug dispersions in lipid matrix can be homogeneous thanks to this quick cooling rate. [1] This process is appropriate for drugs like Ibuprofen as they are dissolved in the lipid phase since they are hydrophobic in nature. (6)

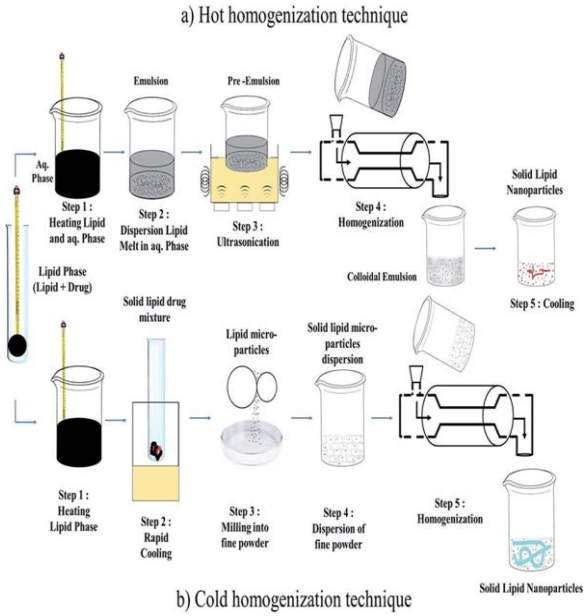

Figure 6: Two methods of homogenization exist: (a)the hot method (b) and the cold method (2)

When different surfactants levels and longer lipid chains were added to the SLNs, the concentration of surfactant significantly affect the physicochemical characteristics of the nanoparticles. (7) The nano formulation's particle size significantly decreases as the surfactant concentration increases. The PDI (polydispersity index) of the finished product is also impacted by surfactant concentration. Surfactants reduce the surface tension of freshly produced nanoparticles and prevent them from aggregating during the homogenization process. (8). Similarly, instability and recrystallization of nanoparticles are brought on by low surfactant concentration.

With increasing the surfactant concentration by 2.5%, it showed a decrease in the PDI. The reason for the PDI decrease could be the existence of a sufficient concentration of surfactant on lipid droplets to preserve the stability and disintegration of the nanodroplets. Surprisingly, PDI was higher at 3% surfactant concentration than 2.5%. EE (entrapment efficiency) and DL (drug loading) increased significantly as the concentration of surfactant increased. This might be explained by the maximum surfactant concentration that is still present on the nano formulation's surface. The formulation with the highest zeta potential or maximum stability of the nano formulation, contained 2.5% surfactant.

The size of nanoparticles is significantly influenced by lipid content. Particle size increased in tandem with a significant increase in lipid concentration. The particle size was found to increase significantly with increasing lipid concentration. With 10% lipid added to the formulation, there were increases in both particle size and PDI. Since there was more lipid available for drug encapsulation, the EE increased noticeably as the lipid concentration rose. However, when lipid concentration increased, drug loading significantly decreased, it might have to do with a reduced drug-to-lipid ratio. There was 5% lipid in the formulation with the highest ZP, which indicates stability in the nano formulation.

The SLNs components have allowed for controlled release because of their solid lipid matrix. These components consist of biodegradable, physiological lipids with minimal cytotoxicity and systemic toxicity. SLN has good compatibility physical stability and increased drug loading. Lipid content (LC), surfactant concentration (SC), and drug concentration (DC) are three formulation elements that significantly impact nanoparticles' physicochemical characteristics and in vivo activities. Furthermore, the quality of the finished product is influenced by other production process parameters, such as homogenization time (HT) and sonication time (ST).

By assessing the SLNs formulation for polydispersity index (PDI), zeta potential (ZP), entrapment efficiency (EE), and drug loading (DL), the formulation drug release can be evaluated. The PDI measures the particle size of the SLN, while the zeta potentials measure the stability of the emulsion formed. The entrapment efficiency and drug loading help to measure the efficiency of the drug in the SLN.

$$\text{Entrapment efficiency (\%)} = \frac{\text{Amount of drug in nano formulation}}{\text{Total amount of drug added.}} \times 100$$

$$\text{Drug loading (\%)} = \frac{\text{Amount of drug in nano formulation}}{\text{Total amount of drug + Total amount of lipid}} \times 100$$

To measure the release of the drugs in the SLN, various methods can be employed, such as the In-vitro release study, where a pre-treated dialysis bag will be filled with plain drug active to be tested and 0.5 g of SLNs. After that, the bag was tied at both ends and put inside a glass jar with a 1000 mL capacity that contained 900 mL of dissolving media. By using the same dissolving media in place of the sample, the sink condition was preserved. After filtering the samples using 0.45 µm filter paper, the amount of drug released was measured using spectrophotometry at 430 nm in wavelength. (9)

CONCLUSION

Colloidal dispersions with altered characteristics of other nanoparticles, including liposomes, microemulsions, suspensions, and polymeric nanoparticles, are known as solid lipid nanoparticles. With the help of SLNs, the main issues with nanoparticles may be avoided, and a drug delivery system that is both chemically stable and physiologically appropriate can finally be accomplished with less restrictions.

At the end of this experiment a better emulsion containing SLN was made using the ultrasonication method. The quality and stability of nano formulation made is largely dependent on the formulation components and manufacturing method including the type of drug been incorporated into the SLN.

The experiment went well in the laboratory but understanding that the loading of the API in the right vesicle helps to improve the drug loading capacity and the drug efficiency.

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