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Review Article

A REVIEW ON SOLID LIPID NANOPARTICLES

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ABSTRACT

Over the past decade, there has been a lot of research on solid lipid nanoparticles (SLNs), also known as lipid carriers. As a new lipid-based drug delivery technology for the topical applications of numerous medicinal drugs, solid lipid nanoparticles (SLNs) have demonstrated promise. SLNs have undergone considerable research on every continent and have become effective nano-sized medication carriers. There is no doubt that nano-formulations are extremely valuable tools for drug delivery applications; the current challenge is how to optimize them to ensure that they are safe, effective and scalable, so that they can be manufactured at an industrial level and advance to clinical use. In this context, lipid nanoparticles have gained ground, since they are generally regarded as non-toxic, biocompatible and easy-to-produce formulations. However, the processes governing SLN cellular uptake and absorption by topical application, as well as the mechanism of SLN drug release, are still unclear and need further research. To make SLNs easier to apply and to improve cutaneous and transdermal administration, it is also crucial to choose the right dose form and formulation base. Additional difficulties that could prevent the clinical translation of SLNs include scaling up and regulatory authorization. Therefore, the main focus of this research is on the various pathways that SLNs use to enter cells and penetrate skin. The physicochemical characteristics of SLNs are then thoroughly discussed, including numerous formulation and dosage form parameters that may affect SLN absorption via the skin. The translational status in relation to scale-up and regulatory issues are also covered in the discussion. Researchers interested in topical uses of SLNs for the effective delivery of medications and cosmetics will find this review to be helpful.

Keywords: Solid lipid nanoparticles, Numerous medicinal drugs, Demonstrated, Medication carriers, Nano-formulations, Scalable, Cellular uptake, Clinical translation, Regulatory authorization, Penetrate skin

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INTRODUCTION

In order for nanotechnology to function, nanoparticles are essential. Between 1 and 100 nanometers in size, nanoparticles can be comprised of carbon, metal, metal oxides, or organic material [1]. It's possible for nanoparticles to have size-related characteristics that deliberately differ from those seen in bulk materials and fine particles. As a result, nanoparticles are smaller than a few 100 nm [2]. The structure of nanoparticles (NPs) is intricate. There are two or three layers in them: (i) a surface layer that has been functionalized by various small molecules, metal ions, surfactants, or polymers The core material is comprised of the central region of NPs, and it is chemically distinct from the shell layer and can be introduced on purpose [3].

Classification of NPs

NPs can be roughly categorized into a number of groups based on their morphology, size, and chemical characteristics. The following list includes some of the well-known classes of NPs based on their physical and chemical properties [4].

Organic nanoparticles

The organic nanoparticles or polymers are also referred to as dendrimers, micelles, liposomes, ferritin, etc. These nanoparticles are biodegradable non-toxic, and some of them, like micelles and liposomes, have hollow centers that are referred to as Nanocapsules and are sensitive to electromagnetic and thermal radiation, including light and heat [5].

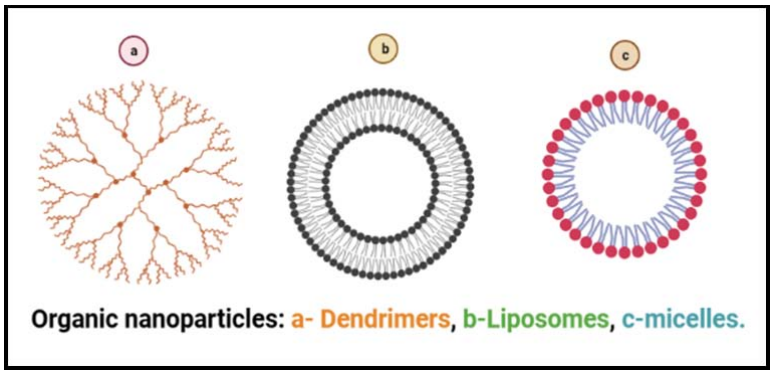

Fig. 1: Organicnanoparticles: a–dendrimers,b–liposomesandc–micelles

Inorganic-based nanoparticles: Metal and metal oxide NPs and NSMs are among these NMs. These NMs can be created synthetically to form metal nanoparticles like Au or Ag NPs, metal oxide nanoparticles like TiO2 and ZnO NPs, semiconductors like silicon

and ceramics [6]; there are two types of inorganic NPs Metal NPs and Metal oxide NPs [7].

Carbon-based nanoparticles

Carbon-based NPs, which include graphene, fullerenes, carbon nanofibers, carbon nanotubes, black carbon, and activated carbon, are NPs whose skeletons are entirely organised from carbon [7].

Synthesis of nanoparticles

For the synthesis of NPs, a variety of techniques may be used; however, these techniques can be roughly categorised into two types, (1) Bottom-up approach and (2) Top-down approach, as shown in fig. 2. Based on their operation, reaction conditions, and established procedures, these techniques are further divided into a number of subclasses [8].

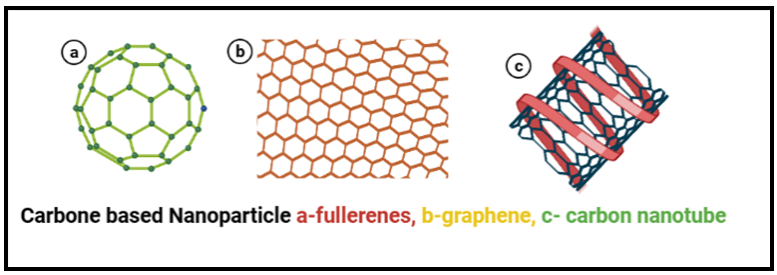

Fig. 2: Carbonbasednanoparticles: a–fullerenes,b–graphene,c–carbonnanotubes,d–carbonnanofibersande–carbonblack

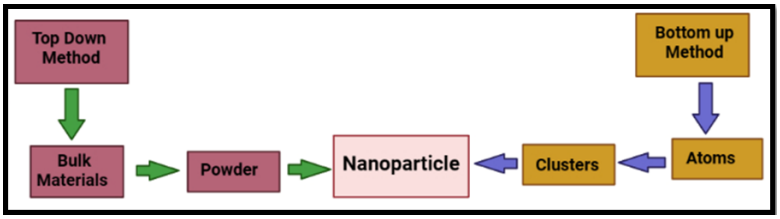

Fig. 3: Flow chart of synthesis of nanoparticles

SLNs

As a result on advancements in biotechnology, biomedical engineering, and nanotechnologies, the field of novel drug delivery systems is expanding exponentially. The development of Nano-sized items carrying the API is a common component of contemporary formulation techniques [9]. Oil-in-water (O/W) emulsions, liposomes, microparticles, and nanoparticles based on synthetic polymers or natural macromolecules have all been explored as particulate drug carriers over the years [10]. In the words of the National Nanotechnology Initiative (NNI), nanotechnology involves the study and application of structures. The overarching objective of nanotechnology is the same as that of medicine: to identify diseases as early and accurately as feasible and to use controlled and targeted medication delivery methods to treat them as well as possible while avoiding any side effects [11]. Lipids have been proposed as an alternate carrier, especially for medications that are lipophilic. Solid lipid nanoparticles (SLNs), the name for these lipid nanoparticles, are gaining a lot of formulators' interest [12]. Wide range in drug delivery technology are being developed at an astounding rate. The two main substances widely supplied to target areas are variously manufactured nanoparticles and medications with poor pharmacokinetic and solubility profiles. Nano lipid dispersions (liposomes, deformable liposomes, virosomes, ethosomes, and solid lipid nanoparticles) are the best colloidal carriers for drug administration due to their biodegradability and nontoxicity. When compared to liposomes and polymeric nanoparticles, solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NSLCs) are dominant [13].

The liquid lipid was replaced by a solid lipid, which later changed into solid lipid nanoparticles, to solve the drawbacks of the oil droplets' liquid nature [14].

There are many different factors contributing to the growing interest in lipid-based systems, some of which are included here [14].

1. Lipids improve oral bioavailability and lower plasma profile variability.

2. Improved lipoid excipient characterization.

3. An enhanced capacity to solve the crucial concerns of knowledge transfer and manufacturing scale-up.

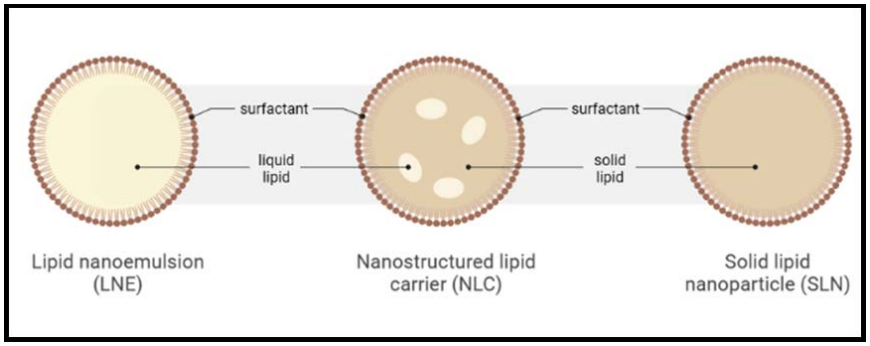

Fig. 4: Schematic presentation of the complete structure of solid lipid nanoparticles

Advantages of SLNs

❖ Small estimate and typically contract measure distribution provides SLNs with natural opportunities to deliver site-specific medicine [15].

❖ Mechanisms used to create conventional emulsions are relevant [15].

❖ To form powdered details, it may be stop-dried [16].

❖ It is possible to establish a gradual, controlled release of dynamic medicine [16].

❖ High concentration of functional compound achieved [17].

❖ Lyophilization possible [17].

❖ Better control of the encapsulated compound's release kinetics [18].

❖ The raw materials needed are the same as those for an emulsion [18].

Disadvantages of SLNs

❖ Inadequate capability for loading drugs [19].

❖ The dispersions have a rather high-water content (70–99.9%) [19].

❖ Probabilities of drug ejection after polymerization during storage [20].

❖ There may be a potential of drug ejection during SLN storage as a result of polymeric transformation [21].

The main goal of solid lipid nanoparticles

According to some, SLN combines the benefits and stays away from the drawbacks of other colloidal carriers. Listed benefits include:

❖ Possibility of targeted drug delivery and controlled drug release [22].

❖ An improved drug's stability [22].

❖ The carrier has no biotoxicity [23].

❖ High drug play role [24].

❖ Stay away from organic solvents [23].

Preparation of solid lipid nanoparticles

Different techniques are used to create SLNs from lipid, emulsifier, and water/solvent; these techniques are mentioned below [25].

1. High-pressure homogenization:

A. Hot homogenization.

B. Cold homogenization.

2. Ultrasonication/high-speed homogenization:

A. Probe Ultrasonication.

B. Bath Ultrasonication.

3. Solvent evaporation method.
4. Solvent emulsification-diffusion method.
5. Supercritical fluid method.
6. Micro emulsion-based method.
7. Spray drying method.
8. Double emulsion method.
9. Precipitation technique.
10. Film-ultrasound dispersion.
11. Using contractor membrane

High-pressure homogenization

The systems used to produce LNPs are many. High-pressure homogenization at high or low temperatures, including hot homogenization and cold homogenization, solvent emulsification, evaporation or diffusion, supercritical fluid (supercritical fluid extraction of emulsions [SFEE]), ultrasonication or high-speed homogenization, [26] and spray drying are frequently used techniques for the preparation of SLNs [27].

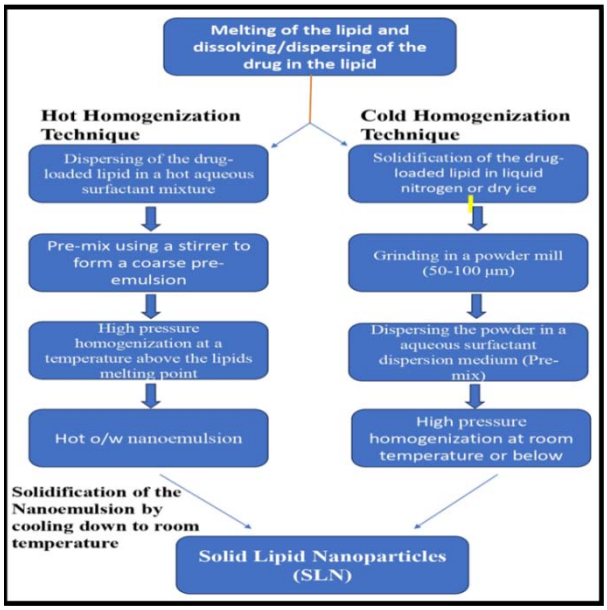

Fig. 5: Schematic procedure of hot and cold homogenization techniques for SLN production

Hot high-pressure homogenization

This approach involves heating the lipid phase to 90 °C before dispersing it into an aqueous phase that contains surfactants at the same temperature. The pre-emulsion is homogenized at 90 °C for three cycles at 5 107 Pa in a high-pressure homogenizer. To solidify SLNs, the created oil-in-water emulsion is then cooled to room temperature [28]. Due to the high kinetic energy of the particles, increasing the homogenization pressure or the number of cycles frequently causes an increase in particle size [23].

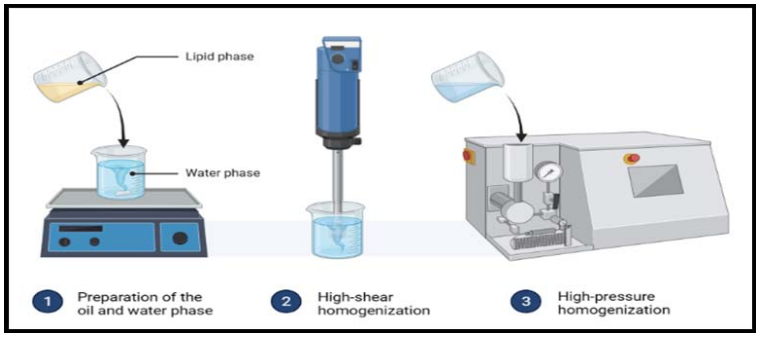

Fig. 6: Hot high pressure homogenizationfor the SLN preparation

Cold high-pressure homogenization

This process involves cooling the molten lipid phase until it solidifies, then grinding it to create lipid microparticles. To create pre-suspension, obtained lipid microparticles are dispersed in a cold, surfactant-containing aqueous phase. The pre-suspension is then homogenized in a high-pressure homogenizer for five cycles at a pressure of 1.5 108 Pa and room temperature [29].

Ultrasonication/high-speed homogenization

SLNs can also be made using high-speed homogenization or ultrasonication methods. It is necessary to combine ultrasonication and high-speed homogenization for lower particle sizes. Although it lowers shear stress, there are several drawbacks, including the possibility of metal contamination and physical instability, such particle development during storage. It uses a bath sonicator or a probe sonicator [30, 31].

Solvent evaporation method

The hydrophobic drug and the lipophilic substance (lipid) are both dissolved in a water-impermeable organic solvent (such as cyclohexane, dichloromethane, toluene, or chloroform) before being emulsified in an aqueous phase using a high-speed homogenizer. The coarse emulsion was immediately run through a micro-fluidizer to increase the effectiveness of fine emulsification. The organic solvent was then mechanically evaporated by stirring at ambient temperature, ideally under decreased pressure (using a rotary evaporator), leaving lipid precipitates as SLNs [32].

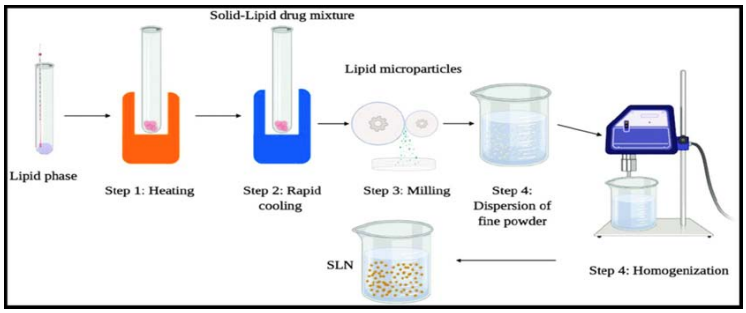

Fig. 7: Cold high pressure homogenizationfor the SLN preparation

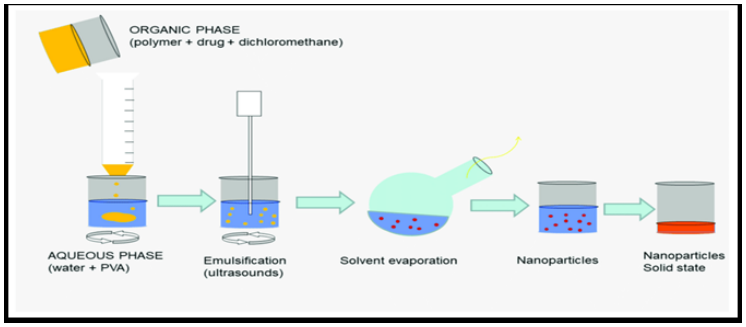

Fig. 8: Solvent evaporation method for the SLN preparation

Solvent emulsification-diffusion method

By using the solvent emulsification-diffusion process, SLNs may also be created. The amount of lipid presents in the organic phase and the type of emulsifier employed both affect the mean particle size. By using this method, particles with typical sizes of 30-100 nm may be produced. The main benefit of this method is that heat is avoided during preparation. Here, the lipid matrix is dissolved in an organic solvent that is inimical to water before being emulsified in an aqueous phase. As a result of the solvent's lower pressure evaporation, the lipid precipitates as nanoparticles in an aqueous media [17, 33].

Supercritical fluid method

This method of producing SLN is very new and offers the benefit of processing without the use of solvents. This platform technology for the creation of powder and nanoparticles comes in a variety of forms. The rapid expansion of the supercritical carbon dioxide solutions (RESS) technique can be used to make SLN. It was wise to use carbon dioxide (99.99%) as the solvent in this procedure [34].

Micro emulsion-based method

SLN preparation methods based on microemulsion dilution were developed by Gasco and colleagues. In general, an optically clear mixture is made up of a low-melting fatty acid (stearic acid), a co-emulsifier (sodium monooctylphosphate), an emulsifier (Polysorbate 20, Polysorbate 60, soy phosphatidylcholine, and sodium taurodeoxycholate), and water [35].

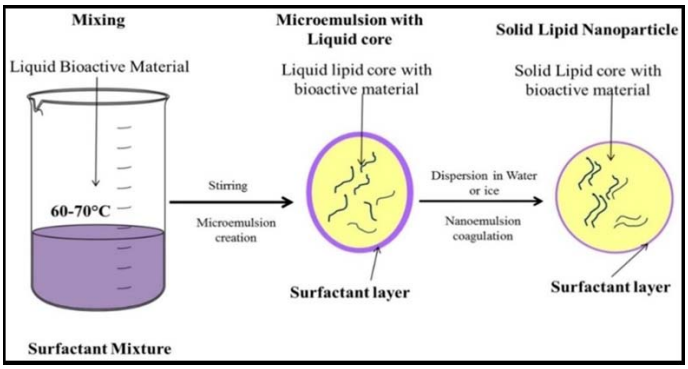

Fig. 9: Representation of SLN production by microemulsion technique

Spray drying method

This technology serves as a replacement for the lyophilization procedure, which produces pharmaceutical products from aqueous SLN dispersion. Although spray drying is a more affordable approach than lyophilization, it is not frequently employed for the synthesis of lipids. Because of the particle aggregation caused by the high temperatures and shear pressures utilised in this method. Lipids having a melting point greater than 70 °C are appropriate for spray drying, according to earlier investigations [12, 36].

Double emulsion method

Warm w/o/w double micro emulsions must be prepared using two different procedures. An aqueous solution containing medicine is first added to a mixture of melted lipid, surfactant, and co-surfactant at a temperature just above the melting point of lipid in order to create a transparent system. The created w/o microemulsion is combined with water, surfactant, and co-surfactant in the second stage to create a clear w/o/w system. It is possible to create SLNs by mixing heated micro double emulsions in cold water, followed by a dispersion media wash using an ultra-filtering system. Because of internal aqueous droplet coalescence inside the oil phase, internal oil droplet coalescence, and layer rupture on the surface of the internal droplets, multiple emulsions are intrinsically unstable [37].

Precipitation technique

Aqueous phase emulsion is created once the lipid is dissolved in an organic solvent (such as chloroform). Nanoparticles are created when the lipid precipitates after the organic solvent has evaporated. An organic solvent (like chloroform) is used to dissolve the glycerides, and an aqueous phase is then used to emulsify the solution. The lipid precipitates, creating nanoparticles, following the evaporation of the organic solvent [38, 39].

Film-ultrasound dispersion

A lipid film is framed, in which there is a watery arrangement that contains the emulsions after the natural arrangements made of lipid and medicine decompress, turn, and dissipate. The SLN with the small and uniform molecular measurement is framed using ultrasound as the test to diffuser in the end [40].

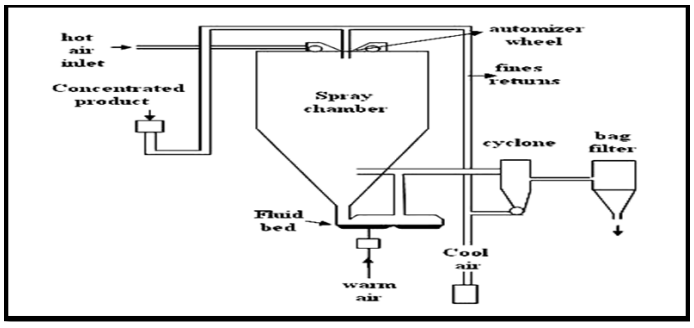

Fig. 10: The spray drying method for the SLN preparation

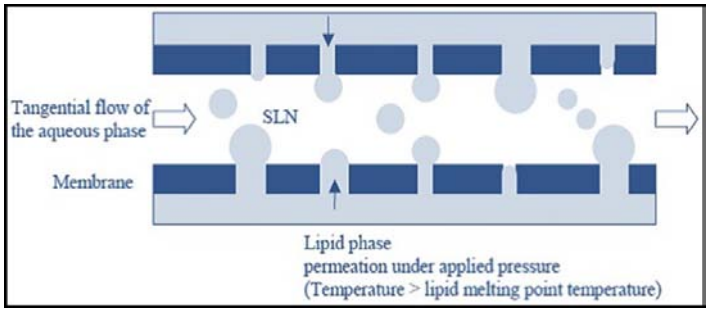

Fig. 11: The membrane contactor for the SLN preparation

Using of membrane

In this method, the fluid stage was pressed at a temperature over the lipid's dissolving function via the pores of the film, allowing the arrangement of tiny beads. While the beads were being framed at the pore outputs, the watery stage was continuously combined with courses inadvertently within the film module. The cooling of the ready at room temperature was used to form SLNs. With the use of a film contactor system, nutrient E stacked SLN are prepared to allow for wide scale creation, and their security is encouraging [40, 41].

CONCLUSION

The last ten years have seen a lot of interest in SLNs and nanostructured lipid carriers as prospective drug delivery (nano) systems. The utilisation of environmentally safe, biocompatible ingredients and processing techniques may be their main advantage. Most of the nanocarriers in this category fall under the low-risk class (class I) of the Nano toxicological categorization system proposed by Keck and Müller due to their size and biodegradable nature. It should be underlined, however, that before progressing these systems to extensive production and commercialization, comprehensive clinical and environmental safety assessment should be carried out. Both the corresponding legal framework and the development of standardised methods to evaluate possible dangers of exposure to nanoparticles are urgently required. Moreover, due to the threat posed by malignant cells and tissues, nanocarriers are suitable for the delivery of anti-cancer drugs. However, as was said for the cases of antibiotics and CNS medications, there are several therapeutic domains that can profit from the application of lipid NPs. It may appear like a difficult situation for the development of this technology given that the oral administration route is the most practical and widely used one for traditional pharmaceuticals and that nanocarriers (including SLNs) supplied through the oral route are not significantly absorbed. This might not be the case, however, for the specific instance of lipid NPs because they have shown that might raise the BA of medications taken orally, which is important when It concerns the (increasingly common) medications with an extremely low water solubility. Unfortunately, more time and money are required for SLN/NLC to demonstrate its therapeutic effectiveness in actual circumstances. The lack of SLNs that have progressed to clinical trials at this time suggests that it will be at least a few years before these technologies reach the pharmaceutical market.

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AUTHORS CONTRIBUTIONS

All authors listed have significantly contributed to the development and the writing of this article.

CONFLICT OF INTERESTS

No conflict of interest

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