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Insights into the Design, Efficacy, and Safety of Nanoemulsion Formulations for Antioxidant and Antihypertensive Therapy

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ABSTRACT:

The kinetically stable colloidal systems, composed of nanoemulsion based nanoscale droplets, provide excellent solubilization formulations for lipophilic phytoconstituents such as curcumin, β-caryophyllene, and many ayurvedic as well as surfactants and essential oils, providing bioavailability and controlled release profiles. The incorporation of generally recognized as safe excipients, including natural oils and surfactants, further increased their use in pharmaceutical and nutraceutical formulations and is beneficial to the human body. In vitro investigations have demonstrated that standardized assays such as DPPH, ABTS, and FRAP indicate enhanced antioxidant properties, whereas angiotensin-converting enzyme inhibition assays validate augmented antihypertensive efficacy, revealing substantial biological activity. In vivo pharmacodynamic evaluations have indicated significant decrements in systemic blood pressure and oxidative stress biomarkers, alongside enhanced bioavailability subsequent to oral administration of nanoemulsion formulations, aimed at therapeutic interventions. Moreover, these delivery systems present a favourable safety profile characterized by negligible cytotoxic effects and the absence of histopathological alterations in principal organ systems. Despite many promising results, challenges remain in some parameters related to nanoformulations, such as scalability and regulatory compliance, and clinical translation, and these need to be addressed human health organizations globally. New formulations such as nanoemulsions and their ingredients, if reduced in cost, will be readily available in the market and there is an urgent

need for standardized protocols and more robust data on human safety in their development, especially long-term exposure and immunological tolerance.

Keywords: Antihypertensive, Antioxidant, Nanoemulsion ,Bioavailability

INTRODUCTION:

The main causes of diseases worldwide are man's daily routine, fast food consumption, lack of exercise, and the strain on the body's blood pressure and respiratory system. These factors are directly linked to heart, kidney, and metabolic disorders and create stress. Traditional Ayurvedic and allopathic antihypertensive and antioxidant treatments, particularly those based on natural phytoconstituents, have low absorption, limited water solubility, and instability under physiological conditions [1–3].

It is imperative that people alter their daily routines to include regular exercise, a diet high in fiber, and adequate sleep in order to treat these problems. Among the many Ayurvedic and allopathic medications on the market, drug delivery methods based on nanoemulsions have become a potent instrument. Cosurfactants and surfactants sustain kinetically stable colloidal dispersions created by dispersing nanoscale oil droplets in water [4]. By shielding sensitive bioactive chemicals, promoting absorption, and enabling sustained release, their small droplet size—typically between 20 and 200 nm—improves therapeutic efficacy [5,6].

The advantages and significance of employing nanoemulsions to provide antioxidant and antihypertensive medications in this condition have been shown by numerous researchers. For instance, following nano emulsification, extracts of β-caryophyllene and Foeniculum vulgare have demonstrated improved neuroprotective and antihypertensive properties [7, 8]. Compared to suspensions employed in traditional procedures, curcumin nanoemulsions have been demonstrated to have greater permeability and bioavailability [9]. Ultrasonication and phase inversion techniques have been successfully used to construct such delivery systems, such as spontaneous emulsification, high-energy, and low-energy systems [10–12].

These medications have been demonstrated to have improved biological activity, decreased toxicity, and targeted delivery when taken orally, topically, or intravenously [13–15]. Researchers created formulations of polyphenols and used essential oils to create nanoemulsified formulations. They then assessed the results using the DPPH and ABTS tests and discovered that the antioxidant activity was noticeably greater [16,17]. Additionally, we discovered that by inhibiting ACE, nanoemulsions of flavonoids and peptides contained in natural medicines also had a strong antihypertensive effect in the human body [18–20].

From a formulation standpoint, we take great care when choosing oil phases (such as medium-chain triglycerides, essential oils) and surfactants (such as Tween 80, lecithin) to guarantee the

formulation's stability over time. Their substantial impact on encapsulation efficiency, zeta potential, and droplet stability is why we chose them [21, 22]. Stable formulations can be created by testing the precise evaluation of drug release kinetics, dispersion stability, and particle morphology made possible by modern characterization technologies including DLS, TEM, and HPLC [23].

When prepared with the right excipients, nanoemulsions are safe to use and have been demonstrated to have low cytotoxicity in humans [24]. Natural food-grade or biodegradable components can be used to create nanoemulsions that are safe for human consumption, satisfy acceptable daily intake requirements, and have shown promise for regulatory approval [25–27].

The scientific momentum and commercial interest in nanoemulsions as effective therapeutics because of their microstructure are building, but there are still issues that need to be resolved, such as large-scale daily production, stability under different storage conditions, and a harmonized regulatory framework [28, 29]. If we look at nanoemulsions from a kinetic perspective, they are stable colloidal dispersions made up of two immiscible liquids (usually water and oil) stabilized by surfactants and co-surfactants. The droplets in nanoemulsions range in size from 20 to 200 nm, and their extremely small size creates a large interfacial area that greatly increases the solubility and bioavailability of lipophilic compounds. [4,3,6]. Additionally, the systems in which they are employed are very small, distinct from microemulsions in that they are translucent and require either spontaneous emulsification procedures or additional energy (such as high-pressure homogenization or ultrasound) to form [4,11].

COMPONENTS OF NANO EMULSION:

With the aid of surfactants and cosurfactants in precisely the right amounts, NEs are colloidal dispersions composed of two phases: an oil phase and an aqueous phase. The performance of NEs is greatly influenced by the characteristics of the phases and surfactant.

Oil and Aqueous phase:

When creating NEs, a range of nonpolar compounds, including free fatty acids (FFA), mineral and essential oils, and other lipophilic nutraceuticals, can be used as the oil phase.The physical and chemical parameters of the oil determine the formation, stability, and features of NEs. Phase, including density, polarity, refractive index, interfacial tension, viscosity, water solubility, and chemical stability[30].Successful NEs produced with various oil and aqueous phases in the presence of a surfactant or surfactants are displayed in below.

Table 1. Lists the various oil phases, aqueous phases, and surfactants used in the formulation of Nano emulsions (NEs).

Nano emulsions	Aqueous Phases	Surfactant/ Co surfactant	Ref.
NEs incorporating citral essential oil	Deionized water	Sorbitane trioleate Polyoxyethylene(10) Oleyl ether Ethylene glycol	30
Wheat bran oil-based nano emulsions	Water	Span-80 and Tween-80	31
Ropinirole hydrochloride	Water	Brij 35 / Isopropyl alcohol (IPA)	32
Beeswax–starch nanoemulsions	Water	Tween-80	33
Vitamin E-enriched NEs	Water	Tween 80	34

Water can be combined with a variety of polar molecules, including proteins, carbohydrates, and others, to create the aqueous phase. The pH, ionic strength, polarity, density, rheology, refractive index, interfacial tension, and physicochemical properties of NEs determine their formulation, stability, and properties. and the aqueous phase's phase behavior, which are determined by the kind and concentration of the components utilized[30]

Surfactants/Emulsifiers

One of the most crucial elements to take into account for the correct design of a product is the choice of an appropriate emulsifier or combination of emulsifiers nanoparticle. A surface-active chemical known as an emulsifier can adsorb to droplet surfaces, promoting droplet breakup and preventing droplets from aggregating.[34]

Thermodynamically stable NEs are created by adding surfactants since they will encourage low interfacial tension, in contrast to emulsions that are micronized by external energy. A transient emulsion is created when water and oil are combined. Nevertheless, due to the

dispersed globules' coalescence, the mixture. When allowed to stand, it will separate into two distinct phases. NEs contain significant amounts of surfactants and emulsifiers from components of generally recognized as safe agents. Proteins, polysaccharides, small molecule surfactants, and phospholipids are a few types of emulsifiers.[30] The concentration and HLB values of surfactants significantly affected the size of the emulsion droplets. The transparent and stable NEs were created[35]. The system tends to stabilize when a surfactant ingredient is added, generating a dispersed phase that presents as a droplet and a continuous phase. In the course of the Droplets form in both phases during the a for mentioned stirring process, with the continuous phases forming as a result of the high instability inside their droplets. For instance, in an oil-in-water (O/W) system created by mixing water and oil, as many drops will form in the water as in the oil. Nonetheless, the water droplets will produce the continuous phase because of their rapid coalescence. This continuous phase is known as the external phase and surrounds the dispersed (internal) phase in the system.[36]

MECHANISM TO ENHANCED BIOAVAILABILITY:

Nanoemulsions, which have a very small oil core, help hydrophobic medications like curcumin and β-caryophyllene become more soluble and passively diffuse over the intestinal barrier [4,9]. It has been demonstrated that the application of surfactants enhances paracellular transport by lowering interfacial tension and avoiding first-pass metabolism[7]. Because lymphatic absorption avoids first-pass metabolism, it raises medication levels throughout the body [10, 23].

FORMATION OF NES:

As mentioned in the section above, NEs are extremely tiny particles that can be obtained by employing high-pressure equipment. NEs can currently be created using both high and low energy emulsification techniques. There are numerous kinds of emulsion systems, depending on the techniques used. consisting of functional chemicals that have been made and studied

High Energy Methods In high energy emulsification, several mechanical techniques like high-pressure homogenization (HPH), microfluidizers, and ultrasonication have been used to create intense disruptive forces like collision, compression, and cavitation, which enable one phase to be disseminated into another as tiny particles droplets. Mechanical equipment is used to create the emulsion in high energy emulsification techniques. Although these high energy techniques are effective in reducing particle size, they are extremely unlikely to work with thermolabile medications and macromolecules such proteins, enzymes, retinoids, peptides, and nucleic acids[30].

High Pressure Homogenization

A special type of high-pressure homogenization device is used to produce nanoscale particles. There is a phase separation between the oil and water as they force through a small input aperture at extremely high pressures (500–5000 psi). Consequently, extremely tiny particles are produced by hydraulic stress and intense turbulence. But this method requires a lot of heat and energy. Pressure and homogenization cycles are the direct causes of particle size. As pressure and homogenization cycles rise, particle size falls[40]

Ultrasonication

High energy shock waves in an ultrasonicator cause cavitation, which causes turbulence and ruptures the droplets. Similar to HPH, ultrasonication is carried out repeatedly until the droplet size stabilizes[42] The interplay between droplet break-up and droplet coalescence governs the generation of NEs droplets. Even though ultrasound uses a lot of shear force to burst droplets, the surfactant's surface activity and concentration both affect how quickly droplets agglomerate[30]

Microfluidization

The process of microfluidization uses a small size fluidizer, a specially made apparatus, to create high pressures between 500 to 20,000 psi, which is similar to Conversely, High Pressure Homogenization and the words are occasionally used interchangeably . In order to force the coarse emulsion to an impingement zone to frame nano-size fine particles, it is first created by combining oil and aqueous phase with an interaction chamber of smaller scale channels. Filtration is then used to obtain uniform particles [41]

Low Energy Methods

Smaller droplets are created in low energy methods when the system transitions from a condition of low interfacial tension to a phase inversion in response to temperature or composition changes [42]

Phase Inversion Temperature

Phase transition during the emulsification process is induced by spontaneous surfactant curvature, which is caused by variations in parameters like temperature and composition[43] There are two types of phase inversion in emulsions: transitional inversion, which is caused by

altering variables that impact the system's HLB, such as temperature and electrolyte concentration, and catastrophic inversion, which is also caused by altering the surfactant's HLB number while maintaining a constant temperature using surfactant mixtures. The PIT method involves mixing non-ionic surfactant, water, and oil at room temperature. Usually, excess oil coexists with o/w micro-emulsions in this combination, and the surfactant monolayer has a positive curvature[44]

Self nanoemulsifying DDs

Nanoemulsion generation is accomplished via the self-emulsification approach without altering the surfactant's spontaneous curvature. The fast diffusion of surfactant and/or co-solvent molecules from the dispersed phase to the continuous phase generates turbulence and produces nano-sized emulsion droplets. The spontaneous emulsification method is another name for the self-emulsification process Diffusion of a hydrophilic co-solvent or co-surfactant from the organic phase into the aqueous phase and the creation of nanoemulsion negative free energy at transitory negative or ultra-low interfacial tensions are the two most often documented methods of nanoemulsion generation from SNEDDS.[45,46]

Solvent Based Methods

Solvent Evaporation Method

This method entails making a drug solution and then emulsifying it in a different liquid that isn't a solvent for the medication. Drug precipitation results from solvent evaporation. A high-speed stirrer can be used to generate high shear forces, which will control crystal development and particle aggregation[46]. The spontaneous and low-energy emulsification procedures described in the production of curcumin nanoemulsions [4] and essential oil-based antioxidant systems [6] are consistent with this technique, even though it isn't often named explicitly.

Co-solvent Evaporation

A combination of two or more volatile solvents, usually an organic solvent like ethanol and a co-solvent like acetone or isopropanol, is used to dissolve the active ingredient. Drugs that are poorly soluble in water become more soluble thanks to this mixed-solvent system, which also makes it easier for them to dissolve into the oil or surfactant phase before evaporating. Even though it isn't called "co-solvent evaporation," a number of research back up comparable techniques. ethanol-assisted spontaneous emulsification to create nanoemulsions laden with curcumin, increasing its absorption and bioavailability [4].dispersion of antioxidant-rich oils in nanoemulsion systems by using food-compatible solvents such ethanol [6]. Similarly,

carriers based on nanoemulsions that carry chemicals obtained from plants using mixed solvent systems [23].

CHARACTERIZATION OF NANOEMULSION:

Making nanoemulsions requires a thorough grasp of their behavior. Let us now look at how we may improve the uniformity, stability, and performance of nanoemulsion-based formulations, and which parameters are necessary to do so.

Droplet Size and the Polydispersity Index (PDI)

If we desire a stable nanoemulsion, the size and long-term stability of the particle size distribution are critical. The average droplet size and PDI are commonly determined using dynamic light scattering (DLS). In this, the particle size is commonly 20-200 nm, while formulations in the nanometer range with PDI values less than 0.3 are dubbed monodisperse. This allows our formulation to be stable and predictable in physiological settings [4, 9, 16].

Zeta Potential

The electrostatic potential at the surface of nanoemulsion droplets, which are composed of oil and water, is very small and provides information about colloidal stability. Measurements of this potential above ±30 mV indicate sufficient repulsive forces to prevent particle aggregation, which is an important factor in long-term stability and shelf life [9, 23].

Encapsulation efficiency (%EE)

Encapsulation is the percentage of active molecule retained in the inner phase of the emulsion and can be high or low depending on the oil, surfactants used, and the process used. Typically, the free drug is separated by ultracentrifugation or dialysis and analyzed using HPLC or UV-Vis spectrophotometry. A high %EE indicates that the hydrophobic bioactives are well-solubilized and protected within the lipid core [6,12].

Morphological Assessment

TME and SEM are used to look at the tiny droplets in a nanoemulsion. These droplets are mostly round and appear to be uniform in size, meaning they are well-formed and because they are very small, they are able to move. When scientists take pictures with this microscope, they often see that the droplets appear to be mostly round and uniform in size across different tests, indicating that the process they used has worked well[13, 16].

Thermodynamics and storage stability

To test a nanoemulsion formulation, the mixture is first frozen and then thawed, or if possible, spun very rapidly. These tests help to see if the mixture stays the same or if the parts start to separate. They also test how well the nanoemulsion formulation stays for a long time,

mainly because these nanoemulsion formulations have some problems like the parts clumping together or floating on top [6,23].

PH and viscosity

The pH is important in nanoemulsions because it helps the drug to work well in various parts of our body, such as the mouth or skin. If it is thick or has a low flow rate, we can say that it is viscous and it is called stickiness. Being viscous is also important because it helps the drug to spread easily and release slowly. We can measure how thick it is using a viscometer. Making sure that the pH and viscosity are correct according to our parameters helps the drug to spread well and be easy to use. [4, 14].

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectroscopy is primarily used to determine the active ingredients in a formulation and their chemical composition. When observed, a number of peaks are observed, which may indicate changes in characteristic peaks or changes in the desired active ingredients and possible drug-excipient interactions, which are important for predicting formulation behavior and stability [9, 23]

IN VITRO AND IN VIVO THERAPEUTIC EVALUATION OF NANOEMULSIONS FOR ANTIOXIDANT AND ANTIHYPERTENSIVE APPLICATIONS:

Nanoemulsion formulations should always be validated using cellular and whole-organism models. How these systems affect therapeutic outcomes can be determined. Nanoemulsions can radically alter the pharmacological profile of poorly soluble plant-based bioactive substances by altering their biochemical availability and biological interactions..

IN VITRO SCREENING FOR ANTIOXIDANT AND ANTIHYPERTENSIVE ACTIVITY:

Embedding active ingredients in nanoemulsions helps to improve radical-scavenging efficiency, as consistently demonstrated in studies using chemical assays such as 2,2-diphenyl-1-picrylhydrazyl,3-ethylbenzothiazoline-6-sulfonic acid and 2,2-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid. Oil-loaded nanoformulations have been shown to significantly enhance in vitro antioxidant responses compared to their encapsulated counterparts [7, 8]. This change is often attributed to the reduced droplet size and improved diffusion, which are more conducive to interacting with free radicals. Antihypertensive activity and ACE inhibition assays reveal another layer of enhancement. Components such as β-caryophyllene and various flavonoids have been shown to exhibit strong enzymatic inhibition when nanoencapsulated, indicating that the delivery format directly affects pharmacodynamic engagement [16, 20]..

IN VIVO EVALUATION OF SYSTEMIC EFFECTS AND BIOAVAILABILITY:

Experimental assessments utilizing animal models indicate that nanoemulsions exhibit superior efficacy compared to conventional formulations, facilitating a systematic analysis of their physiological effects on the human organism. Specifically, nanoemulsions incorporating phytochemical constituents have demonstrated the capacity to attenuate hypertension in rat models while concurrently reinstating endothelial functionality [1,2]. This observation suggests a mechanism of direct therapeutic intervention as opposed to mere symptomatic relief. Furthermore, pharmacokinetic studies validate these benefits, enabling precise assessment of therapeutic efficacy. The application of nanoemulsions in drug delivery not only enhances bioavailability but also facilitates the systemic distribution of hydrophobic agents, thereby prolonging their biological efficacy. One specific study demonstrated that the nano formulation approach produced increased plasma retention and a superior distribution profile compared to traditional drug administration techniques [10]. Supplementary analyses indicated reduced oxidative stress biomarkers, indicating systemic protection within the experimental subjects [18].

EVALUATION OF TOXICOLOGICAL PROFILES, SAFETY PARAMETERS, AND BIOCOMPATIBILITY OF NANOEMULSION-BASED DRUG DELIVERY SYSTEMS:

In order to ensure the safety of human health and regulatory compliance, it is necessary to evaluate the consensus and unhealthful components in the formulation. The clinical and therapeutic shell requires a complete evaluation of their biocomposition and inviolability profile to include the formulation of the formulation and it should always be done. They understand how their lipophilic agents, surfactants and emulsifying agents are designed and the elements in the formulation affect the human body

IN VITRO CYTOTOXICITY ASSESSMENT:

Cytotoxicity is frequently evaluated by using assects such as the formulation of the cells in contact with the formulation, using ashes such as 3-(4,5-dimethylthiazol-2yl)-2,5-diphynyltetrazolium bromide and Tripan Blue. Sessa et al.[7] And Sharma et al [9] It was found that employment for food-grade surfactants like Twin 80 and Lesthin results in high cell viability, until the concentration remains below the safe limit. Atanase [23] said that the size and surface fee of the droplet is important to reduce cellular toxicity.

IN VIVO TOXICITY AND HISTOLOGICAL EVALUATION:

The animal-based model serves as the evaluative framework for the formulation, emphasizing its effects on designated organ systems within the test subjects. According to research conducted by Rehman et al.[1] alongside findings reported by Ali et al.[18] it was observed that oxidative stress in the cerebral tissue of both protected and treated subjects diminished subsequent to the administration of the formulation. Additionally, Khan et al.[20] reported no pathological alterations in the principal organs associated with these systems, indicating that the formulation effectively fulfills its intended function without exacerbating distress within the observed systems.

REGULATORY FRAMEWORK AND GENERALLY RECOGNIZED AS SAFE (GRAS) ASSESSMENTS:

The safety of nanoemulsion is mainly dependent on the regulatory acceptance of their individual components, especially classified as the GRS (GRS) Shah et al.[6] especially safe. Jadhav et al. [13] Ensuring the use of the right surfactants, choosing the right dose, and strictly adhere to the guidelines established by authorities like FDA and EMA are the necessary steps. These remedies guarantee the safety of the product, effectiveness and adherence to international standards, increasing the trust of the customer and the reliability of the industry Atanase [23].

CLINICAL OUTLOOK AND FUTURE DIRECTIONS:

Nanoemulsions have exhibited significant potential in human therapeutics, demonstrating substantial advancements. Despite the encouraging outcomes observed in preclinical formulations, their clinical implementation remains constrained. This limitation is principally attributed to the necessity for exhaustive safety data to guarantee patient safeguarding. Furthermore, challenges associated with the establishment of scalable manufacturing processes present additional obstacles. Mitigating these impediments is critical for the transference of nanoemulsion technology from experimental settings to standard clinical practice, thereby expanding therapeutic alternatives.[1,6,23]

Nanoemulsion formulations contain bioactive ingredients that are therapeutic to the human body, including antioxidants and antihypertensive agents—particularly curcumin, β-caryophyllene, and various polyphenols—that have shown significantly increased oral bioavailability and therapeutic efficacy in preclinical animal studies [2, 9, 16]. However, inter-individual variability in pharmacokinetics, stability of these formulations under physiological

conditions, and lack of data on long-term administration present significant challenges for regulatory progress [6, 13, 23].

Humans have made great progress and this is the era of technology and the advancement of nanotechnology offers promising opportunities to overcome these limitations that are being explored in human health and treatment systems in a shorter time and at a lower cost and to optimize nanoemulsion formulation parameters - such as surfactant concentration, oil type and emulsification energy - to achieve nanoformulation, greater reproducibility and targeted delivery [6, 23]. In addition, smart nanoemulsions that release their payload in response to internal cues such as pH, enzymes or redox status are gaining traction as precision delivery systems [10, 23].

Transdermal, nasal, and pulmonary formulations are being explored to improve patient compliance by avoiding first-pass metabolism [14, 18, 23]. They offer new promise for chronic diseases such as hypertension, which require consistent and predictable medication regimens.While excipients such as Tween 80, lecithin, and MCT oil are GRAS-certified and widely used in approved nanoformulations [6, 13], specific guidelines for nanocarrier systems—toxicity limits, biodegradation, and pharmacokinetics—are still evolving and are in dire need of development [6, 23]. Greater engagement between regulatory agencies, researchers, and clinicians is needed to establish clear safety benchmarks and approval frameworks.

Considering the importance of the human body and the diseases it can cause, nanoemulsions are in great need of advancement. Nanoemulsions offer unique advantages in terms of tunable properties, biocompatibility, and multifunctionality. However, to fulfill their clinical promise, formulation strategies must be tailored to patient-specific needs and comply with international safety standards.

CONCLUSION:

There are many promising delivery systems in nanotechnology that are being used for human therapeutics. Drug delivery systems based on nanoemulsions have emerged as a transformative platform to enhance the solubility, stability and bioavailability of phytochemicals with known antioxidant and antihypertensive properties and are expected to find wide application in human therapeutics in the coming era. In particular, for the use of curcumin, β-caryophyllene and polyphenols and many other ayurvedic medicines and for such hydrophobic compounds, the

reviewed literature has consistently shown that nanoemulsions offer significant advantages in overcoming the limitations of conventional formulations and their beneficial effects on the human body at low doses. Nanoemulsions have been shown in animal studies to enhance pharmacokinetic parameters in this dosage form, which can help with the release of frequently administered drugs, and have been confirmed by extensive in vitro and in vivo studies. In addition, the favorable safety profile, as reported in various cytotoxicity and histological assessments, makes nanoemulsions attractive candidates for long-term use, demonstrating how they can be a useful therapeutic approach in humans and animals. Despite many promising results, challenges remain in some parameters related to nanoformulations, such as scalability and regulatory compliance, and clinical translation, and these need to be addressed by human health organizations globally. New formulations such as nanoemulsions and their ingredients, if reduced in cost, will be readily available in the market and there is an urgent need for standardized protocols and more robust data on human safety in their development, especially long-term exposure and immunological tolerance. If we look to the future, the integration of advanced technologies such as AI-guided optimization and stimulus-response systems - along with interdisciplinary collaboration - is expected to accelerate the clinical acceptance of nanoemulsion-based therapies. This will allow us to take maximum care of human health using new technologies and they will be used to treat more people. These systems hold great promise not only for managing hypertension and oxidative disorders but also as a comprehensive platform for precise phytopharmaceutical delivery.

DECLARATION OF CONSENT:

We, the authors of the manuscript titled **Insights into the Design, Efficacy, and Safety of Nanoemulsion Formulations for Antioxidant and Antihypertensive Therapy** declare that the work is original, has not been published or submitted elsewhere, and that all authors have read and approved the final version of the paper. All authors consent to the publication of this manuscript in the journal and accept responsibility for its content.

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