INTERNATIONAL JOURNAL OF ADVANCES IN PHARMACY MEDICINE AND BIOALLIED SCIENCES
An International, Multi-Disciplinary, Peer-Reviewed, Open Access, Indexed, Triannually Published Journal
|www.biomedjournal.com|
ISSN 2348-2109

Nanoemulsion technology in unani medicine

Mohd. Aamir Mirza[1], Mohammad Jameel[2], Mukhtar Azam Khan[3], Zeenat Iqbal[4]

[1]Ranbaxy Laboratories Ltd, Sector 18, Gurgaon (Haryana), India.
[2]Regional Research Institute of Unani Medicine, (CCRUM), Aligarh, Uttar Pradesh, India.
[3]Department of Pharmaceutical Medicine, Faculty of Pharmacy, Jamia Hamdard, New Delhi, India.
[4]Dept. of Pharmaceutics, JamiaHamdard, New Delhi, India.

MINI-REVIEW ARTICLE

ARTICLE INFORMATION

Article history
Received: 5 March 2015
Revised: 25 March 2015
Accepted: 30 March 2015
Early view: 20 April 2015

*Author for correspondence
E-mail: aamir_pharma@yahoo.com

QR Code

ABSTRACT

One of the basic differences between modern medicine (Allopathic) and indigenous medicine (like Unani) is that the earlier deals with a particular constituent/component/moiety while systems like Unani medicine relies on holistic approach. Converting entire crude form of a drug into a dosage form poses problems to a pharmaceutical scientists which result into a large dosage size, increased dosing regimen, inadequate mixing of different crude drugs and patient non-compliance (geriatrics, pediatrics and non-conscious). Now we are laden with techniques like nanotechnology (e.g., NE technology). By judicious exploration of technology we can think of dosage forms that can address the challenges being faced and also complying with formula of ancient scriptures (Qrabadeen). This may be successfully explored in liquid dosage forms like Jushanda, Khasanda, Haleeb, Sharbat and other types of sayyal. It can also be explored for external dosage forms (liquid and semi-solid). A genuine effort and ability to think out of the box would definitely pave the way for amalgamation of NE technology with Unani system of medicine.

INTRODUCTION

The belief that natural medicines are much safer than synthetic drugs has gained popularity in recent years and led to tremendous growth of phyto-pharmaceutical usage. On the other hand ancient scriptures of different civilization (Greek, Indian, Chinese etc.) are abundant with well proven usage of different herbs for the treatment of mankind and animals too. Unani system of medicine is one of them and well structured and documented. In recent patent controversies of turmeric and Neem, antique literatures of Unani system (Qarabadeen) played a major role in strengthening our case.

One of the basic differences between a modern medicine (Allopathic) and indigenous medicines (including Unani) is that the earlier deals with a particular constituent/component/moiety while the other relies on holistic approach. Converting entire crude form of a drug into a dosage form doesn't offer much space to a pharmaceutical scientists which result into a large dosage size, increased dosing regimen, inadequate mixing of different crude drugs and patient non-compliance (geriatrics, paediatrics and non-conscious).Previously herbal drugs could not attract scientists towards the development of novel drug delivery systems due to processing, standardising, extracting and identification difficulties. Other limitations were instability in acidic pH, liver metabolism etc. which led to drug levels below therapeutic concentration in the blood resulting in less or no therapeutic effect. Now we are equipped with modern sophisticated techniques (analytical, formulation and clinical). Novel technologies used in drug delivery are well proven for their curative potential for particular disease by targeting exactly the affected zone inside a patient's body and transporting the drug to that area. It is also advantageous in delivering the herbal drug at predetermined rate and delivery of drug at the site of action which minimizes the toxic effects with the increase in bioavailability of the drugs. In novel drug delivery technology, control of the distribution of drug is achieved by incorporating the drug in carrier system or in

changing the structure of the drug at molecular level. For last one decade many novel carriers such as liposomes, nanoparticles, phytosomes and implants have been reported for successful modified deliveryof various herbal drugs e.g. curcumin, quercetin, silybin, ginkgo etc. Incorporation of herbal drugs in the delivery system also aids to increase in solubility, enhanced stability, protection from toxicity, enhanced pharmacological activity, improved tissue macrophage distribution, sustained delivery and protection from physical and chemical degradation.By judicious exploration of technology we can think of dosage forms that can address the challenges being faced, complying with formulas of Qrabadeen and also establish its authenticity clinically. In Table 1 some herbal drugs have been enlisted that are being used in Unani and Ayurvedic systems of medicine. Preclinical and clinical efficacies of most of them have also been tested. But usually herbal medicine has relied on tradition that may or may not be supported by empirical data. Evidence-based verification of the efficacy of herbal medicinal products/botanicals is still lacking in general. However, in recent years, data on evaluation of the therapeutic and toxic activity of herbal medicinal products became available.

Nanonization possesses many advantages, such as increasing compound solubility, reducing medicinal doses, andimproving the absorbency of herbal medicines compared with the respective crude drugs preparations. Nanoemulsion (NE) is one of them, has a potential to carry both hydrophilic and lipophilic components of crude drugs. It is a type of colloidal system with particles varying in size from 10 nm to1000 nm (Ratnam, Ankola et al., 2006).

Generally, NE consist ofoil phase, surfactant and aqueous phase which represented the oil droplet size in the range of 50-200 nm dispersed in the aqueous phase using the appropriate surfactant and their concentration. Currently, there are growing interest of essential oil which are prepared in term of NEs such as curcumin (Ahmed, Li et al. 2012), eucalyptus oil (Saranya, Chandrasekaran et al. 2012) and lemonoil (Rao and McClements 2012). In this article we will discuss the potential of Nanoemulsion technology to deal with different drugs/dosage forms of Unani system of medicine.

NANOEMULSION IN UNANI SYSTEM

NEs are the emulsions of O/W or W/O type having the size range of few microns/nanometres. They areprepared by using the surfactants which are considered safefor the human use and approved by the FDA. These types ofemulsions have higher surface area and hence can easily penetrate through biological membrane. They are also non toxic and nonirritant in nature and can be used in the animals and veterinary (Shah, Bhalodia et al. 2010)purpose. NE can be prepared by the high(Lieberman, Rieger et al. 1998)pressure homogenization and micro-fluidisation technique.

Reducing droplet sizes to the nanoscale leads to some very interesting physical properties, such as optical transparency (Figure 1) and unusual elastic behaviour. In the world of nanomaterials, NEs hold great promise as useful dispersions of deformable nanoscale droplets that can have remarkably varying flow properties and optical properties ranging from opaque to nearly transparent. Moreover, it is very likely that NE will play an increasingly important role commercially, since they can typically be formulated using significantly less surfactant than is required for nano structured lyotropicmicro emulsion phases. Such phases are actually quite different (Mason, Graves et al. 2006). Lyotropic liquid crystals are equilibrium structures comprised of liquids and surfactant, such as lamellar sheets, hexagon- ally packed columns, and wormlike micellar phases, that form spontaneously through thermodynamic self assembly. By contrast, NEs do not form spontaneously; an external shear must be applied to rupture larger droplets into smaller ones. Compared to microemulsion phases, relatively little is known about creating and controlling NE. This is primarily because extreme shear, well beyond the reach of ordinary mixing devices, must be applied to overcome the effects of surface tension to rupture the droplets into the nanoscale regime (Mason, Graves et al. 2006). In Table 2 some commercially available NEs have been shared that further authenticates its applicability in drug delivery.

NE technique can be explored for both types of liquid dosage forms (Sayyal), internal and external. They are more demanding in case of oral drug delivery considering the bulky size of dosage units. Dispensing single drugs (Mufradaat) into NEis not a big challenge. But compound drugs (Murakkabat) possess a big challenge. Nearly all different forms of drugs can be converted into NE like solid (Jamid), semisolid (neemjamid) and liquid (sayyal) like curcuminpowder and various oils (roghan badaam, babchi oil, neem oil etc). Solid drugs (Jamid mufradaat) are first converted into suitable oil or aqueous phase by solubilising into suitable oil while oils are taken as such or by solubilising into oil. The overall drug loading into dosage form (NE) depends upon the solubility of drug in the oil. It has successfully addressed the bioavailability problems of curcumin. Today curcumin has been widely acknowledged globallyas a"wonder drug of the future" because of its great potential abilities to prevent and treat a wide spectrum of incurable andchronic diseases. However, the major problem limiting the exploitation of its potentially valuable therapeutic effects is its low bioavailability (Dandekar, Jain et al. 2010). In practice, only very low or undetectable levels of curcumin can be achieved in blood byoral administration of curcumin. The low bioavailability of curcumin has been attributed to its very low aqueous solubility, tendency to degrade in the gastrointestinal tract in the physiological environment, high rate of metabolism, and rapid systemic elimination. The low bioavailability of curcumin has sofar limited its medical use. It has been suggested that a person

isrequired to consume large doses (about 12-20g/day) of curcumin inorder to achieve its therapeutic effects on

Table 1. A collection of commonly used herbs in Ayurvedic and Unani system of medicine. Botanical names and family are also mentioned.

S.No.	Common name	Ayurvedic / Sanskrit name	Unani Name	Botanical name	Family	Parts used	Dose
1.	Gunchi, Ratti	Gunja, Kakanantika, Kakapilu, Raktika, Kakadani	Ghogchi	*Abrus precatorius* Linn.	Fabaceae	Root, Leaves, Seeds	0.5-1.5 ratti
2.	Circita	Apamargah, Mayoorah,Markatapippalee, Durgrahah	Chiraita	*Achyranthes aspera* Linn.	Amaranthaceae	The whole plant	5- 7 gm
3.	Bilva	Vilva, Maloorah, Sreephala, Sadaphala, Sailoosha.	Bael (Belgiri)	*Aegle marmelos* Linn. Corr	Rutaceae	Leaves, Root, Fruits	2-3 gm
4.	Kulanjan	Rasna, Sugandhamoola, Kulanjana	Rausana	*Alpinia calcarata* Rox	Zingiberaceae	rhizomes	
5.	Satavar, Satamuli	Satavari, Abhiru, Sahasravirya	Satawar	*Asparagus recemosus* Wild	Liliaceae	Root	7-10 gm
6.	Bachnag, Meetavish	Vatsanabha, Halahala, Pranahara	Beesh (Meetha zehar)	*Aconitum napellus* Linn, *Aconitum ferox*	Leguminosae	Root tuber	1- 2 chawal
7.	Baach, Vacha	Vacha, Ugragandha, Golomi, Jatila, Shatgrandhi, Sataparvita	Baach	*Acorus calamus* Linn.	Araceae	Rhizomes	1-3 gm
8.	Adusa, Arusa	Vasa, Vasaka, Vrisha, Vrishaka, Simhasya, Vishnu, Vajidanta, Adaroosha	Adusa	*Adhatoda vasica*	Acanthaceae	Whole plant	10-20 gm
9.	Siris	Sireesha, Bhandi, Fanjhi, Sukataru, Mrdupushpa	Siras	*Albizia lebbeck* Linn. Benth	Fabeaceae	Bark, Flowers, Seeds	3-6 gm
10.	Beluli, Lasan	Lasuna, Ugragandha, Bhootaghni, Rasona	Lahsan	*Allium sativum* Linn.	Liliaceae	Bulb	3 gm
11.	Gheekaumar, Ghikumari	Kumari, Grithakumari, Grihakanya	Ghekwar	*Aloe vera, A. barbadensis* Miller	Liliaceae	Leaves juice	1-4 ratti
12.	Bilatti kat hal	Kshudrapanasa	Kathal	*Artocarpus communis* Forst.	Moraceae	Fruits, Latex	
13.	Isvarmul	Garalika, Gandhanukuli, Garudi	Zaravand	*Aristolochia indica* Linn.	Aristolochiaceae	Whole plant	1-2 gm
14.	Vansooran, Bansooran	Vanasoorana, Vajrakanta, Kandala	Zamikand	*Amorphophallus companulatus*	Araceae	Corns	2-10 gm
15.	Semul, Semar	Salmali, Mocha, Picchila, Raktapushpa, Stirayu,	Sembhal	*Bombax ceiba* Linn.	Bombacaceae	Resin, Leaves, Bark, Thorns	5-10 gm
16.	Palas, Dhak	Palasa, Kimsuka, Raktapushpa, Ksharasreshta	Plaas	*Butea monosperma* Lam. Taub	Leguminoseae	Seeds	3-5 gm
17.	Rayi	Srashapa, Rajita, Aasuri	Raai	*Brassica compestris*	Brassicaceae.	Seed, Oil	0.5-1 gm
18.	Brabmbhi	Brahmi, Trayamana, Seetakamini, Trayanthi, Bhekaparni	Brahmi	*Bacopa monnieri* Linn. Pennell	Scrophulariaceae	Whole plant	3-5 gm
19.	Akavana, Aka, Mandara	Arka, Sooryahvaya,Vasuka, Ksheeraparni, Alarka, Asphoda,	Madar (Aak)	*Calotropis procera*	Asclepiadeceae	Root, Latex, Flower and Leaves	0.5-1 gm
20.	Amaltas, Girimala	Aragvadha, Kritamala, Rajavriksha, Chaturangulam, Deerkhaphala	Amaltaas	*Cassia fistula* Linn.	Caesalpiniaceae	Whole plant	2-4 gms
21.	Bharangi	Brahmanayashtika, Kharashakha, Padma, Kasajith, Barbura	Baharangi	*Clerodendrum serratum* Linn.	Verbenaceae	Root and Leaves	3-6 gms
22.	Dhaniyam	Dhanyaka, Dhanaka, Chatra, Kustumburu, Vitunnaka	Dhaniya	*Coriandrum sativum* Linn.	Apiaceae	Leaves, Fruits	Leaves- 10-20 g,fruit- 5-7 g
23.	Balsam tree	Ikkata, Ikkada	Balsan	*Commiphora caudata*	Burseraceae	Bark, Leaves	
24.	Baranimbu, Bijapura	Matulunga	Baranimbu	*Citrus medica* Linn.	Rutaceae	Fruits, Root and Leaves	10-20 ml juice
25.	Dattura	Dhattura, Dusthara, Unmatta, Durdhura	Dhatura	*Datura metel* Linn.	Solanaceae	Whole plant	30-60 mg
26.	Willow		Baide musk	Salix spp.	Salicaceae	Bark	10-50 g extract
27.	Juniper Berries	Havusa, Hapusa	Abhal (Arar)	*Juniperus communis*	Cupressaceae	Dried fruits	3-5 gms
28.	Guduchi	Amratavalli	Gilo	*Tinospora Cordifolia* Wild	Menispermaceae	Whole plant	3-6 gms

Note: The information has been extracted from The Ayurvedic Pharmacopoeia of India (1st and 3rd edition) and Makhzanul Mufradat by Hakim Kabiruddin.

Table 2. Commercial nanoemulsion formulations along with their manufacturers.

Drug /Bioactive	Brand Name	Manufacturer	Indication
Dexamethason	Limethason	Mitsubishi Pharmaceutical, Japan	Steroid
Propofol	Diprivan	Astra Zaneca	Anaesthetic
Flurbiprofenaxtil	Ropion	Kaken Pharmaceutical, Japan	NSAIDs
Vitamins A, D, E and K	Vitalipid	Fresenius Kabi Europe	Parenteral nutrition
Palmitate alprostadil	Liple	Mitsubishi Pharmaceutical, Japan	Vasodilator, platelet inhibitor

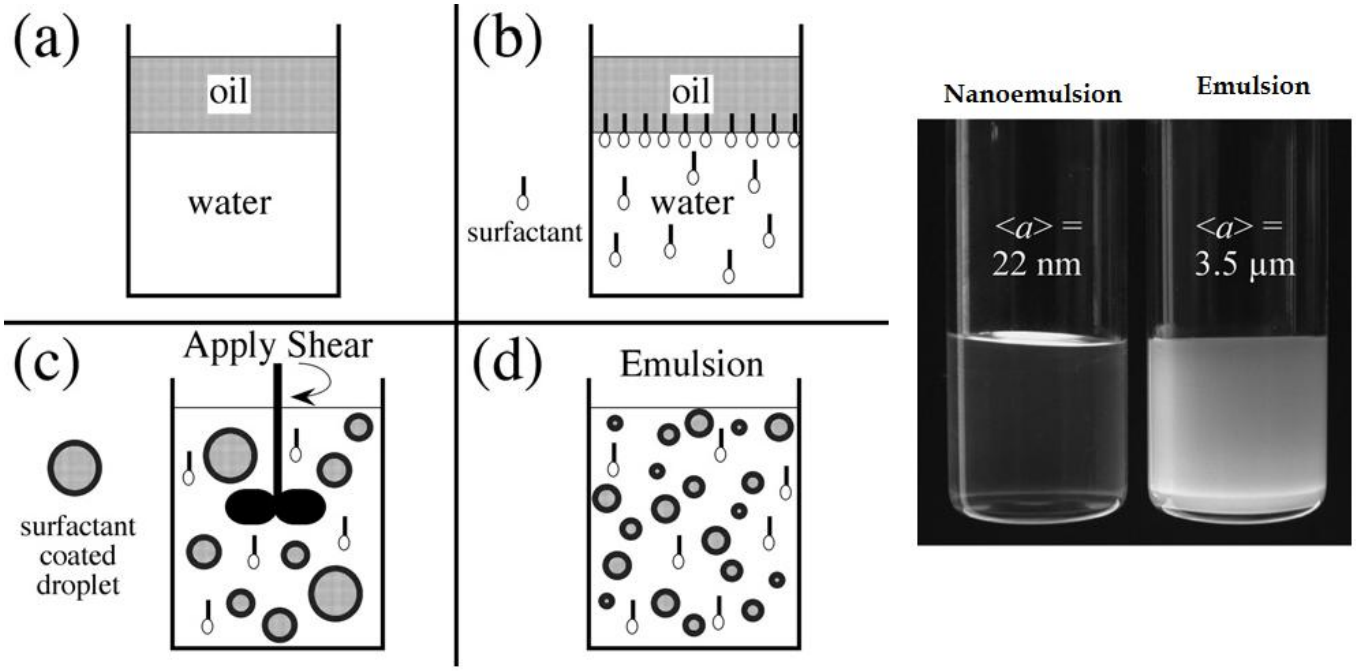

Figure 1. General method of preparation of Emulsion (a, b, c and d). Difference in transparency between Emulsion and Nanoemulsion are also evident in the figure.

the human body (Dandekar, Jain et al. 2010). That means one has to swallow 24 to 40 curcumin capsules of 500 mg each. These doses are considered to be too high, and therefore, not feasible to be incorporated in clinical trials due to unbearable after-taste to the palate, possibility of giving rise to nauseatic feeling and perceived toxicity issues. One of the solution to this conundrum was the development of NE of curcumin (Rachmawati, Budiputra et al. 2014).

On the other hand components of a compound drug vary in nature like solubility (lipophilic/hydrophilic), consistency and susceptibility to different conditions. Here we havealso a good alternative in the form of NE. Lipophilic drugs/extracts can be solubilised in a suitable oil carrier and any of the oil can also be taken as a carrier if it suitable dissolves other lipophilic components. Similarly hydrophilic components can be separately converted into an aqueous medium. Both the differently natured solvents can be transformed into a single transparent NE by the techniques mentioned above. But formulation optimization process of compound drug is exhaustive as compared to single drugs.

If dare to think out of the box, two systems of medicine can also be amalgamated. A synergistic NE was formulated using two drugs of different origin Tea tree oil and Itraconazole for vaginal candidiasis (Mirza, Ahmad et al. 2013). The dual loading of Itraconazole and tea tree oil in a single formulation seems promising as it elaborated themicrobial coverage. Despite being low solubility of Itraconazole in tea tree oil, a homogeneous, transparent and stable solution of both was created by co-solvency using chloroform. Complete removal of chloroform was authenticated by Gass chromatography-mass spectroscopy and the oil solution was used in the development of NE which was further translated into a gel bearing thermo sensitive properties.

CONCLUSION

Above evidences put a strong rational for the exploration of NE technology for drugs and dosage forms being used in Unani system of medicine. By implication of these modern technologies therapeutic efficacy and acceptability of these indigenous medicines can be improved along with acceptable dosage sizes, dosing regimen, and patient compliance.

REFERENCES

Ahmed K, Li Y, McClements DJ, Xiao H. Nanoemulsion-and emulsion-based delivery systems for curcumin: encapsulation and release properties. Food Chemistry. 2012; 132: 799-807.

Atul Bhattaram V, Graefe U, Kohlert C, Veit M, Derendorf H. Pharmacokinetics and bioavailability of herbal medicinal products. Phytomedicine.2002; 9:1-33.

Dandekar PP, Jain R, Patil S, Dhumal R, Tiwari D, Sharma S, et al. Curcumin-loaded hydrogel nanoparticles: Application in anti-malarial therapy and toxicological evaluation. Journal of Pharmaceutical Sciences. 2010;99(12):4992-5010.

Lieberman HA, Rieger MM, Banker GS. Pharmaceutical Dosage Forms--Disperse Systems: Marcel Dekker; 1998.

Mason T, Graves S, Wilking J, Lin M. Extreme emulsification: formation and structure of nanoemulsions. Condensed Matter Physics. 2006; 9:193-9.

Mirza MA, Ahmad S, Mallick MN, Manzoor N, Talegaonkar S, Iqbal Z. Development of a novel synergistic thermosensitive gel for vaginal candidiasis: An in vitro, in vivo evaluation. Colloids and Surfaces B: Biointerfaces. 2013;103:275-82.

Rachmawati H, Budiputra DK, Mauludin R. Curcumin nanoemulsion for transdermal application: formulation and evaluation. Drug Development and Industrial Pharmacy. 2014(0):1-7.

Rao J, McClements DJ. Lemon oil solubilization in mixed surfactant solutions: Rationalizing microemulsion& nanoemulsion formation. Food Hydrocolloids. 2012;26(1):268-76.

Ratnam DV, Ankola D, Bhardwaj V, Sahana DK, Kumar M. Role of antioxidants in prophylaxis and therapy: A pharmaceutical perspective. Journal of Controlled Release. 2006;113(3):189-207.

Saranya S, Chandrasekaran N, Mukherjee A. Antibacterial activity of eucalyptus oil nanoemulsion against Proteus mirabilis. International Journal of Pharmacy and Pharmaceutical Science. 2012;4: 668-71.

Shah P, Bhalodia D, Shelat P. Nanoemulsion: A pharmaceutical review. Systematic Reviews in Pharmacy. 2010;1(1):24.

Tiyaboonchai W, Tungpradit W, Plianbangchang P. Formulation and characterization of curcuminoids loaded solid lipid nanoparticles. International Journal of Pharmaceutics. 2007;337(1):299-306.

Verma H, Prasad SB, Yashwant SH. Herbal Drug Delivery System: A Modern Era ProspectiveInternational Journal of Current Pharmaceutical Research. 2013;4:88-101.