NANO-DRUG DELIVERY SYSTEMS, THE WAY FOR MORE EFFECTIVE DRUGS .

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CONTENTS

BACKGROUND

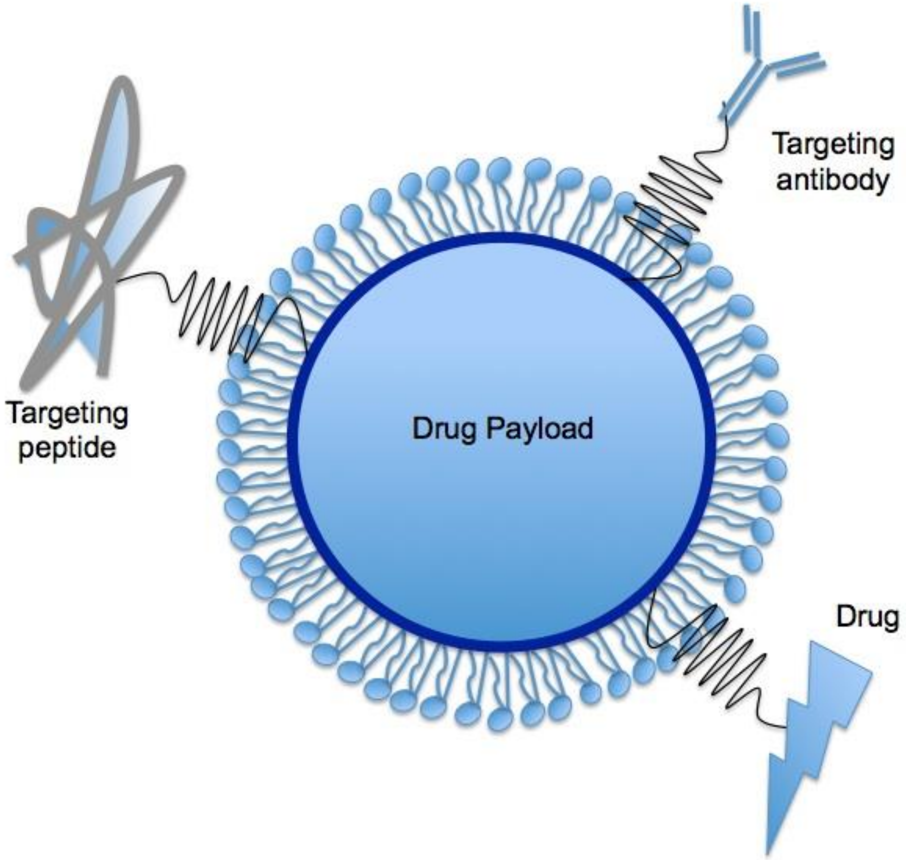
WHAT IS PHARMACEUTICS?

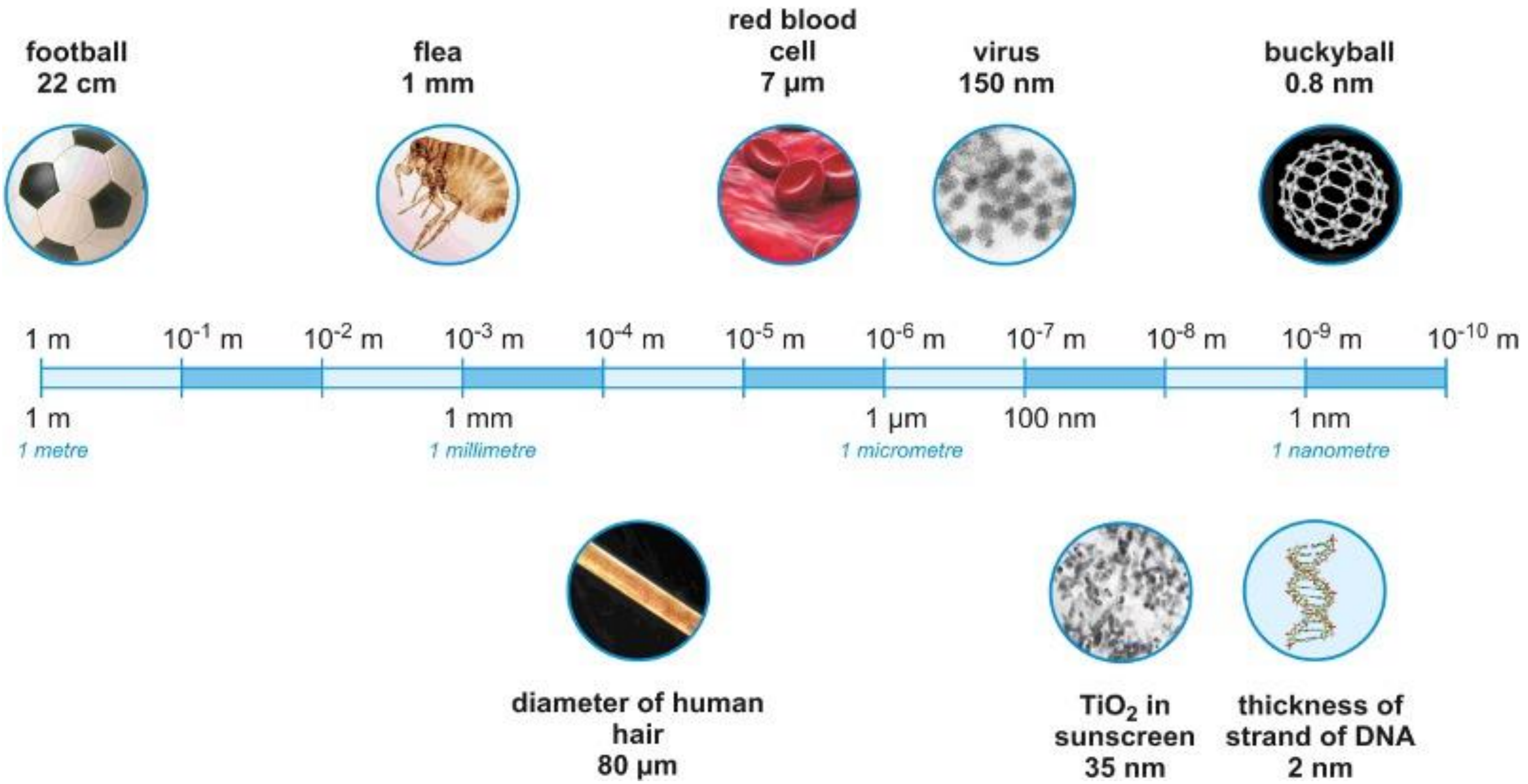
The art and applied science of dosage form design.

Conversion of drug substance to pharmaceutical preparation .

particular pharmaceutical product containing active and inactive pharmaceutical ingredients formulated into the particular dosage form.

TYPES OF NANOPARTICLES FOR DRUG DELIVERY

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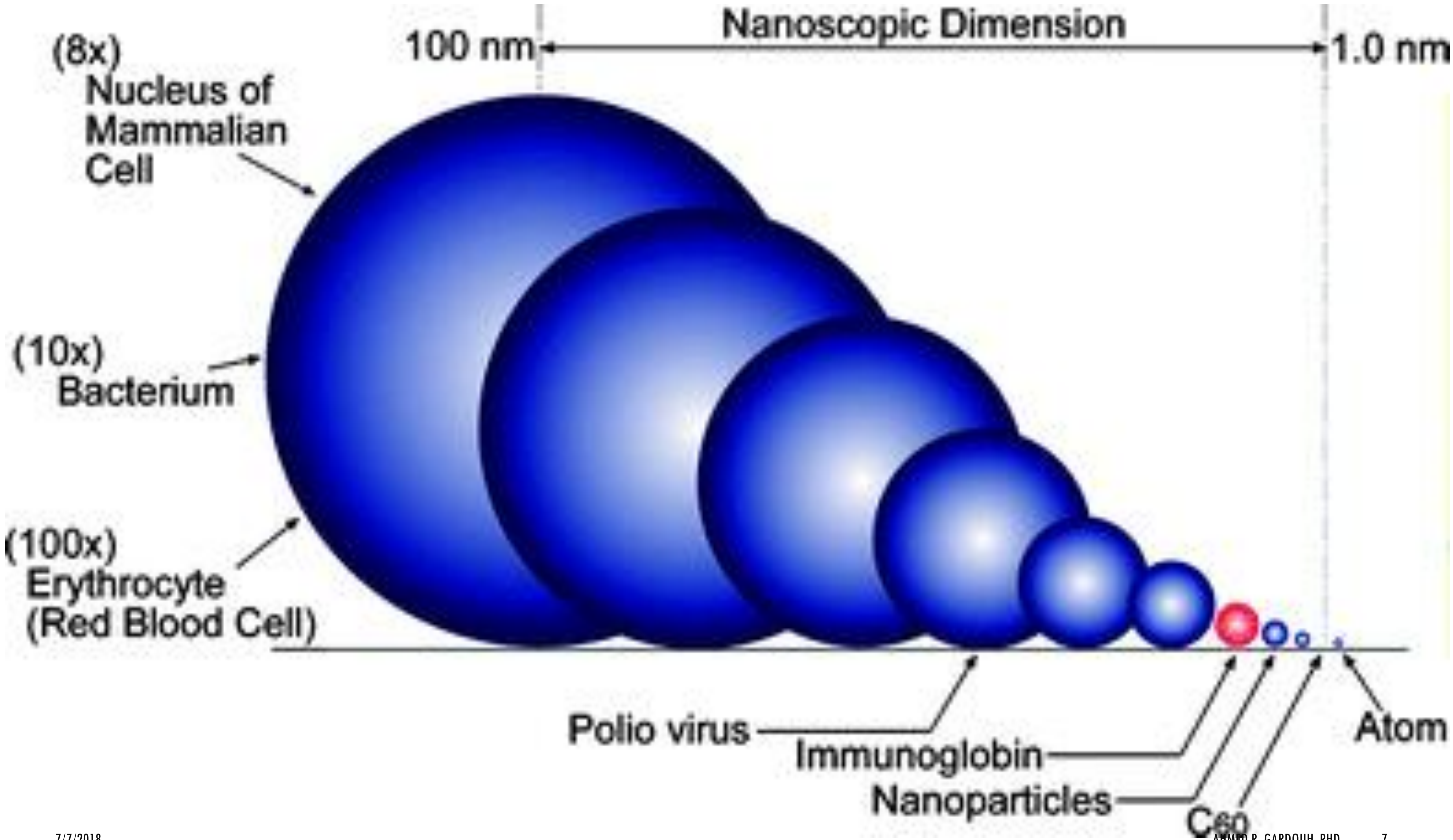
22 cm
flea
1 mm
red blood
cell
7 µm
virus
150 nm
buckyball
0.8 nm
1 m
10^{-1} m
10^{-2} m
10^{-3} m
10^{-4} m
10^{-5} m
10^{-6} m
10^{-7} m
10^{-8} m
10^{-9} m
10^{-10} m
1 m
1 metre
1 mm
1 millimetre
1 µm
1 micrometre
100 nm
1 nm
1 nanometre
diameter of human
hair
80 µm
TiO_2 in
sunscreen
35 nm
thickness of
strand of DNA
2 nm


Nanoscopic Dimension
100 nm
1.0 nm
(8x)
Nucleus of
Mammalian
Cell
(10x)
Bacterium
(100x)
Erythrocyte
(Red Blood Cell)
Polio virus
Immunoglobin
Nanoparticles
C60
Atom

lipid based nanoparticles

-Nano-emulsions

-self-nanoemulsifying drug delivery system (SNEDDS)

- solid lipid nanoparticles

- lipid nanocapsules

- nanosuspension

- liposomes

- layersomes

- liquid crystalline nanoparticles

- lipid-drug conjugates

POLYMER BASED NANOCARRIERS

-polymeric nanoparticles

- polymeric micelles

- polymer-drug conjugates

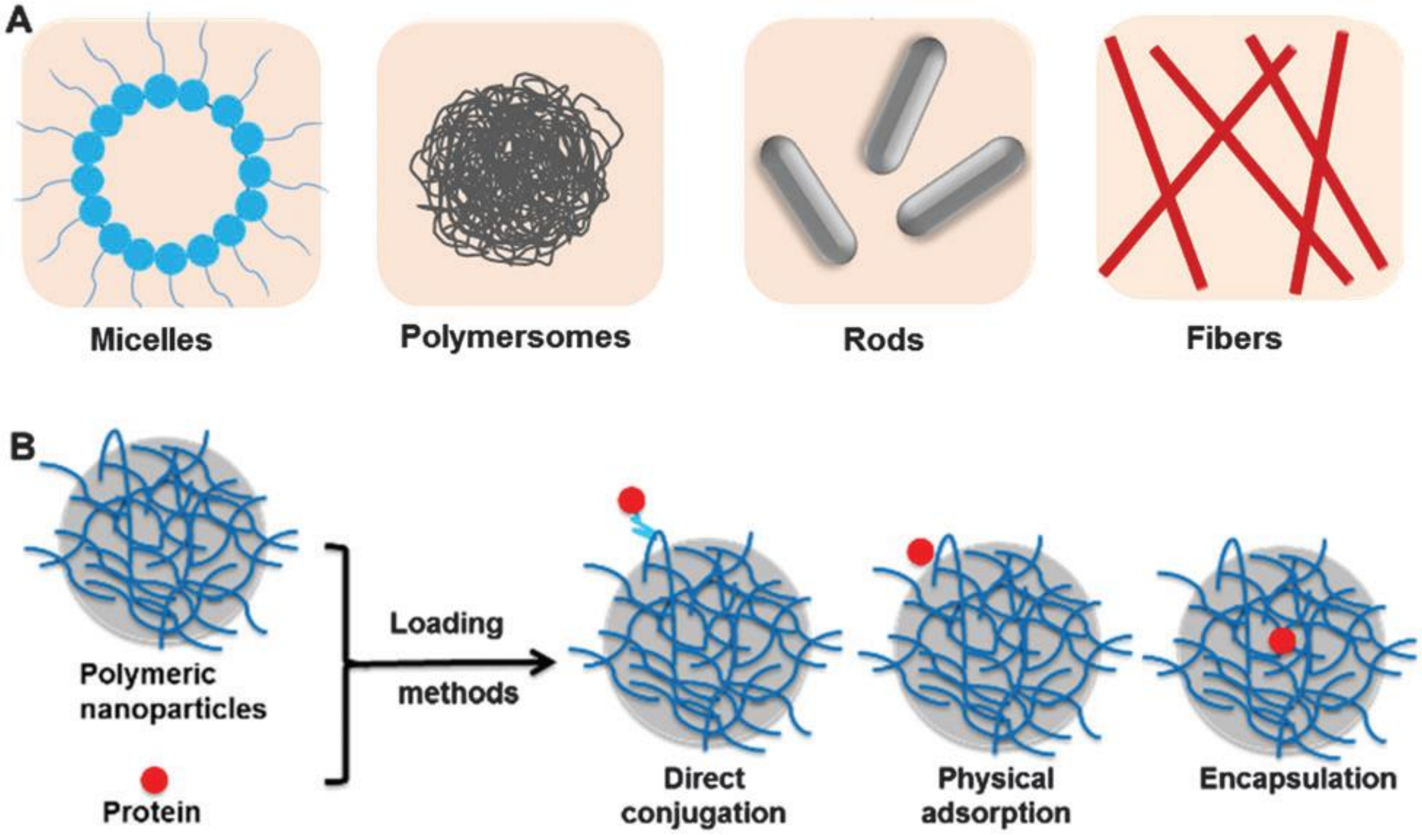
-Drug nanocrystals

-Dendrimers

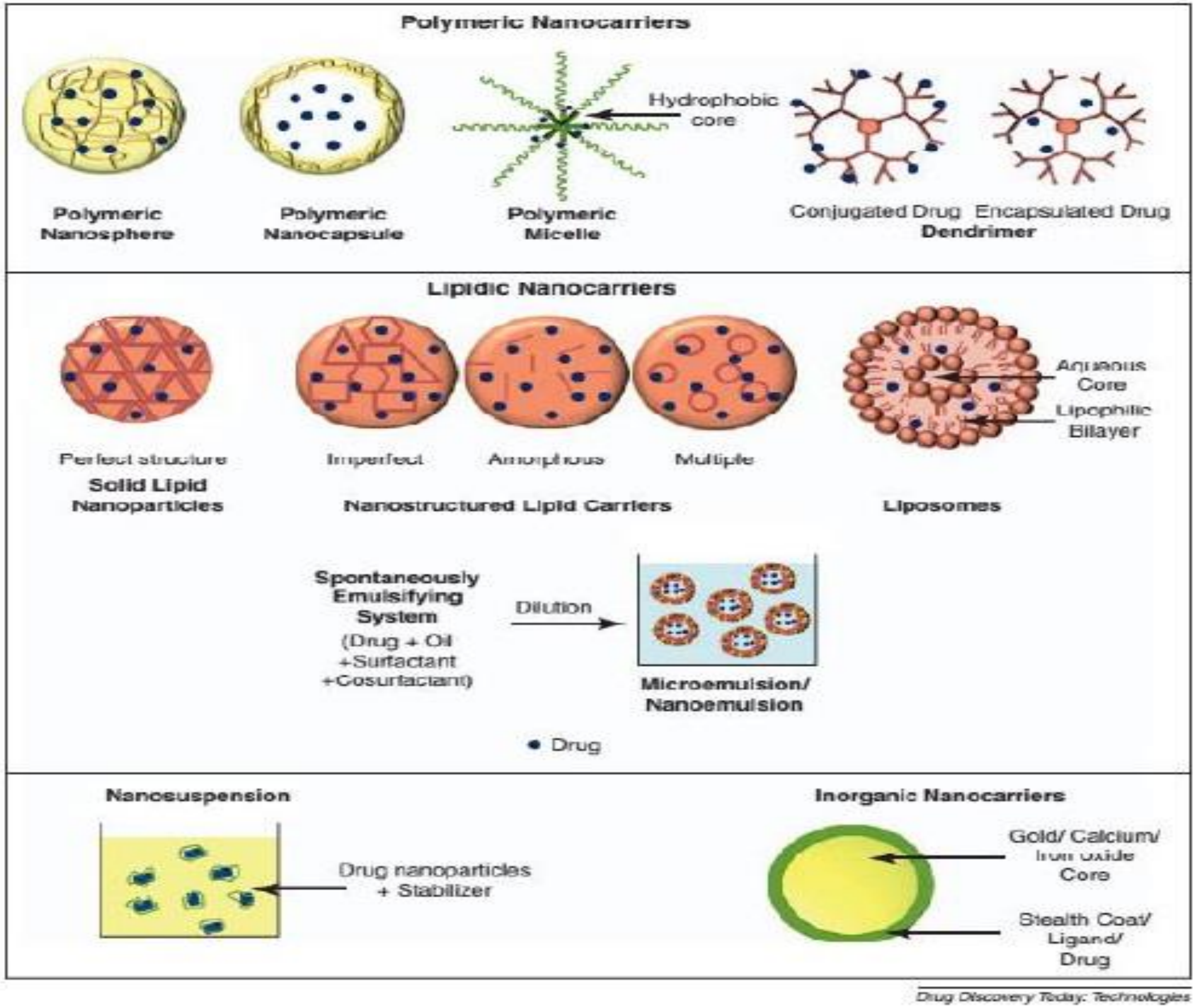
- Carbon nanotubes

-Silica and silicon nanoparticles

- Nanogels and so on (**Ratnam et al., 2009**).



Types of some lipid and polymer nanoparticles (Hong Zhao et al., ***J. Mater. Chem. B,*** 2016,4, 4060.



EXAMPLES OF VARIOUS NANO-ARCHITECTURES AVAILABLE FOR ORAL DRUG DELIVERY (**DESAI ET AL., 2012**)

DISADVANTAGES OF MOST NAN-DRUG DELIVERY SYSTEMS:

Disadvantages of liposomes:

Low solubility

Short half-life

Phospholipid may undergo oxidation and hydrolysis

Production cost is high.

Leakage and fusion of encapsulated drug molecules.

Fewer stability.

Disadvantages of polymeric nanoparticles:

The technique is not suitable to all drugs.

Post preparative steps, such as purification and preservation, incomplete or discontinuous film.

Inadequate stability of certain active components.

Disadvantages of nano-emulsion

1. Nanoemulsions show poor drug loading capacity.

2. Show drug expulsion during storage.

3. Relatively high water content of the dispersion (70-99.0%) is observed in nano-emulsion.

Disadvantages of solid lipid nanoparticles

1. Limitation in drug loading capacity.
2. Drug expulsion during storage.
3. High water content of aqueous SLN dispersions (70–95%).

INCORPORATION OF ACTIVE INGREDIENT IN NANOPARTICLES

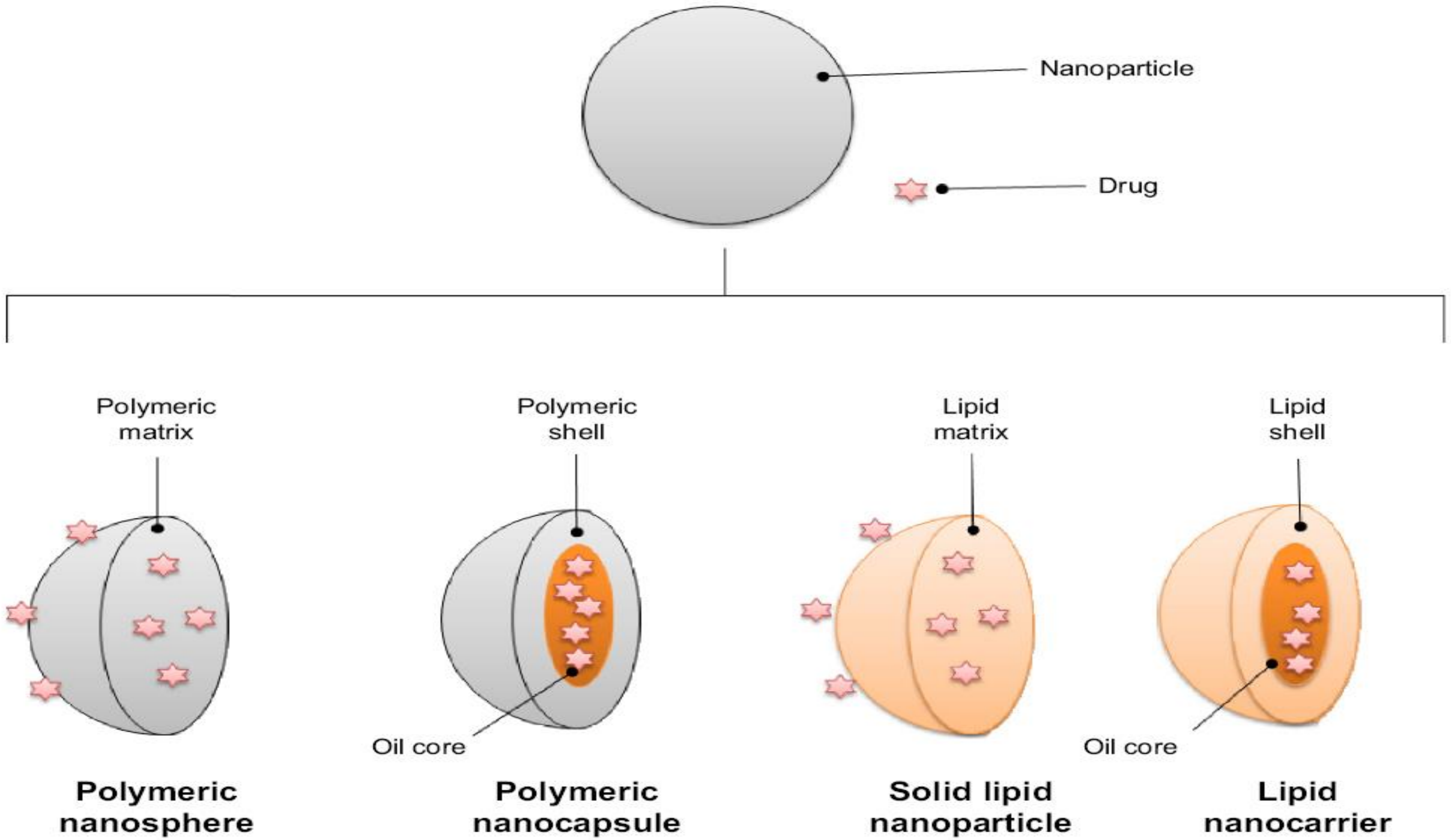


Figure 2 Schematic differences between nanocapsule, nanostructured lipid carrier, polymeric nanoparticle, and solid lipid nanoparticle drug delivery systems.

METHODS OF PREPARATION

1. Cold and hot homogenization methods
2. Spray drying methods
3. Ultrasonic methods
4. Simple methods for ease of scale up

EXAMPLES OF PUBLISHED WORK

British Journal of Pharmaceutical Research
3(3): 326-346, 2013

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Design and Characterization of Glyceryl Monostearate Solid Lipid Nanoparticles Prepared by High Shear Homogenization

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Authors' contributions

This work was carried out in collaboration between all authors. Author ARG designed the study, wrote the protocol, and wrote the first draft of the manuscript. Author HMG managed the analyses of the study, managed the literature searches and overall revision and submission. Authors SG, HMG and MMG supervised the entire research. All authors read and approved the final manuscript.

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Design, formulation and *in-vitro* characterization of Irbesartan solid self-nanoemulsifying drug delivery system (S-SNEDDS) prepared using spray drying technique

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Controlled release of insulin from folic acid-insulin complex nanoparticles

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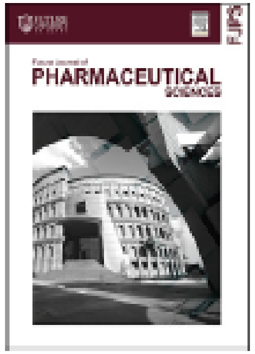

Formulation and *in-vitro* evaluation of pantoprazole loaded pH-sensitive polymeric nanoparticles

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Accepted Manuscript

Title: Ginkgo Biloba Extracts-loaded Starch Nano-spheres: Preparation, characterization, and in vitro release kinetics

Authors: Tao Wang, Caie Wu, Gongjian Fan, Tingting Li, Hao Gong, Fuliang Cao

PII: S0141-8130(17)32120-7
DOI: http://dx.doi.org/doi:10.1016/j.ijbiomac.2017.08.012
Reference: BIOMAC 8004

To appear in: *International Journal of Biological Macromolecules*

SNEEDS AND SSNEEDS

SNEEDs are isotropic mixtures of oil, surfactant, co-surfactant and the drug that form fine oil-in-water (o/w) nanoemulsion when introduced into aqueous phases under gentle agitation.

LIMITATIONS OF SELF-NANOEMULSIFYING DRUG DELIVERY SYSTEMS

high production cost, incompatibility problems with capsule shell , low drug portability and stability, drug leakage and precipitation, low drug loading, few choices of dosage forms and irreversible drugs/excipients precipitation.

S-SNEDDS

This drug delivery system combines the advantages of liquid SNEDDS with those of a solid dosage form and overcomes the limitations associated with liquid formulations

The resulting powder may then be filled directly into hard gelatin capsules or mixed with suitable excipients before compression into tablets.

NOVEL SOLID SELF-NANOEMULSIFYING DRUG DELIVERY SYSTEM (S-SNEDDS) FOR ORAL DELIVERY OF OLMESARTAN MEDOXOMIL: DESIGN, FORMULATION, PHARMACOKINETIC AND BIOAVAILABILITY EVALUATION

AIM OF STUDY

Study aimed towards the development of S-SNEDDS of OLM by a spray drying technique using Aerosil 200 as solid carrier

Preparation and Evaluation of OLM S-SNEDDS

Buchi Mini Spray Dryer

PHARMACOKINETIC STUDY

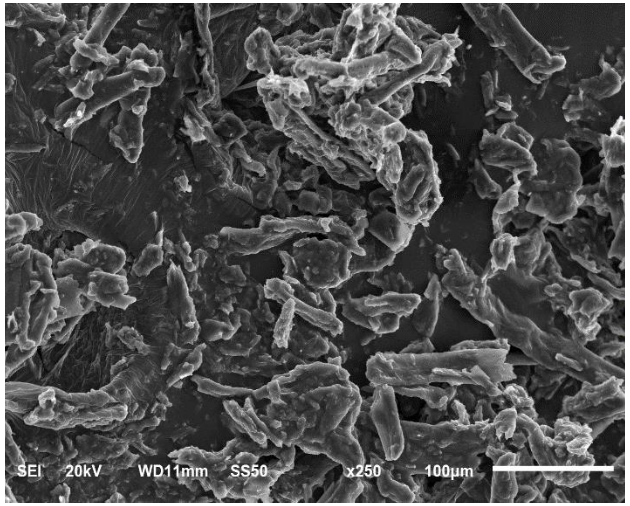
PREPARATION AND EVALUATION OF OLM S-SNEDDS

Two optimized SNEDDS formulae were selected to be converted into S-SNEDDS.

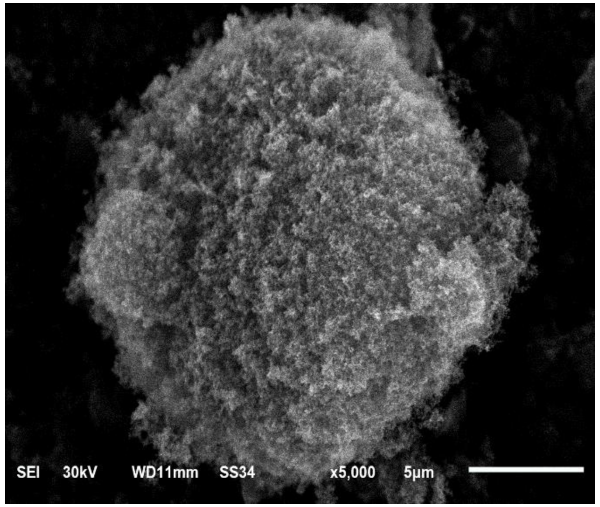
MICROMERITIC PROPERTIES FOR OLM

Formula	F3	F4
Angle of Repose	27·64°±1·03	22·79°±2·22
Bulk Density (g/ml)	0·49±0·02	0·51±0·03
Tapped Density (g/ml)	0·59±0·02	0·54±0·01
Carr's index (%)	14·32±1·72	12·41±0·95
Hausner's ratio	1·22±0·10	1·08±0·08

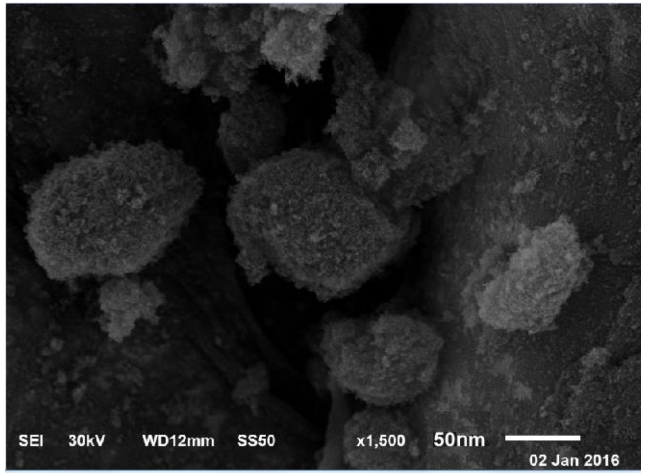
2. SCANNING ELECTRON MICROSCOPY (SEM)



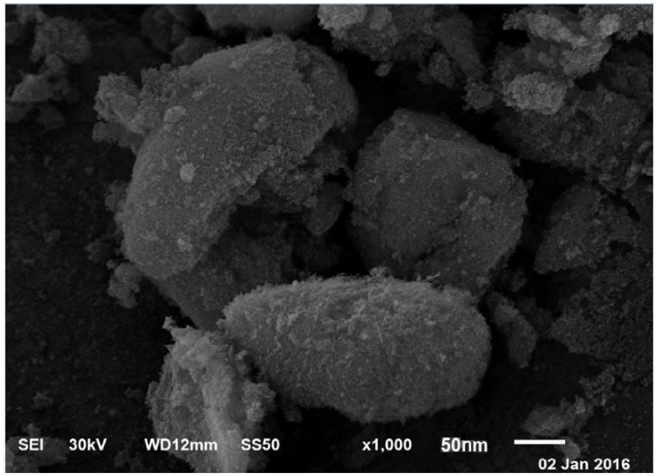
OLM



Aerosil 200


SEI 30kV WD12mm SS50 x1,500 50nm
02 Jan 2016

OLM (F3)


SEI 30kV WD12mm SS50 x1,000 50nm
02 Jan 2016

OLM (F4)

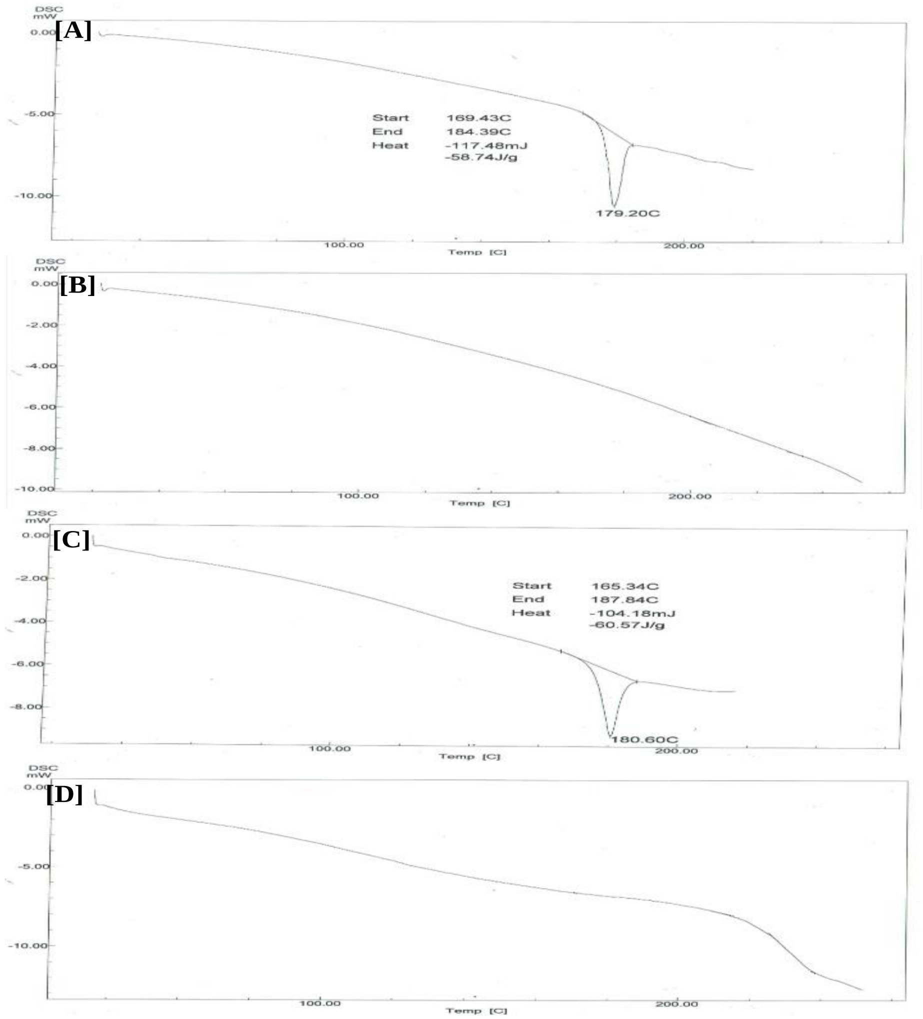
DSC thermograms of

(A)pure OLM

(B) Aerosil 200

(C) physical mixture of OLM and Aerosil 200

(D) OLM S-SNEDDS formula (F3)



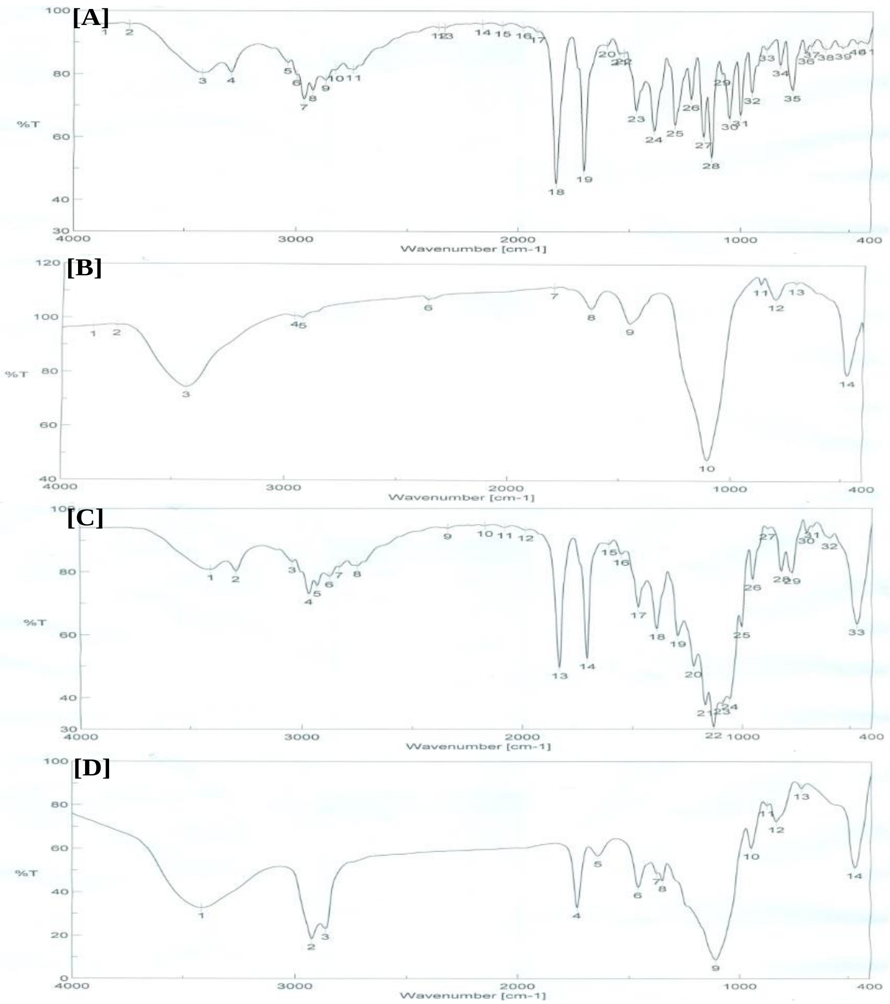
FTIR spectra of

(A) Pure OLM

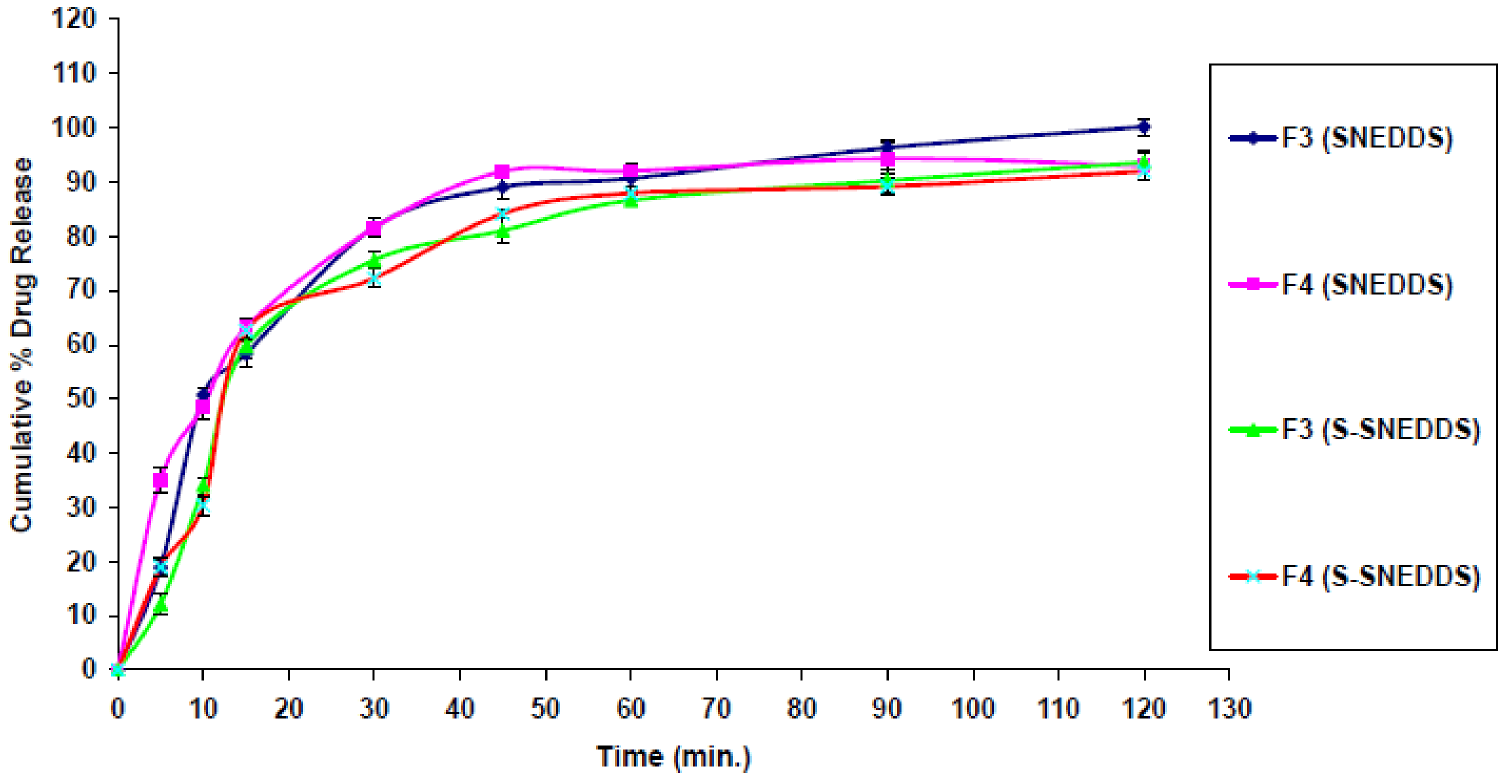
(B) Aerosil 200

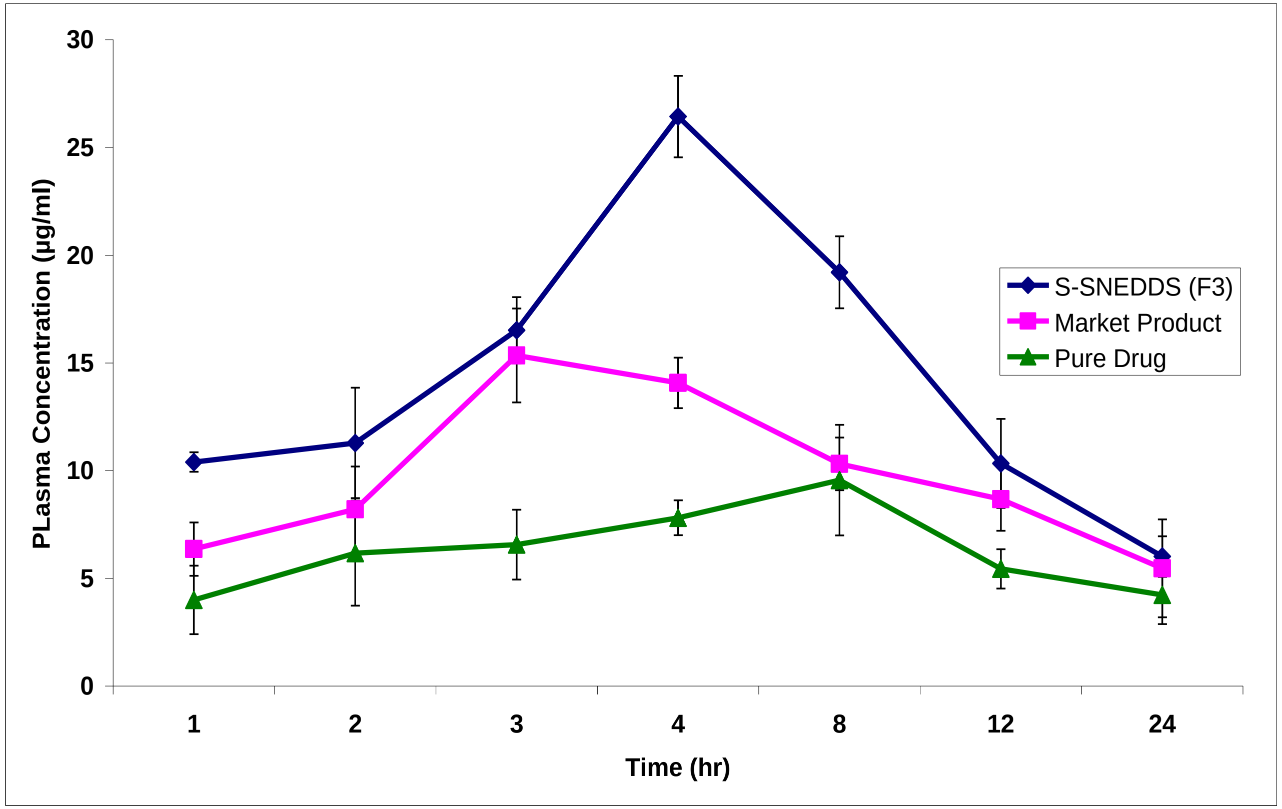
(C) Physical mixture of OLM and Aerosil 200

(D) OLM S-SNEDDS formula (F3)



COMPARISON STUDY OF IN VITRO RELEASE PROFILES OF OLM SNEDDS FORMULAE AND S-SNEDDS FORMULAE (F3 & F4).





Plasma concentration-time profiles of OLM after oral administration of optimized S-SNEDDS formula (F3), Marketed product and pure drug in rats (n=6)

PHARMACOKINETIC PARAMETERS OF OLM AFTER ORAL ADMINISTRATION OF OPTIMIZED S-SNEDDS FORMULA (F3), MARKETED PRODUCT AND PURE DRUG IN RATS.

PK Parameters	S-SNEDDS (F3)	Marketed Product	Drug Suspension
C_{max} (μg/mL)	26.4320 ± 1.89	15.3365 ± 2.18	9.5562 ± 2.37
t_{max} (h)	4	3	8
AUC_{0-24h} (μg·h/mL)	299.7304 ± 4.15	208.3887 ± 6.47	143.2684 ± 3.59
$t_{1/2}$ (h)	7.2489 ± 1.87	6.2488 ± 0.94	6.0896 ± 1.02
K_e (h^{-1})	0.0956 ± 0.002	0.1109 ± 0.004	0.1138 ± 0.001

The relative bioavailability of OLM in S-SNEDDS formula was about 1.44 fold compared with marketed product.

Conclusion

SNEDDS are promising carriers for the oral delivery of OLM.

S-SNEDDS can be considered as novel and commercially feasible alternative to current marketed OLM.

Finally, the oral delivery of hydrophobic drugs can be made possible by S-SNEDDS.

YOU CAN CITE THIS WORK THROUGH

Nasr, A.; Gardouh, A.; Ghorab, M. Novel Solid Self-Nanoemulsifying Drug Delivery System (S-SNEDDS) for Oral Delivery of Olmesartan Medoxomil: Design, Formulation, Pharmacokinetic and Bioavailability Evaluation. *Pharmaceutics* **2016**, *8*, 20.

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Article

Novel Solid Self-Nanoemulsifying Drug Delivery System (S-SNEDDS) for Oral Delivery of Olmesartan Medoxomil: Design, Formulation, Pharmacokinetic and Bioavailability Evaluation

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Abstract: The main purpose of this study was to develop a solid self-nanoemulsifying drug delivery system (S-SNEDDS) of Olmesartan (OLM) for enhancement of its solubility and dissolution rate. In this study, liquid SNEDDS containing Olmesartan was formulated and further developed into a solid form by the spray drying technique using Aerosil 200 as a solid carrier. Based on the preliminary screening of different unloaded SNEDDS formulae, eight formulae of OLM loaded SNEEDS were prepared using Capryol 90, Cremophor RH40 and Transcutol HP as oil, surfactant and cosurfactant, respectively. Results showed that the mean droplet size of all reconstituted SNEDDS was found to be in the nanometric range (14.91–22.97 nm) with optimum PDI values (0.036–0.241). All formulae also showed rapid emulsification time (15.46 ± 1.34–24.17 ± 1.47 s), good optical clarity ($98.33\% \pm 0.16\%$–$99.87\% \pm 0.31\%$) and high drug loading efficiency ($96.41\% \pm 1.20\%$–$99.65\% \pm 1.11\%$). TEM analysis revealed the formation of spherical and homogeneous droplets with a size smaller than 50 nm. In vitro release of OLM from SNEDDS formulae showed that more than 90% of OLM released in approximately 90 min. Optimized SNEDDS formulae were selected to be developed into S-SNEDDS using the spray drying technique. The prepared S-SNEDDS formulae were evaluated for flow properties, differential scanning calorimetry (DSC), scanning electron microscopy (SEM), reconstitution properties, drug content and in vitro dissolution study. It was found that S-SNEDDS formulae showed good flow properties and high drug content. Reconstitution properties of S-SNEDDS showed spontaneous self-nanoemulsification and no sign of phase separation. DSC thermograms revealed that OLM was in solubilized form and FTIR supported these findings. SEM photographs showed smooth uniform surface of S-SNEDDS with less aggregation. Results of the in vitro drug release showed that there was great enhancement in the dissolution rate of OLM. To clarify the possible improvement in pharmacokinetic behavior of OLM S-SNEDDS, plasma concentration-time curve profiles of OLM after the oral administration of optimized S-SNEDDS formula (F3) were compared to marketed product and pure drug in suspension. At all time points, it was observed that OLM plasma concentrations in rats treated with S-SNEDDS were significantly higher than those treated with the drug in suspension and marketed product.

Keywords: Olmesartan; solid self-nanoemulsifying drug delivery system (S-SNEDDS); Capryol 90; Cremophor RH40; Transcutol HP; Aerosil 200; spray drying

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time for questions