TARGETED DRUG DELIVERY SYSTEM

❖ CONTENTS:-

- Concept
- Approaches
- Advantages
- Disadvantages
- Introduction to liposomes
- Niosomes
- Nanoparticles
- Monoclonal Antibodies & their applications

❖ CONCEPT:-

Targeted drug delivery is a system of specifying the drug moiety directly into its targeted body area (organ, cellular and subcellular level of specific tissue) to overcome the aspecific toxic effect of conventional drug delivery, thereby reducing the amount of drug required for therapeutic efficacy delivery.

Targeted is special form of drug delivery system where medicament is selectively targeted only to site of action.

This means of delivery is largely founded on nanoparticles.

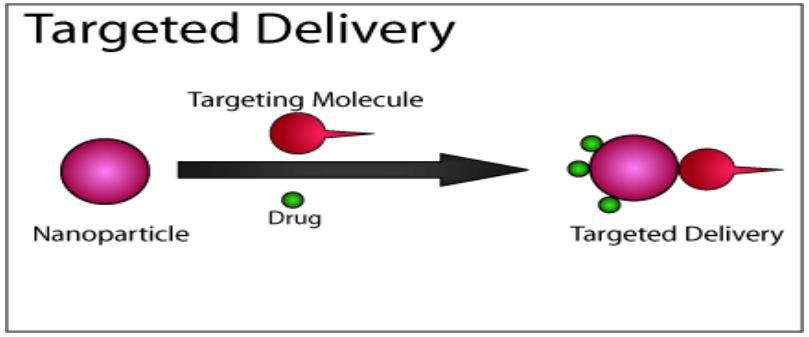


FIG. (1): CONCEPT OF DRUG TARGETING

❖ APPROACHES:-

The basic approaches for targeting the drug to specific site based on different research outcome may be categories broadly in to following:

1. Controlling the distribution of drug by incorporating it in carrier system.
2. Altering the structure of the drug at molecular level.
3. Controlling the input of the drug into bio-environment to ensure a programmed and desirable bio-distribution.

For the fulfilment of this conditions, two approaches are used extensively

1 .Passive targeting. 2. Active targeting

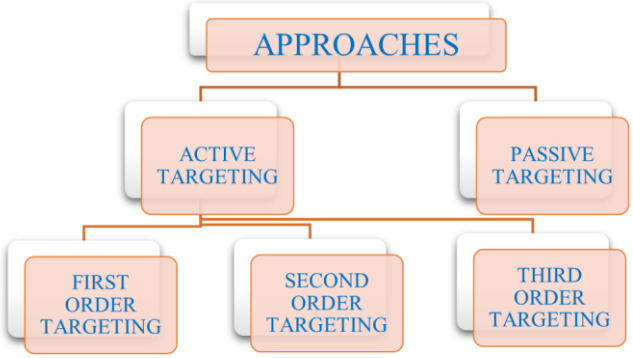


FIG. (2): APPROACHES OF DRUG TARGETING

- **PASSIVE TARGETING:-**

  System that target the systemic circulation are generally characterized as "passive" delivery system.

- **ACTIVE TARGETING:-**

  Conceptually, Active targeting exploits modification or manipulation of drug carrier to redefine its biofate.

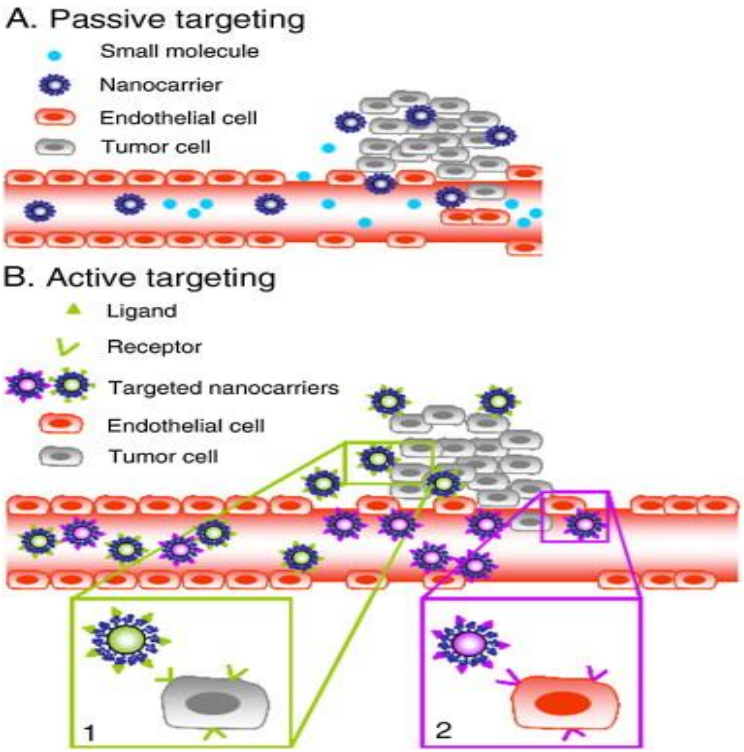


FIG. (3): ACTIVE AND PASSIVE TARGETING

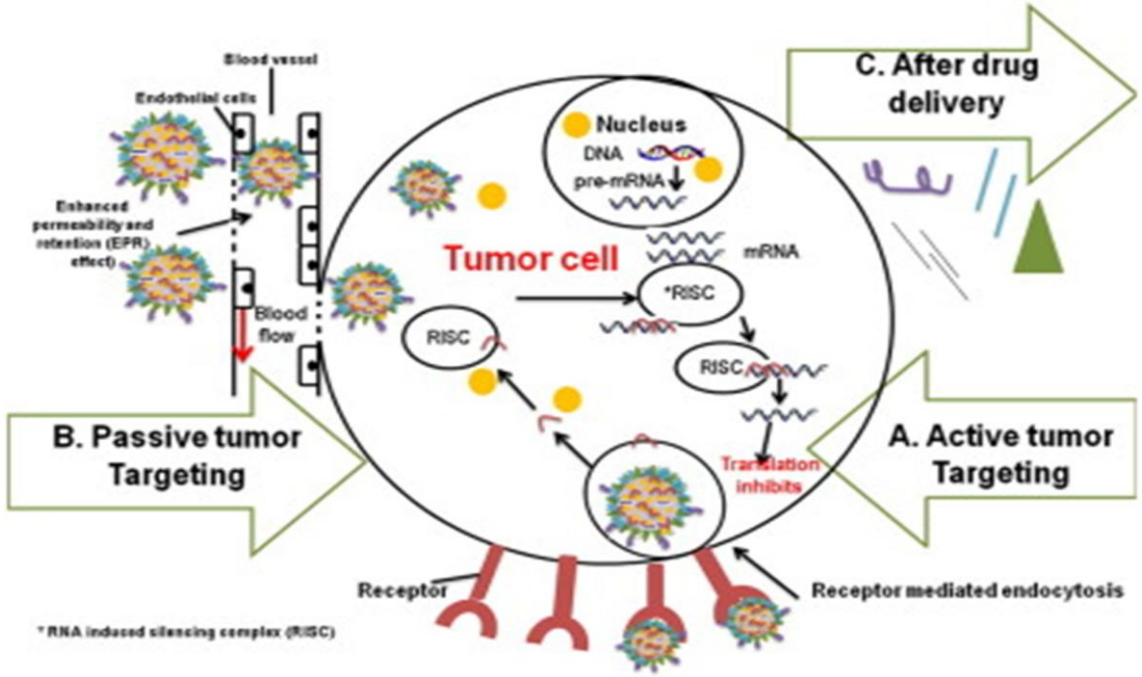


FIG. (4): CONCEPT OF ACTIVE AND PASSIVE TARGETING SYSTEM

❖ ADVANTAGES:-	❖ DISADVANTAGES:-
1) Toxicity reduced, decreased harmful systemic effect. 2) Drugs smaller dose gives desired effect. 3) Avoidance of first pass metabolism.	1) Requires highly sophisticated technology for formulations. 2) Requires skill for manufacturing. 3) Drug loading is usually low, For e.g. micelles.

❖ HISTORY:-

The concept of targeted drugs was first proposed on 1906 by scientist “Paul Ehrlic”. As a theoretical concept it become most popular and site-specific treatment, but still the “Magic Bullet” continues to be a challenge to implement clinically. Then Bangham’s observation (1965) led to discovery of Artificial vesicular system based on phosphor lipid amphiphiles.

FIG. (5): Paul Ehrlic

❖ LIPOSOME :-

The name liposome is derived from two Greek words: 'Lipos' meaning fat and 'Soma' meaning 'Body'.

Liposomes are concentric bilayered vesicles in which an aqueous volume is entirely enclosed by a membranous lipid bilayer mainly composed of phospholipids.

Liposome was found by Alec Bangham of Babraham Institute in Cambridge, England in 1965. In 1990, drugs with liposome and Amphotericin B were approved by Ireland.

Liposomes are spherical, self- closed structure formed by one or several concentric lipid bilayer with an aqueous phase inside.
There are no. of component of liposomes however lecithin (mix of phospholipids) and cholesterol being main components.
They have to be specified designed to release the encapsulated drug in target site.

Provides selective passive targeting to tumor tissues

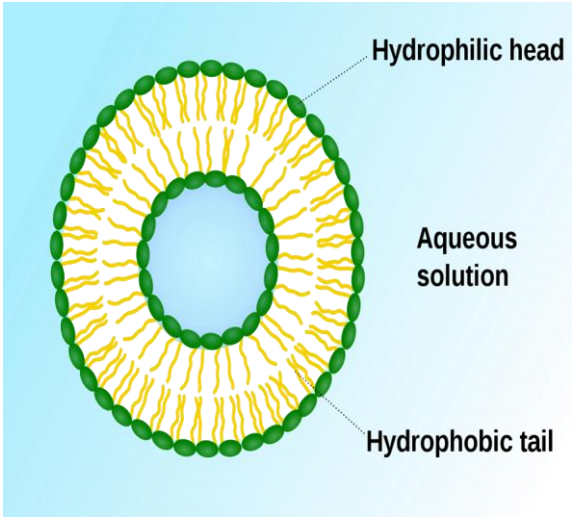


FIG.(6): STRUCTURE OF LIPOSOME

ADVANTAGES:-

1) Biocompatible
2) Completely Biodegradable
3) Non-toxic
4) Flexible
5) Non-immunogenic
6) Provide selective passive targeting to tumors
7) Increase efficacy and therapeutic index.
8) Can be formulated into multiple dosage form.

DISADVANTAGES:-

1) Production cost is high.
2) Leakage and fusion of encapsulated drug or molecule.
3) Short half life
4) Low solubility
5) Sometimes phospholipid undergoes oxidation and hydrolysis like reaction.
6) Fast elimination from blood and localization in reticuloendothelial system

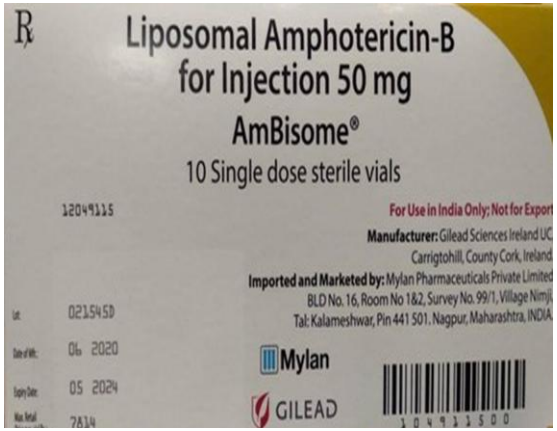


FIG.(7):MARKETED PRODUCT OF LIPOSOME

TYPES OF LIPOSOME:- LAMELLA: is a flat plate like structure that appears during the formation of liposomes. The phospholipid bilayer first exists as a lamella before getting converted into spheres.

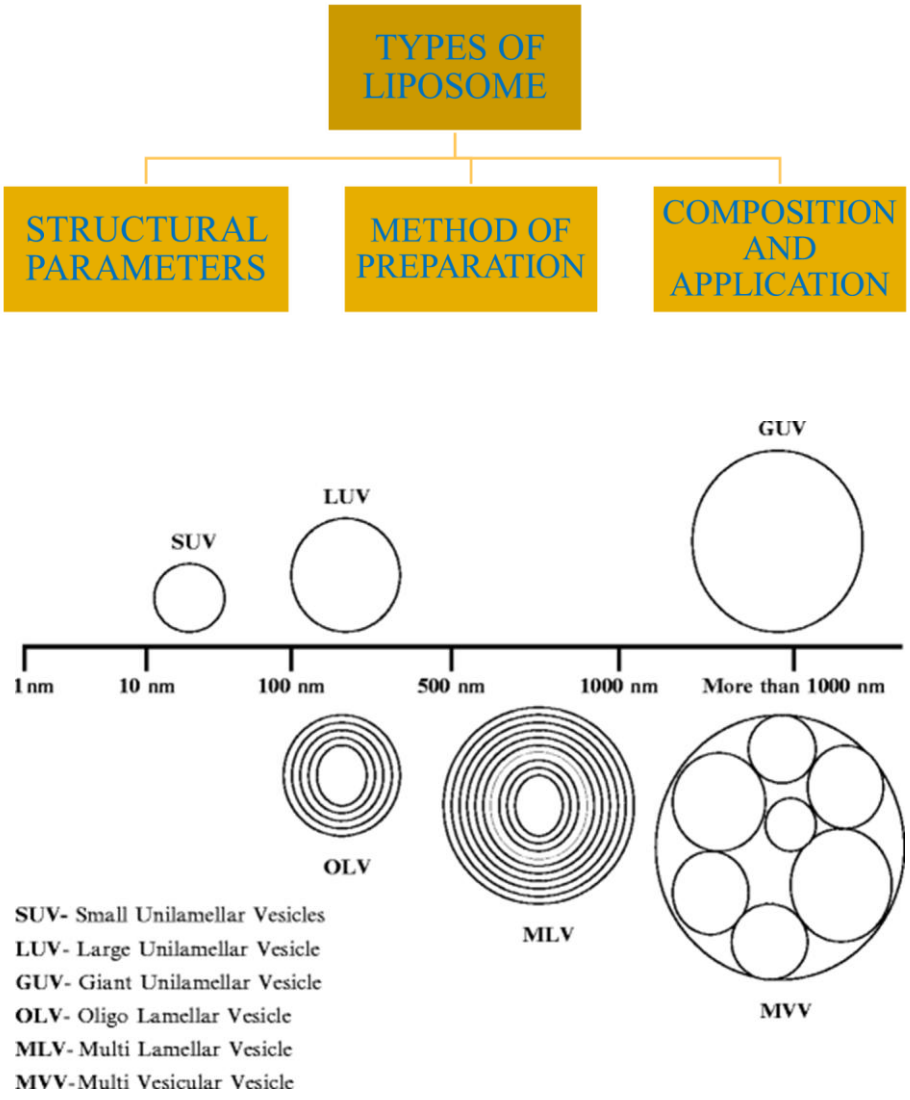
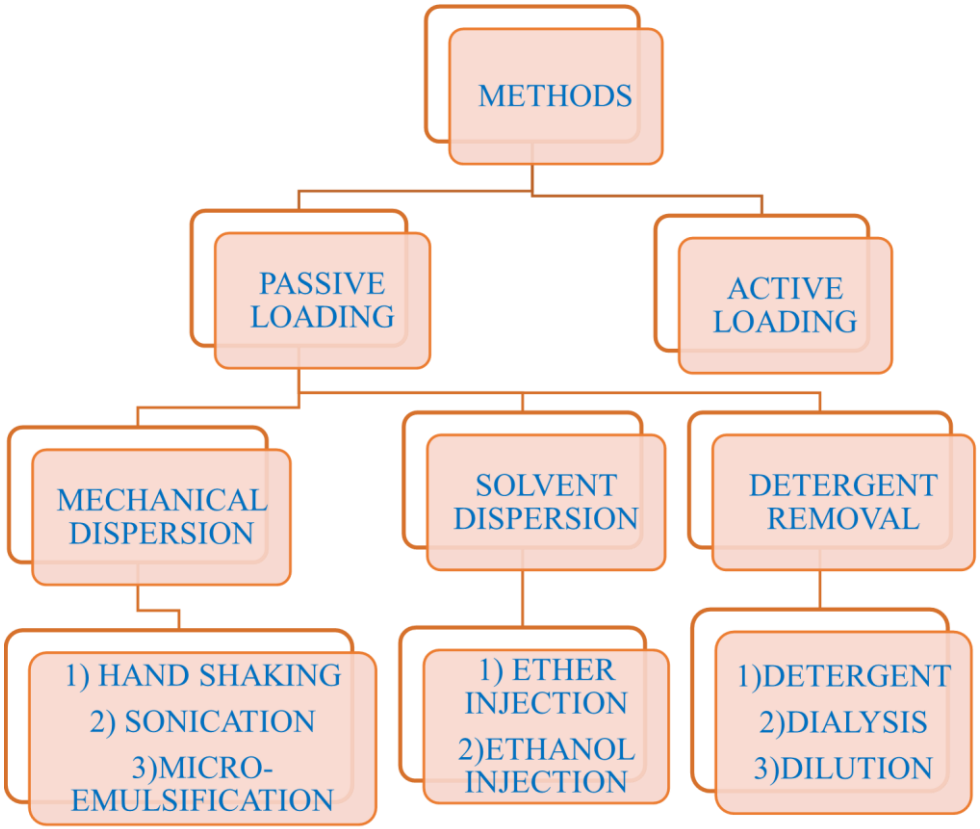


FIG. (8): SIZE RANGES OF LIPOSOMES

METHOD OF LIPOSOME PREPARATION:-



APPLICATIONS OF LIPOSOME:-

SOLUBALISATION	SUSTAINED RELEASED	ACCUMULATION
• FUNGAL INFECTION • EX:- • AMPHOTERICIN B, DOXORUBIN	• CANCER • EX:- • SYSTEMIC ANTINEOPLASTIC DRUGS	• CARDIOVASCULAR DISEASE • EX:- • PROSTAGLANDINS

❖ NIOSOME:-

Niosomes are non-ionic surfactant based unilamellar or multilamellar bilayer vesicles.

These are formed upon hydration of non-ionic surfactants with or without incorporation of Cholesterol.

The niosomes are very small and microscopic in size. Their size lies in the nanometric scale.

Both hydrophilic & lipophilic drugs, can be entrapped either in aqueous layer or in lipid layer.

The two main components used for the preparation of niosomes are,

1. Cholesterol 2. Non-ionic Surfactant.

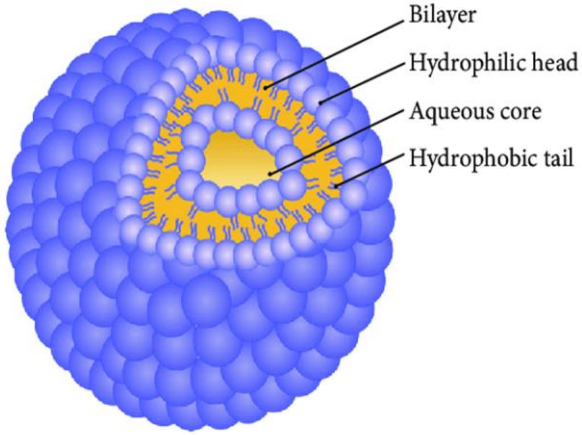


FIG. (9): STRUCTURE OF NIOSOME

ADVANTAGES:-

- They are osmotically active &stable.
- They increase the the stability of the entrapped drug.
- Biodegradable, non-immunogenic &biocompatible.

DISADVANTAGES:-

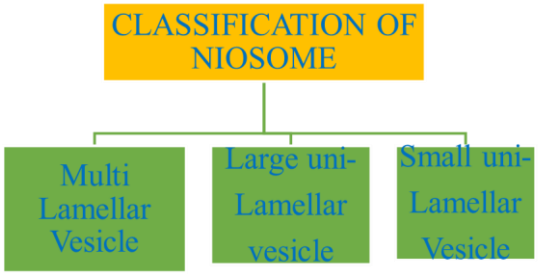
- Aggregation
- fusion
- Leaking of entrapped drug.

FIG. (10): MARKETED PRODUCT OF NIOSOME

METHOD OF PREPARATION:-

- Hand shaking method
- Reverse phase evaporation technique
- Ether injection method
- Multiple membrane extrusion method

CLASSIFICATION:-



APPLICATIONS:-

1) Drug Targeting
2) In Diagnosis
3) Leishmaniasis
4) Delivery of Peptide Drugs
5) Niosomes as a carriers for haemoglobin
6) To organs other than RES.

❖ NANOPARTICLES:-

Nano derives from the Greek word ‘Nanos’ means dwarf or extremely small.

Nano capsules are the ones in which the drug is confined to an aqueous or oily core surrounded by a shell- like wall.

Alternatively the drug can be covalently attached to the surface or into the matrix

Nano particle are 10-1000 nm (1µ) sized solid, colloidal particles.

One can distinguished two types of nanoparticles:

1. Nanospheres
2. Nanocapsule

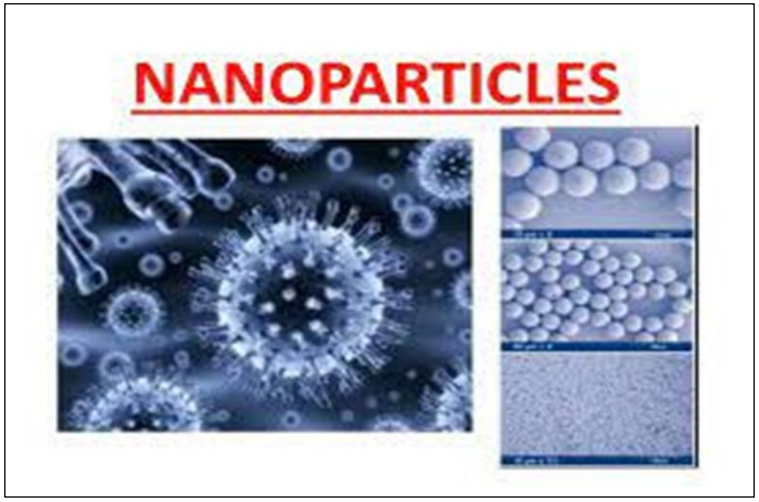


FIG. (11): STRUCTURE OF NANOPARTICLES

METHOD OF PREPARATION:-

a) Amphiphilic Macromolecules Cross Linking	• Heat crosslinking • Chemical crosslinking
b) Polymerization Method	• Emulsion polymerization • Dispersion polymerization • Interfacial condensation polymerization • Interfacial complexion
c) Polymer Precipitation Method	• Solvent evaporation method • Solvent displacement • Salting out

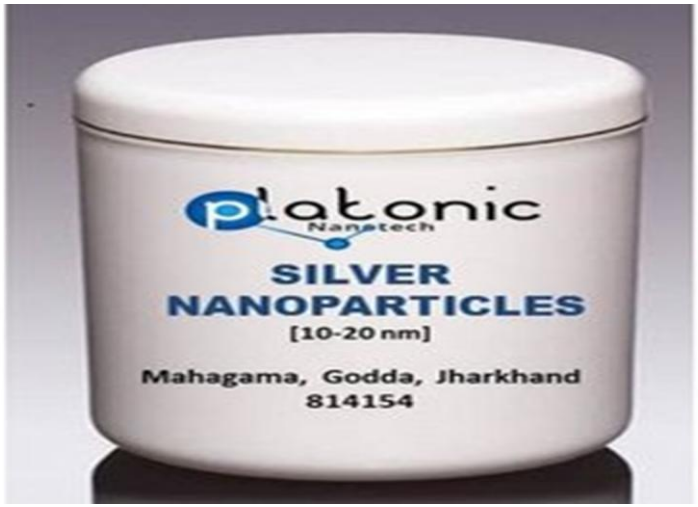


FIG. (12): MARKETED PRODUCT OF NANOPARTICLES

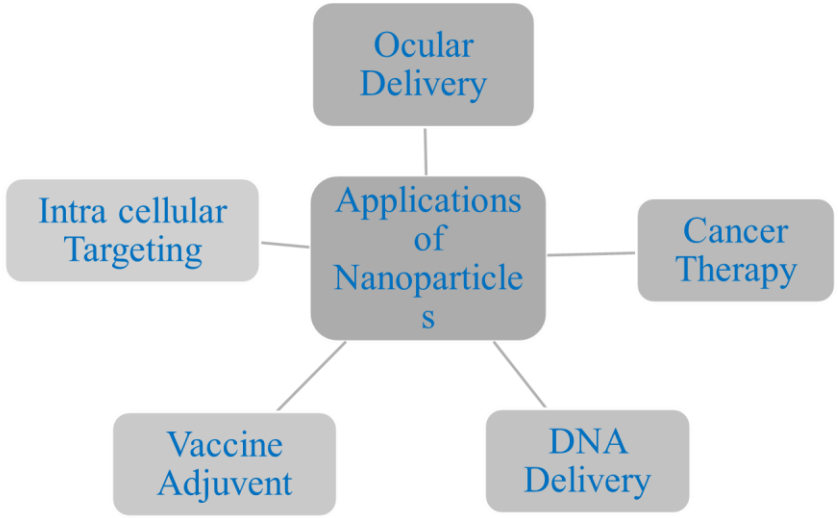
ADVANTAGES: -

1) More uniform effect of drug.
2) Reduction in frequency of dosage.
3) Site specific targeting.
4) Various routes of administration.
5) Better drug utilization and less side effects

DISADVANTAGES: -

1) High cost
2) Productivity more difficult.
3) Reduced ability to adjust the dose.
4) Requires high skill to manufacture.
5) Highly sophisticated technology.
6) Difficult to maintain stability of dosage form.

APPLICATIONS:-



❖ MONOCLONAL ANTIBODIES:-

ANTIBODY: - is a protein used by immune system to identify and neutralize foreign objects like bacteria and viruses. Each antibody recognizes a specific antigen unique to its target.

MONOCLONAL ANTIBODIES: - are identical immunoglobulin's, generated from a single B – cell clone.

These antibodies recognize unique epitopes or binding sites on a single antigen

Derivation from a single B – cell clones and subsequent targeting of a single epitome is what differentiates monoclonal antibodies from polyclonal antibodies.

Various clinical and pre-clinical studies have been performed with monoclonal antibodies and derivatives.

--Most of studies based on antigen recongnistution by antibodies and to develop cancer therapy.

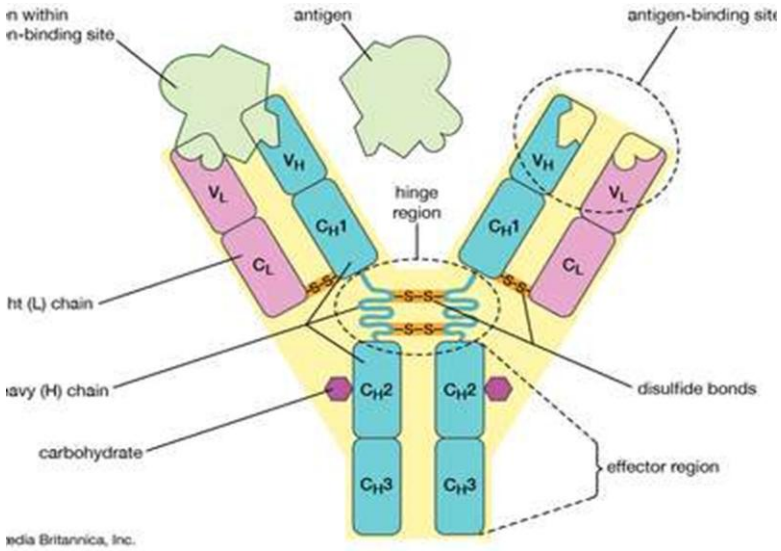


FIG. (13): MONOCLONAL ANTIBODY

ADVANTAGES:-

- Side effects can be treated
- Bind to specific diseased
- Treat wide range of conditions

DISADVANTAGES:-

- Time consuming project
- Very expensive
- 99% of the cells do not survive.
- Possibility ofgenerating immunogenecity

APPLICATION:-

- For immunosuppression
- For Cancetr Diagnosis
- For Antigen Purification
- For Passive Immunisation
- For Biochemical Analysis

METHOD OF PREPARATION:-

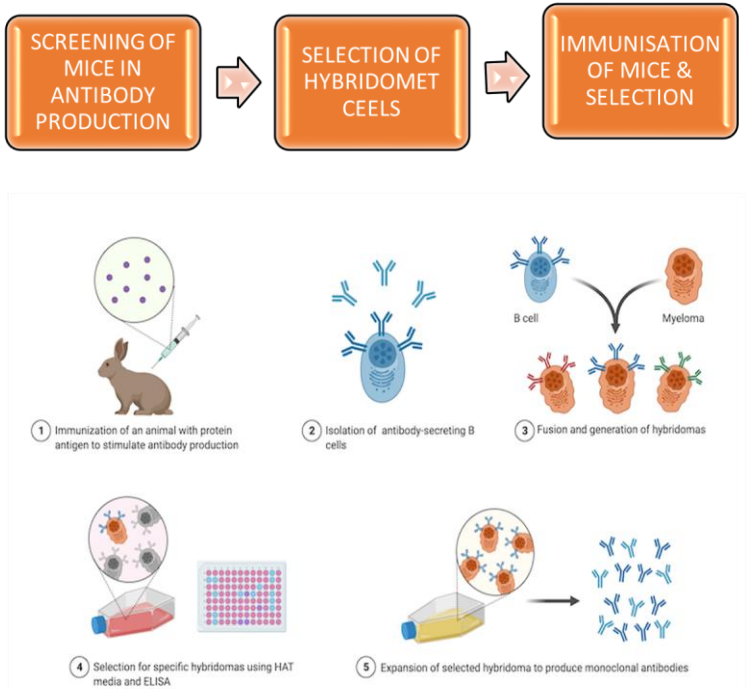


FIG. (14): PREPARATION OF ANTIBODIES

REFERENCE:-

1) S. P. Vyas and R. K. Khar, Targeted and Controlled Drug Delivery System, Novel Carrier System., 1st edition: 2002, Pg. No. 42-43, CBS Publishers & Distributed Pvt. Ltd.
2) Nagoba Shivappa et. al, American Journal of Pharmatech Research , A review on targeted drug delivery 2018, 8(4), ISSN:2249-3387
3) H. S. Mahajan et.al., Pharma times, Targeted Drug Delivery System, Vol 39- No.2, February 2007, Pg. No. 19
4) Dr. Aijaz. A. Shaikh et. al., Text book of Novel Drug Delivery System, edition 2019, Pg. No. 145-165, by PV Publication .

PREPARED BY: - 1) Bilkis Pathan

2) Alfiya Pansare

GUIDED BY: - Dr. S.Mantry

DEPARTMENT: - Pharmaceutics

SUBJECT: - Novel Drug Delivery System

CLASS:- Final Year B.Pharm.

ACEDMIC YEAR: - 2021-2022