Magnetic Drug Targeting

ADVANTAGES

- Therapeutic responses in target organs at only 1/10th of the free drug dose.
- Controlled drug release within target tissues for intervals of 30 min to 30 h, as desired.
- Avoidance of acute drug toxicity directed against endothelium & normal parenchymal cells.
- Adaptable to any part of the body.

DISADVANTAGES

- It is expensive
- It needs miniaturized specialized magnet for targeting, advanced techniques for monitoring, & trained personnel to perform procedures.
- Magnet must have relatively constant gradients, in order to avoid focal overdosing with toxic drugs.
- A large fraction (40 – 60 %) of the magnetite, which is entrapped in the carriers, may be deposited permanently in target tissues.

Magnetic delivery systems

- Magnetic microspheres
- Magnetic nanoparticles
- Magnetic liposomes
- Magnetic emulsion
- Magnetic resealed erythrocytes

Monoclonal antibody based targeted drug delivery

- The recognition site for the monoclonal antibody should be located on the surface of the cell.
- The antibodies should have sufficient tumor tissue specificity.
- The extent of localization of the antibody at the target site. Biodistribution of the drug–antibody conjugate in the body relative to that of the parent antibody.
- Stability of the drug–antibody conjugates in blood.
- The host toxicity of the conjugate. The conjugate must be biodegradable and non-immunogenic. Drugs should be released upon interaction between the carrier molecule and the cell.

Approved Monoclonal Antibodies

Antibody	Target	Indication
Trastuzumab	HER2	Breast Cancer
Bevacizumab	VEGF	Lung Cancer
Cetuximab	EGFR	Colorectal carcinoma
Panitumumab	EGFR	Colorectal carcinoma

Immunoconjugates

- The possibility of raising monoclonal antibodies against cell surface markers allow tumor site targeting discretely.

- Many cytotoxic drugs have been conjugated with monoclonal antibodies. These conjugates have been used to study drug localization in tumors and modulation o drug toxicity. They have been found to be useful in the management of various types of carcinomas.

- The conjugation of antibodies developed against a specific tumor determinant with another recognition component provides them dual specificity to target the drug or toxin intracellularly.

Bispecific antibodies

- The approach has been mainly suggested for immunotherapy of immunological disorders especially those related to lack of MHC restricted recognition by immune effectors cells.

- Bispecific antibodies against tumor endothelium & tissue factors (the initiator of the intrinsic pathway of blood conjugation) have also been proposed for synergistic effects.

Immunotoxins

- These are conjugates of antibody (Mab & Fab) fragments & toxins, in which cell binding moieties of the toxins are replaced with specific binding chain of the antibodies.

Advantages

- The naturally occurring toxins used have very specific biological pathways in producing their cytocidal effects.

- The cytotoxic activity of the toxin that is conjugated to the antibody does not involve any other secondary agent(s).

- Theoretically, immunotoxins should not bind to non-malignant cells, and even if they do bind, the internalization of the agent should not be sufficient to neutralize the therapeutic effect.

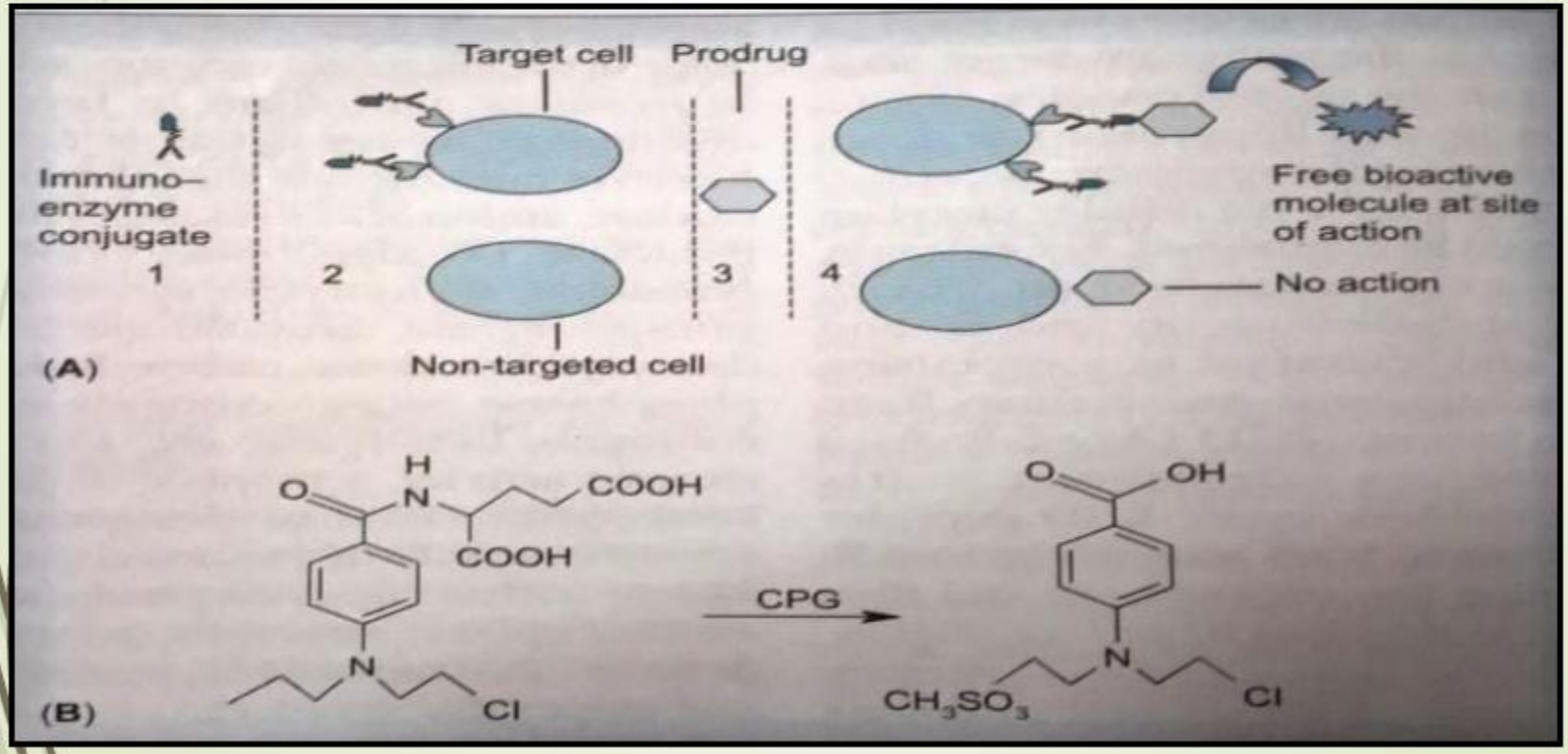
Prodrugs

- Prodrug is an inactive pharmacological moiety developed to optimize pharmacokinetics or site selectivity of a drug.
- Since the prodrug has low cytotoxicity prior to its activation, it has very few chances of its encounter with healthy cells.
- In general, selective enzyme expression, hypoxia, & low extracellular pH at tumor site is utilized for prodrug activation.
- ADEPT has been investigated in the treatment of tumors, where an antibody-enzyme conjugate is administered systemically, where it clears from the circulation & localizes to its target by virtue of the antibody binding to its specific biomarker on the tumor.

Enzymes & prodrugs used for ADEPT

Enzymes	Prodrug	Reactivity
Alkaline Phosphatase	Doxorubicin	Hydrolysis of Phosphate Group
	Etoposide	
β lactamase	Mitomycin	Cleavage of Lactam Ring
	Paclitaxel	

Schematic representation of ADEPT



Conclusion

Targeted drug delivery essentially implies for selective and effective localization of the pharmacologically–active moiety at preidentified target(s) in therapeutic concentration.

Various strategies such as active targeting, passive targeting etc. can be applied to achieve efficient drug targeting.

The targeted delivery is of great importance in cancer chemotherapy which always demands for reduction in adverse effect.