Distinct characteristics of nab Paclitaxel from solvent based Paclitaxel in anti tumour activity:

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ABSTRACT:

The plasma paclitaxel-time profile is sensitive to tissue distribution and decomposition of paclitaxel-carrier complexes, but the tissue distribution profile is highly sensitive. Tissue distribution is carrier complex system-dependent, making the paclitaxel plasma profile a poor predictor of clinical outcomes.[1]This review provides a summary of Paclitaxel involving the use of albumin as a drug delivery tool for getting better the pharmacokinetics of a drug by developing the targeted drug delivery systems in antitumour activity. Nanotechnology is a highly active research area due to its potential to enhance the solubility of Paclitaxel and improve its pharmacokinetic profile and decrease side effects, target tumor sites passively or actively.[2] Albumin, a unique nanocarrier with an extended serum half-life of 19 days, can interact with overexpressed receptors in diseased tissues and cells, allowing active targeting of disease sites without specific ligands.[3]

INTRODUCTION:

Human serum albumin, an abundant protein in the body, is used in various applications such as nephrotic syndrome, blood replacement, burn treatment, and cancer treatment. It is also a versatile drug delivery tool, used in conjugates, nanoparticles, and complexes loaded with drugs, peptides, and antibodies.[4] Albumin is highly soluble in hydrophobic drugs like paclitaxel and can be transported across blood vessels via the gp60 albumin receptor, activating caveolae-mediated endothelial transcytosis. It is abundant in tumors, where tumor cells use it as energy and nitrogen source.[5] Nanotechnology holds significant potential in pharmaceutical applications, especially in drug delivery, as nanomaterials enable efficient administration, protection, and transport of therapeutic agents, but their structure can limit targeted delivery.[3]

Solvent based Paclitaxel:

Paclitaxel (PTX) is a crucial chemotherapeutic agent from the taxane family. The widely used medication paclitaxel is used to treat lung, breast cancer and for the second-line treatment of AIDS-related Kaposi's sarcoma[6] by promoting tubulin to assemble into abnormal microtubules, which causes chromosomal missegregation and prevents mitosis and cell division, ultimately leading to the death of tumour cells.[7]

Paclitaxel's clinical development is hindered by its low solubility and lack of modifiable functional moieties. The selection of a suitable delivery system is crucial for improving its clinical development, safety, and efficiency, as it lacks modifiable functional moieties in its structure.[8] PTX, a P-gp substrate, has poor aqueous solubility and low permeability due to its molecular weight, hydrogen bond acceptor, and polar surface area. This results in a permeability coefficient of 10-6 cm/s, making it difficult to deliver via oral routes. Consequently, PTX is administered via intravenous (IV) with a suitable cosolvent, causing adverse effects like acro-anesthesia and neurovirulence, leading to pain and high costs.[8] Due to the low water solubility of Paclitaxel, it is formulated in a mixture of Cremophor EL and dehydrated ethanol. However, Paclitaxel has severe side effects, necessitating the development of alternative formulations. Non-toxic nano-delivery systems can protect the drug, lower toxicity, increase circulation half-life, improve pharmacokinetic profiles, and improve patient compliance, while reducing side effects.[2]

Solvent free Paclitaxel with nab technology:

Taxanes are the microtubule stabilizers that inhibit mitosis, motility, and intracellular transport, leading to apoptotic cell death. They are hydrophobic and have side effects like hypersensitivity reactions and neuropathies. Cremaphor EL is the most feasible option for solubilizing paclitaxel for intravenous administration. To improve therapeutic index, solvent-free formulations and delivery systems have been investigated, with nab-paclitaxel being the first successful attempt.[9] Nab-paclitaxel is a solvent free paclitaxel formulation for drug delivery based on nab-technology, Clinical trials show it improves response rates and progression-free survival in breast cancer patients. It is currently being studied for lung and ovarian cancers. The nab formulation allows safe infusion without premedications, with peripheral sensory neuropathy and myelosuppression as main adverse effects. [10]

The study compared the delivery efficiency of various nanoformulations in various tissues. Paclitaxel showed weak delivery efficiency in most tissues, except for the intestine and fiver. Nanoformulations like m-nab-P (mouse albumin nab Paclitaxel) and nab-P improved delivery efficiency in most tissues. Nab-P was associated with greater efficiency in pancreas, stomach, kidney, lung, spleen, and bone.[11]Recent studies show that nab-paclitaxel has distinct pharmacologic features compared to sb-paclitaxel (solvent based Paclitaxel), which may contribute to differences in clinical safety and efficacy. Nab-paclitaxel has faster and deeper tissue penetration and slower elimination compared to sb-paclitaxel. Tissue distribution depends on the drug carrier complex, indicating that more paclitaxel may enter the tumor and reduce systemic exposure duration. This may explain the lower frequency of severe adverse events like neutropenia with nab-paclitaxel despite higher dose intensity.[10]

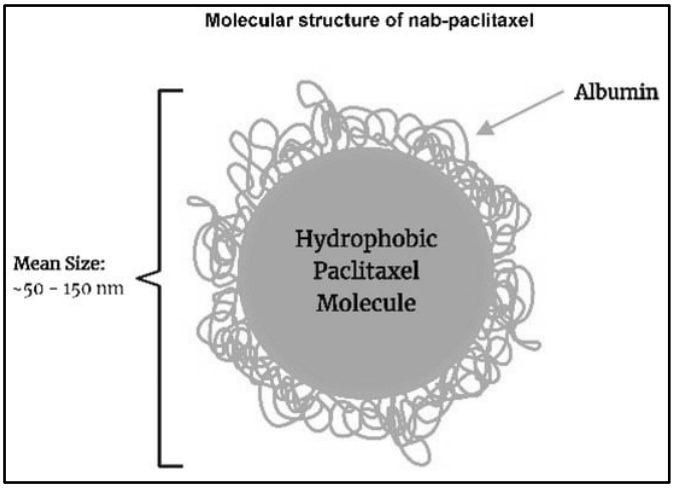

Fig: 1[12]

CONCLUSION:

The clinical success of nab-paclitaxel demonstrates the significant potential of nab technology and albumin-based drug delivery platforms, leveraging the natural properties of albumin and tumor biology. Human serum albumin is a versatile drug delivery tool used in various applications, including nephrotic syndrome, blood replacement, burn treatment, and cancer treatment. Nanotechnology holds significant potential in pharmaceutical applications, especially in drug delivery. Paclitaxel, a crucial chemotherapeutic agent, is used to treat lung, breast cancer, and AIDS-related Kaposi's sarcoma. However, its clinical development is hindered by low solubility and lack of modifiable functional moieties. Non-toxic nano-delivery

systems can protect the drug, lower toxicity, increase circulation half-life, improve pharmacokinetic profiles, and improve patient compliance. Solvent-free paclitaxel with nab technology has been investigated for improving therapeutic index, response rates, and progression-free survival in cancer patients. This review emphasizes albumin's importance as a nanodrug delivery carrier for hydrophobic drugs, leveraging its passive and active targeting potential. Nab-paclitaxel showed superior transport across endothelial cells, greater penetration and cytotoxic induction in xenograft tumors, and enhanced extravascular distribution in patients, indicating its distinct clinical efficacy and toxicity profile.[5]

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