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A REVIEW ON ADVANCEMENT OF CONTROLLED RELEASE TECHNOLOGIES IN PHARMACEUTICALS

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ABSTRACT

The number of clinical applications for nanoparticles has exploded recently. Nanoparticles were created to circumvent systemic, microenvironmental, and cellular biological obstacles. Precision medicines, which use tailored ways to improve therapy efficacy, have overcome patient heterogeneity. Still, one-size-fits-all nanoparticles are produced. In the age of precision medicine, nanoparticles made of lipids, polymers, and inorganic materials may now be created with greater precision than ever before. This review focuses on non-personalized and precise nanoparticle applications. Our research shows that intelligent nanoparticle design can boost efficacy in general distribution applications while allowing customized designs for precision applications, eventually improving patient outcomes.

INTRODUCTION

Many promising treatments have failed due to poor delivery systems. The therapeutic landscape has changed due to changing drug delivery requirements, methodologies, and technology. Small-molecule medicines were the most popular treatment at the time.1,2 Initially, delivery attempts aimed to improve drug solubility, release, action, and pharmacokinetics 5,6. Various treatments have been developed over time. Biological macromolecules include proteins, peptides, monoclonal antibodies, nucleic acids, and living cells.3,4,5 Other issues arose from novel activities, such as protein and peptide stability and intracellular transport requirements (especially for nucleic acids).7 New drug delivery systems were required to solve these concerns. There are five therapeutic classes: nucleic acids, peptides, proteins, and cells. Modifying the drug's microenvironment, establishing an interface (i.e., a drug delivery system) to manage interactions between the drug and its microenvironment (Fig. 1).[8]

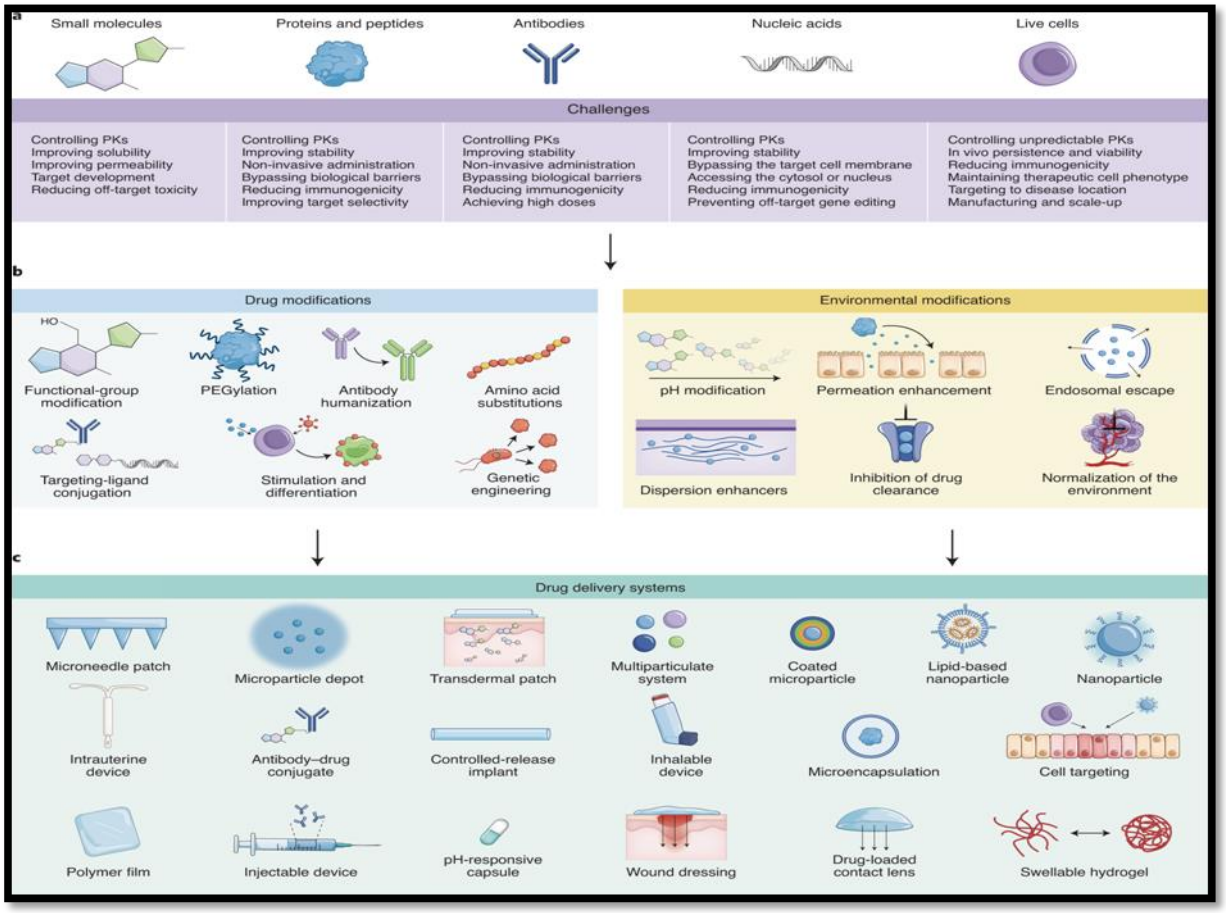

Fig: 1 Class of therapeutic and delivery paradigms

3DP technologies applicable for pharmaceutical development

Various 3DP systems have been produced by altering the energy, material, and mechanical factors. [7,8] 3DP technologies like inkjet, nozzle deposition, and laser writing are widely utilized in the pharmaceutical industry and categorized into various subtypes based on materials and energy sources. 3DP technologies have various qualities, which are summarised here.

Printing-based inkjet (IJ) system

Inkjet systems (CIJ and DOD) print on demand or continuously (DOD). In CIJ and DOD technologies, high-pressure pumps create droplets 10–50 m in diameter and 0.5–70 pL in volume. [9]The drop size, speed, and interval must be adjusted in both IJ systems. Also, fluid viscosity must be considered. The DOD system supports thermal and piezoelectric printer heads. Thermal DOD printing is used to heat and expel ink by forming bubbles. An acoustic pulse generated by a piezoelectric crystal's rapidly changing form is sufficient to produce ink. Thermal DOD is only suited for volatile liquids, whereas piezoelectric is suitable for a wide range of liquids. Piezoelectric DOD can be used at room temperature with less volatile and biocompatible liquids than thermal DOD, which can reach temperatures up to 300 °C.[10]

Drop-on-solid and drop-on-drop deposition are both DOD technologies. Drop-on-drop deposition uses drops to build a 3D structure with high precision. This direct writing IJ-printing technology can manufacture nanoscale drug delivery systems with varied geometries. A droplet's diameter is 100 nanometers.[11] To guarantee rapid jetting and solidification, the printed fluid must be flawless. The printed fluid's viscosity and volatility must be carefully controlled to minimize coffee ringing, fluid

leakage, and nozzle blockage. The ideal viscosity is found to be between 8 and 14 cps. [13] The drug's physical, therapeutic, loading, and stability qualities are all examined. It is possible to pharmacoprint an extensive range of pharmaceuticals using drop on solid deposition, which is more versatile than drop on a drop. [14]Powder bed 3DP uses a process called drop-on-solid deposition. It is also called drop-on-powder or drop-on-bed deposition, binder jetting, plaster printing, or powder bed 3DP (a liquid ink). After the 3D structure is constructed, the platform is lowered, and a new powder layer is applied. [12-15]A 200 microns high ink-binding powder bed with particle sizes of 50 to 100 microns is used to generate 3D objects. Layer thickness and spacing can be changed to optimize layer adherence. To produce high-quality goods, powder bed reactivity with binder ink and topological features must be considered. [16]

Nozzle-based deposition systems

The most common printing-based IJ technique lacks hardness, has a rough surface, and has modest drug loadings. Solid components are mixed with the binder and then placed straight into the build chamber during 3D printing.[17] The method has two subcategories: fusion deposition modeling (FDM) and microsyringe pressure aided microsyringes (MPAM) (PAM). FDM is also one of the most extensively used 3DP technologies, with numerous applications. In FDM, an extruded thermoplastic polymer filament is layered onto a build plate and solidifies instantly. Figure 1a shows FDM in operation. The API and thermoplastic polymer are melted together before extrusion.[18]Flexible manufacturing technology (FDM) can produce complicated pharmaceuticals with complex geometries at a low cost. One of the technology's flaws is the need for biodegradable thermoplastic polymers with suitable extrusion melt viscosity.[19]

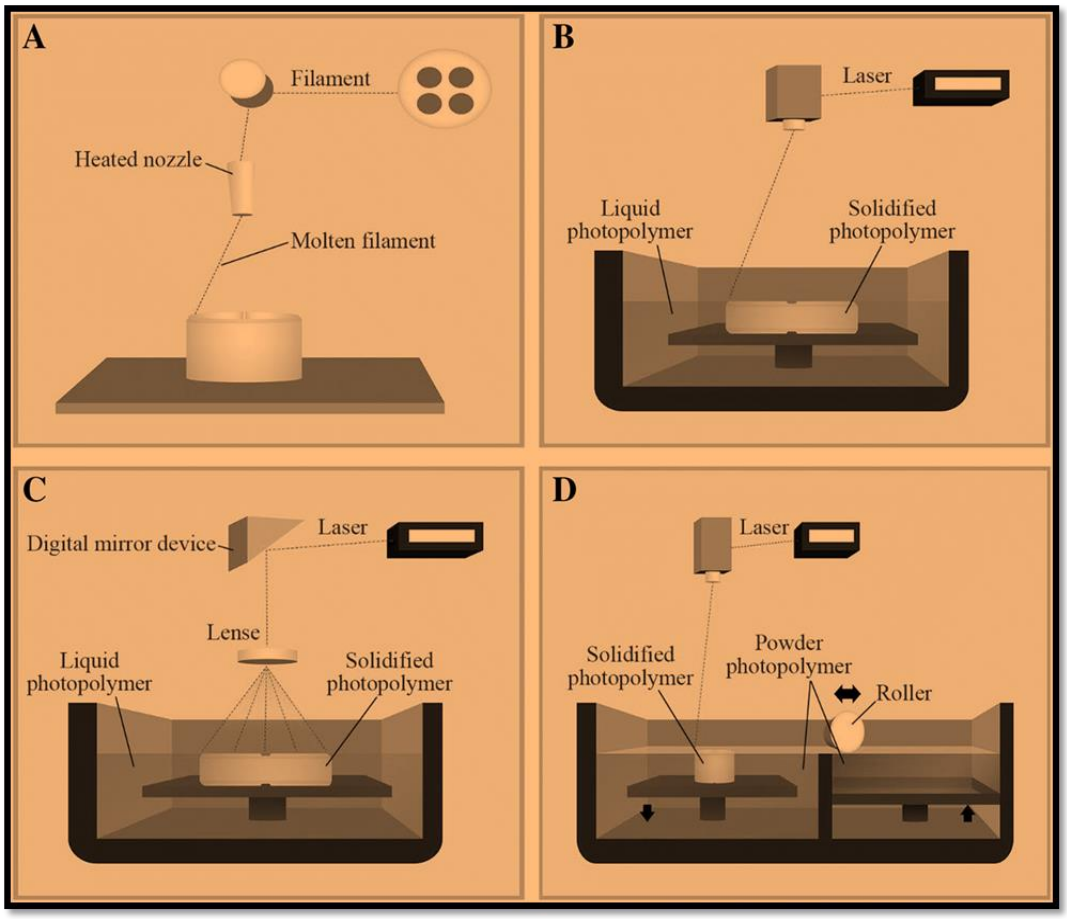

Fig: 2 Graphical illustrations of 3DP processes. A- FDM printer, B- SLA printer, C- DLP printer, D -SLS printer

This study intends to improve patient response to therapy and focuses on biomaterials and biomedical engineering advances in nanomedicine. 20 The Review's executive summary covers NNI and PMI aims. 21 Even though this study involves precision diagnostics, we predict that delivery of precision medicine therapies will significantly impact the future use of NPs in diagnostics. The limitations of biology and rational NP designs that try to transcend these limitations are also discussed. Several decades of NP research distribution and administration patterns are also discussed.22Several developing trends will benefit NP-based precision cancer therapeutics and immunotherapy, as well as in vivo gene editing (Fig. 3).

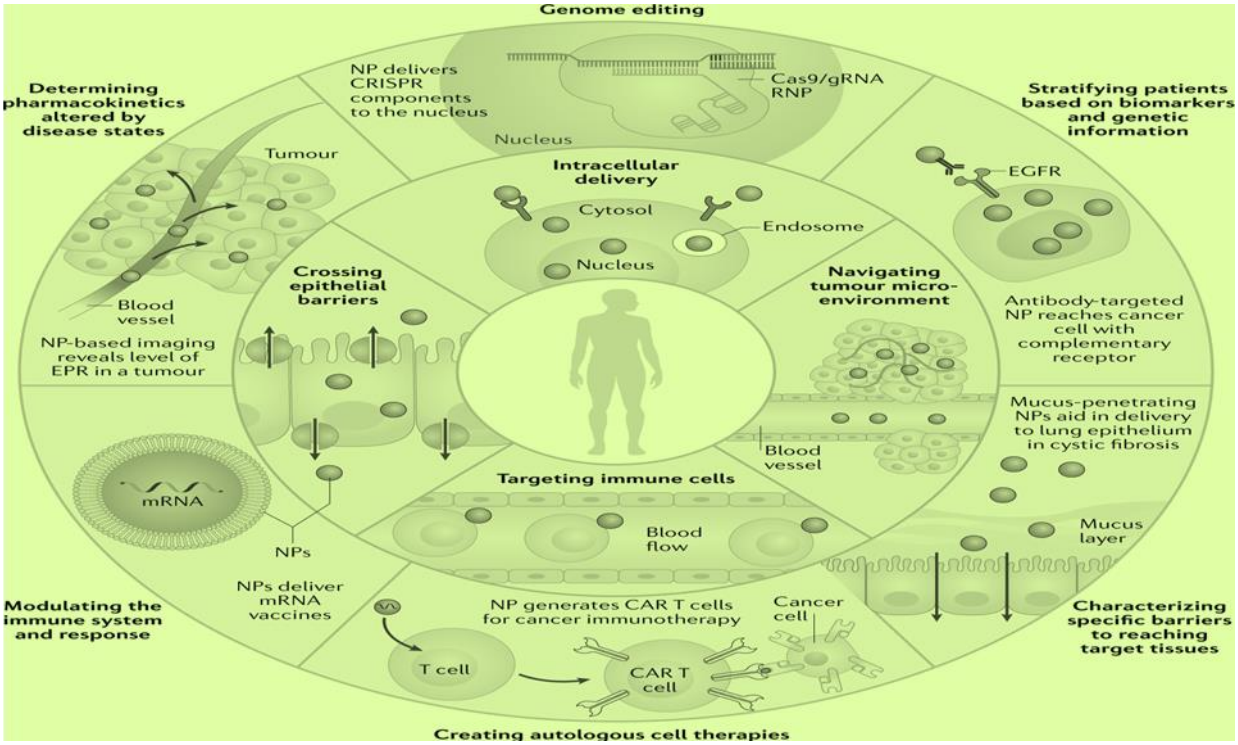

Fig 3: Biological barriers to precision medicine applications.

Therapeutic Approaches

The lack of understanding of the disease's physics and dynamics has made finding a remedy difficult. Treatment for vitiligo aims to prevent white spot growth, promote repigmentation, and reduce stress. [24]The most common treatments for vitiligo are medication and phototherapy. Corticosteroids, including betamethasone dipropionate, clobetasol dipropionate, and mometasone furoate, have been used to treat vitiligo. Recent guidelines advocate tacrolimus and pimecrolimus as first-line treatments for vitiligo. [25] Face leukomas respond well to glucocorticoids and calcineurin inhibitors in clinical trials. The buildup of ROS in the epidermis also contributes to melanocyte failure. [26] The oxidation-antioxidant system can be repaired by antioxidants that remove ROS and hydrogen peroxide. [27] Oral antioxidants such as polypodium leucotomos, vitamin E, and minocycline are used to cure vitiligo. Phototherapy, such as NB-UVA and PUVA, can be used without medicine. Phototherapy is very successful in inducing repigmentation, whether used alone or in combination with the drugs listed above. 28

Vitiligo can take months or years to appear. Long-term use of some medications or therapies may result in adverse side effects. Skin shrinking, acne, and folliculitis are long-term glucocorticoid use side effects. 29 Corticosteroids in high amounts may cause side effects. So corticosteroids are not recommended for vitiligo. Although tacrolimus is clinically similar to glucocorticoids and has similar therapeutic benefits, a recent study shows it does not affect segmental vitiligo. After two

weeks, the most common calcineurin inhibitor adverse effect is burning.[30] The high cost of calcineurin inhibitors relative to corticosteroids may cause financial hardship for patients. Antioxidant medications have no adverse side effects. [31]Due to the small number of participants in most trials, vitiligo patients should not use topical antioxidants. Non-drug treatments like phototherapy for vitiligo require patients to go twice or three times per week. Despite improved success rates, recurrence rates remain high. More than half developed white blotches on their tanned skin within a year of stopping their medicine. Phototherapy can cause hazardous side effects such as headaches, nausea, and eye and kidney damage. These procedures can cause skin cancer. The NHS only recommends phototherapy as a last resort when all other methods have failed. Nano-drug delivery systems have become increasingly popular to improve drug penetration via the skin. Using nanovesicles provides several advantages over other approaches. [32]Examples are nanoparticles, microemulsions, and lipid carriers. Few nanomedicine research specifically target vitiligo treatment.

Natural product-based nanotechnology and drug delivery

According to the WHO,[33] traditional medicine meets or exceed the population's basic health needs. Researchers are studying plant species' bioactive components, chemical makeup, and pharmacological potential to create new active chemicals with fewer adverse effects. There is still much room to develop new and highly effective drugs from natural compounds found in plants. Finding active chemicals in nature is difficult since the metabolite composition of live organisms might alter in response to stressful circumstances. [34]A pharmaceutical industry relationship has been developed. Less synthetic substances on the market mean more research into natural active molecules. Medicines from higher plants have been developed and commercialized. Among the commercially available medications containing natural therapeutic agents are Artemotil (derived from Artemisia annua L.), Reminyl® (an acetylcholinesterase inhibitor obtained from Galanthus woronowii Losinsk), and Paclitaxel® (derived from Taxus brevifolia plant; v) (silymarin from Silybum marianum).[34]

Many natural substances have already been shown beneficial. Plants include a variety of bioactive substances such as alkaloids, flavonoids, and phenolic compounds. [35] However, due to their inability to cross lipid membranes, these chemicals have lower bioavailability and efficacy. Because of their high systemic clearance, many medicines require frequent or large dosages. Natural product-based nanomedicine solutions may overcome hurdles like those listed above as nanotechnology improves. Medical nanotechnology research has been going on for a while. As a result, it is now possible to combine a large variety of compounds and combinations. They can also change the chemical's properties and behavior in the body.[36] They also increase the solubility and stability by combining molecules with varying degrees of hydrophilicity and lipophilicity to maximize bioavailability and activity. In the quest for novel therapeutic options in modern medicine, the combination of release mechanisms and natural chemicals may help delay the establishment of drug resistance.[37]

Natural products are split into two categories: those used mostly for synthesis and those intended to treat specific illnesses. Cancer, the world's most prominent cause of death, is extensively studied. Nanomedicine is being used to treat a range of other illnesses and malignant cells. Figure 4 depicts the extraction of plant-derived biochemicals and their usage in nanomedicine. Pharmaceutical companies have always sought new and better ways to develop new treatments and improve existing ones.[38] These new formulations have been made possible by nanopharmaceuticals, nanodiagnostics, and the integration of diagnosis and treatment. The rapid advancement of nanotechnology has played a role. [39,40]

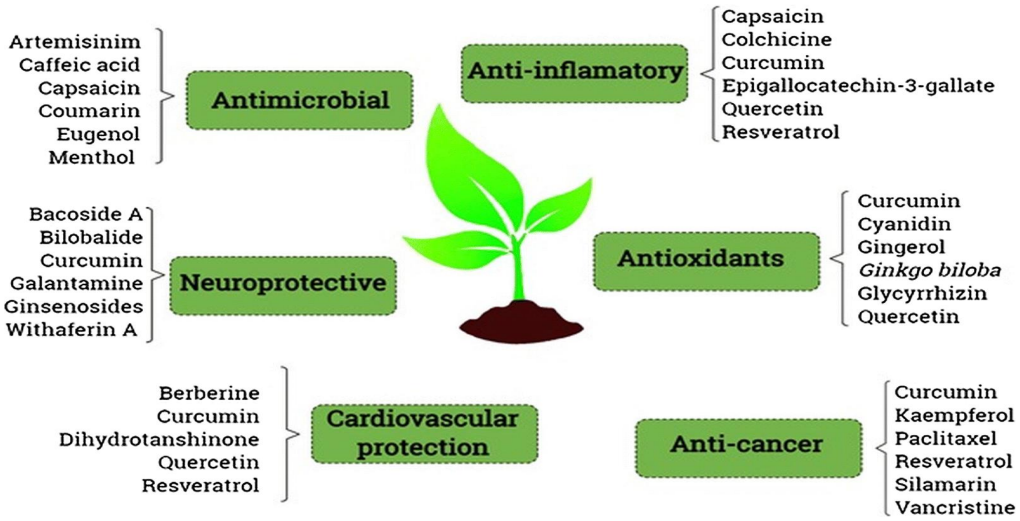

Fig: 4 For example, these are some examples of natural chemicals taken from higher plants used in nanomedicine. In some cases, these extracts are currently on the market, while others are being tested in clinical trials, yet scientists are scrutinizing others.

CONCLUSION

This article discusses new nanomedicine developments in medication delivery and diagnostics. They can diagnose, precisely convey to targets, and sense or activate elements in a live system. Nanoscale materials are defined. Aiming for better drug absorption, bioavailability, and controlled release was the initial goal of nanotechnology. For example, nanotechnology has increased the efficiency of known bioactive chemicals, a common aspect of nanomedicine. There are several ways to use nanotechnology to treat curcumin, resveratrol, and other compounds. Crystal nanoparticles, liposomes, micelles, and superparamagnetic dendrimers have all boosted the efficiency of these natural compounds.

Natural biomaterials are in high demand due to their biodegradability, biocompatibility, renewable resources, and low toxicity. Crosslinking strategies are improving the stability of polysaccharides and proteins in industrial processing and biological matrices nowadays. Surfactant-free surfactant polymerization and evaporate liquids nanoparticles have also been used (nanospheres and nanocapsules). In recent years, nanomedicine research has focused on combining therapy and diagnosis (theranostic), using cancer as an example. In cancer therapy, iron oxide-coated hyaluronic acid as a biopolymeric substance has been employed.

The FDA has approved many more commodities and clinical studies. Nanomedicine has already changed the creation and administration of medications in biological systems. Thanks to nanomedicine, we can now identify and treat diseases simultaneously.

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