

Igniting Innovation: Plasma's Dominance in The Future of Drug Delivery

Vareesha Karimella *¹, Venu Gopalaiah Penabaka ², Yadala Prapurna Chandra ³

1. IV Year B. Pharmacy, Ratnam Institute of Pharmacy, Pidthapolur (Village), Muthukur (Mandal), Nellore (Dist), Andhra Pradesh-524346, India.
2. Professor, Head of the Department, Vice-Principal. Department of Pharmaceutics, Ratnam Institute of Pharmacy, Pidthapolur (Village), Muthukur (Mandal), Nellore (Dist), Andhra Pradesh-524346, India.
3. Professor, Principal, Department of Pharmacology, Ratnam Institute of Pharmacy, Pidthapolur (Village), Muthukur (Mandal), Nellore (Dist), Andhra Pradesh-524346, India.

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*Address for Correspondence:

Vareesha Karimella, IV Year B. Pharmacy, Ratnam Institute of Pharmacy, Pidthapolur (Village), Muthukur (Mandal), Nellore (Dist), Andhra Pradesh-524346, India.

Abstract

Historically, plasma the liquid part of ancestry has been used for medicinal purposes in several ways, including drug delivery. Plasma-located drug delivery orders have shown promise for reserved and planned drug delivery, regaining their therapeutic efficacy and minimizing side effects. This study surveys recent research on the use of red bodily fluid in pharmacological dosage forms or other consumable forms, such as skin-derived nanoparticles, liposomes, and micelles. This plasma will be the future top marketing in the world. The future directions and recent studies are the pathways that ensure its capabilities in curing disease and how effective it is going to work in curing and preventing diseases.

Keywords: Nanoparticles, Pharmacodynamics, Pharmacokinetics, Bioavailability.

Introduction:

The fourth state of matter, plasma, has become a cutting-edge and exciting tool for medication delivery systems. In contrast to traditional drug delivery techniques, plasma-based drug delivery combines the therapeutic agents targeted and controlled release with the versatility of plasma technology to provide special benefits. This novel strategy has a great deal of promise to improve medication efficacy, lessen adverse effects, and improve patient outcomes ¹.

A relatively new and exciting technology that has the potential to enhance the efficacy, safety, and convenience of drug delivery is plasma-based delivery. The liquid component of blood known as plasma contains a variety of substances, including proteins, nutrients, and hormones. It is a biocompatible, flexible substance that can be used to administer drugs to specific tissues or organs.

Plasma is now recognized as a valuable therapeutic agent due to its appealing protein composition and immune-stimulating properties. Red bodily fluid has also become a valuable form of drug transmission orders in the modern era. Body tissue has been utilized as a nudity material to create a variety of pharmaceutical ingredients, including liposomes, plasma-derived nanoparticles, and micellar forms for medications and other consumable forms ^{2,3}. In (Figure 1)

Drug portions of drugs or other consumable forms are pharmaceutical advances that have one or more movement additives and are intended to be administered to patients via a range of routes, including oral, injectable, and current methods. These formulations aim to lower the probability of side effects while guaranteeing appropriate medication delivery to the operating site. The creation and design of drug dosage forms are crucial to their delivery, and it is these forms that ensure the safe and effective administration of medications. Pharmacological dosage forms need to consider several aspects, such as the intended target site, the delivery mechanism, and the physicochemical properties of the medication. Several alternative drug dosage forms exist that can be produced, including pills, capsules, shots, creams, and gels ⁴.

Recent years have seen a significant increase in interest in plasma as a component in the development of pharmacological dosage forms because of its potential to enhance drug distribution and therapeutic outcomes. In Plasma, the liquid portion of blood is made up of a wide range of chemicals, including coagulation factors, proteins, enzymes, and antibodies. Because plasma has unique properties that may affect the pharmacokinetics and pharmacodynamics of a particular substance, it must be considered when creating pharmacological dosage forms.

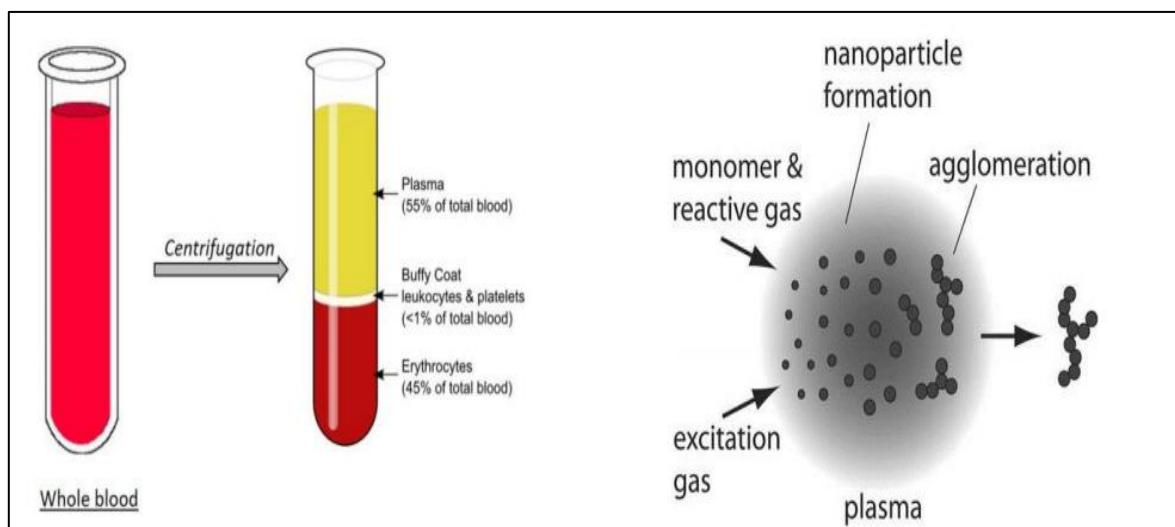


Figure 1: Separation of plasma by centrifugation at 1,500×g for 10 minutes at 4°C

In addition to examining current research and potential future directions for the use of plasma in the formulation of medication dosage forms, this article aims to provide a general overview of the significance of drug dosage forms in drug delivery, the role of plasma in drug dosage form formulation, and the interactions between medications and plasma components.

Overview of Plasma Technology: Ionized gases with free electrons and positively charged ions make up plasma, a state of matter. Because of its high energy, this state can produce a wide range of reactive species, which makes it an adaptable medium for drug delivery applications. Utilizing plasma's

ability to alter a material's surface characteristics, plasma-based drug delivery enables controlled drug release ⁵.

Interaction of Plasma Components and their Relation to Drug ^{6,7}:

In addition to a variety of proteins, including albumin, immunoglobulins, fibrinogen, and coagulating determinants, plasma is a complex mixture of water, electrolytes, hormones, and enzymes.

The following is a list of some of the more significant skin areas and how drugs interact with them (Figure 2):

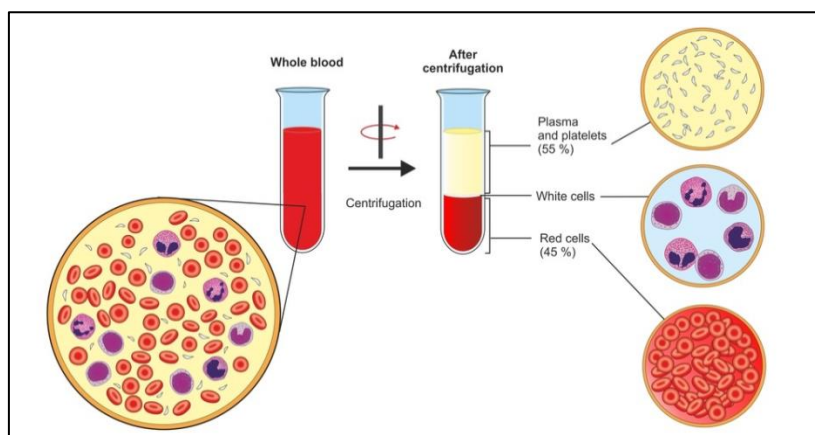


Figure 2: The elements of blood

Albumin:

The most prevalent protein in plasma, albumin is necessary for fatty acid and medication transportation, pH regulation, and oncotic pressure maintenance. Many different drugs, including ones with bitter or unclear ingredients, as well as the drug's pharmacodynamics. For example, binding to albumin can make a drug's half-life longer and prevent consent from being allured.

Immunoglobulins:

An array of proteins known as immunoglobulins serves as an immune response's fault-finder. Proteins with this property can bind to drugs and allow them to alter the pharmacodynamics and pharmacokinetics of the drug. For example, immunoglobulin can bind to a drug and keep it from getting to the intended site, which lowers the drug's bioavailability.

Clotting factors:

The coagulation components fibrinogen, prothrombin, factors, VII, VIII, IX, X, XI, and XII. are present in plasma. These proteins, which are essential to the coagulation cascade, can interact specifically with heparin and warfarin, two anticoagulants. The safety and effectiveness of some medications may be impacted by interactions between clotting factors and other medications.

Fibrinogen:

A protein found in body tissue, fibrinogen aids in blood clotting by identifying errors. Certain drugs, like clopidogrel and anesthetics, which have antiplatelet effects, can bind to fibrinogen. The pharmacokinetics and pharmacodynamics of medication may be impacted by these interactions ⁸.

Critical Confluences: Mapping the Most Important Interactions Between Medications and Plasma ⁹⁻¹⁰

Protein binding:

A lot of drugs have a strong affinity for plasma proteins like globulin and albumin, which can serve as carriers of these drugs. The drug's bioavailability, consent, and elimination can all be impacted by the effectiveness of protein binding. Because protein-binding sites are satiated, well-protein-bound medications for example offer the possibility of a longer half-life and discounted approval. Adverse effects, toxicity, and drug accumulation could arise from this.

Enzymatic absorption:

A range of drug-metabolizing enzymes, such as esterases and cytochrome P450 (CYP) enzymes, are present in plasma. These enzymes can change a drug's pharmacological characteristics and bioavailability by changing it into active or inactive metabolites. The activities of these enzymes may be influenced by variations in genetics, drug interactions, and medical conditions.

Immunoglobulin binding:

Drugs can bind to immunoglobulins, altering their distribution and elimination mechanisms. Immunoglobulins can also trigger immunological responses and hypersensitivity reactions [3]. For example, in certain situations, sensitive reactions to specific medications may arise due to the formation of drug-antitoxin aggregates.

Coagulation factors:

A range of coagulation factors are present in plasma and may interact, at least somewhat, with other anticoagulant drugs such as warfarin and heparin. These interactions can impact the efficacy and safety of the medication by changing the clotting cascade and increasing the risk of grieving or coagulating.

pH and electrolyte balance:

These factors may affect the solubility, stability, and absorption of drugs in plasma. Changes in plasma pH and electrolyte balance can affect drug disposition and metabolism through their effects on the activity of drug transporters and enzymes.

Smart Dosing: The Role of Plasma in Next-Generation Drug Dosage Forms

There are several uses for plasma in drug dosage forms or other consumable forms ^{11,12,13}:

Surface Modification of Drug Carriers:

A variety of drug carriers, including liposomes, microspheres, and nanoparticles, can have their surface characteristics changed by a plasma treatment. Researchers can improve the surface wettability, charge, and functional groups of these carriers by exposing them to plasma. Drug carriers perform better as a result of these modifications, which also affect drug-loading capacities, release kinetics, and interactions with biological tissues.

Dosage form sterilization by plasma:

Pharmaceutical dosage forms are sterilized using plasma technology. A cold sterilization technique called plasma sterilization efficiently gets rid of microorganisms without affecting the stability of medications or other ingredients in the dosage form. This is especially crucial for sensitive medications and biologics.

Plasma-derivative nanoparticles:

Small pieces of body tissue made of proteins, known as plaque-derived nanoparticles, can transport drugs to their desired locations. These elements have demonstrated the ability to transport drugs to specific instruments or organs, such as intelligence, where drug transport is usually difficult because of the ancestry-intelligence barrier.

Plasma-Modified Liposomes:

Liposomes are lipid-based vesicles that are employed in a variety of pharmaceutical formulations as drug carriers. Liposome surfaces can be altered by plasma treatment, which can affect the stability, effectiveness of drug encapsulation, and release properties of the particles. This method improves liposomal drug delivery systems' functionality.

Micelles:

Self-massed nanoparticles composed of amphiphilic particles; micelles can represent medications for target delivery. Previous studies have created amphiphilic particles that form micelles using plasma proteins. It's possible that micellar development was done to reduce the drug's release and increase its ability to heal.

Plasma Engineering: Innovations in Drug Formulation and Preparation Methods ^{14,15}

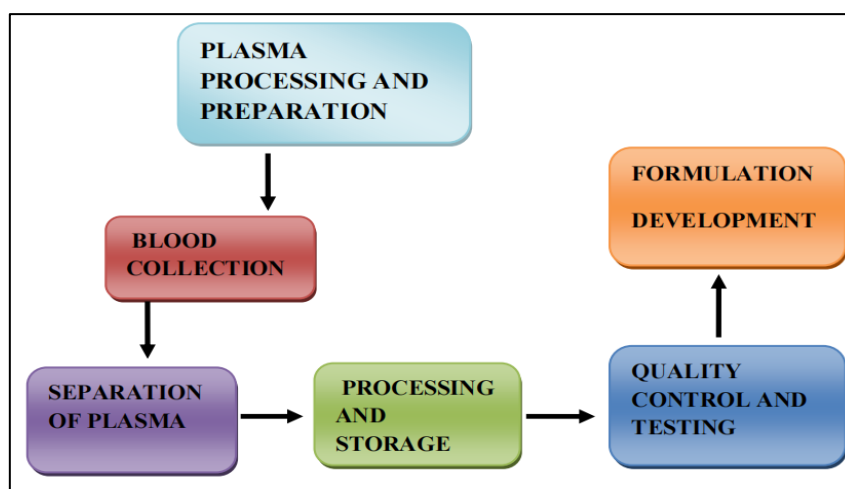


Figure 3: The plasma processing and preparation techniques

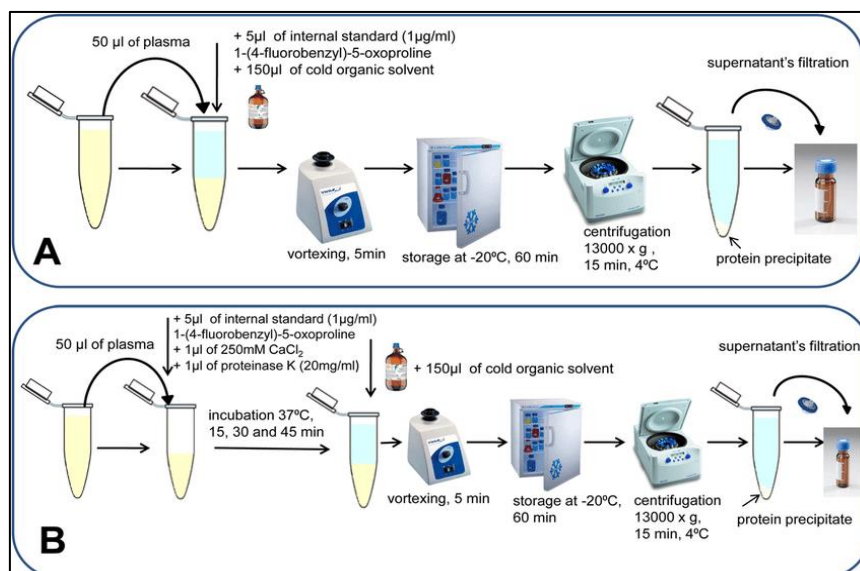


Figure 4: Centrifugation process

Blood collection:

Plasma can be produced using blood from humans or animals. Human plasma is frequently extracted from willing donors who meet strict eligibility requirements. During the collection phase, a sterile needle and collection bag are usually used to draw blood from the arm or the neck.

Plasma separation:

After the blood is drawn and transferred to a sterile container, the plasma is separated using a centrifuge from the red blood cells and other biological components. The separation process can be carried out using a variety of techniques, including membrane filtration, density gradient centrifugation, and differential centrifugation. As shown in Figure 4,5,6



Figure 5: Plasma separator PT tubes,



Figure 6: Centrifuge machine

Processing and storage:

The plasma may undergo further processing to remove contaminants and pathogens after separation. Common processing techniques include solvent/detergent treatment, heat treatment, and nanofiltration. Another method for extending the stability and shelf-life of plasma is to freeze or lyophilize it (freeze-dry).

Drug Loading:

Add the drug to the sample that has been modified by plasma, if applicable. Certain carriers' ability to load drugs can be increased by plasma treatment, which improves the effectiveness of drug encapsulation.

Quality control and testing:

To ensure their safety and efficacy, plasma products must undergo rigorous testing before being used in drug dosage forms. Testing for infectious diseases like HIV, hepatitis B and C, and West Nile virus is part of this. Another method of evaluating the quality of a plasma product is to test it for clotting factors, protein content, and other characteristics.

Formulation development:

Following processing and testing, the plasma product may be used as a component in drug dosage forms such as injectables, inhalables, or oral formulations. The steps in the formulation development process include selecting the appropriate excipients, improving the stability and bioavailability of the formulation, and conducting additional safety and efficacy testing.

Reporting and Documentation:

Keep a record of every step of the process, including the formulation specifics, characterization outcomes, and plasma parameters that were employed. Compile records and reports for future use and regulatory compliance.

Medication therapy is efficiently delivered in vivo by plasma polymerized nanoparticles.

By integrating several classes of molecules into a single nanostructure, improving the active targeting of therapeutic agents, and enabling novel combination therapies, multifunctional nanocarriers, or MNCs, hold the potential to improve therapeutic outcomes. Nevertheless, a single

therapeutic agent can only be carried by nanocarrier platforms that are presently authorized for clinical use. One of the biggest technological obstacles to clinical translation has been the synthesis of more complex MNCs, which is complicated and expensive. Here, we demonstrate how easily and affordably multiple therapeutic cargoes can be delivered by plasma polymerized nanoparticles (PPNs), which are synthesized in reactive gas discharges. This process is compatible with upscaling commercial production. In difficult-to-transfect cells, delivery of siRNA against vascular endothelial growth factor (VEGF) at incredibly low concentrations (0.04 nM) dramatically decreased VEGF expression. When hard-to-transfect cells were compared to commercial platforms with higher doses of siRNA (6.25 nM), the reduction in VEGF expression was significant. In mice with orthotopic breast tumors, PPNs containing siVEGF and standard of care Paclitaxel (PPN-Dual) at lower doses (<100 µg/kg) synergistically altered the tumor microenvironment and dramatically slowed tumor growth. PPNs are a novel type of nanomaterial that can be used to deliver medicines and are easily functionalized in any type of laboratory environment without requiring additional purification or wet-chemistry steps.

Present Pinnacles and Future Horizons ¹⁶

Development of new body tissue-located drug formulations:

Scientists are looking into cutting-edge techniques to include red blood cell constituents in medication formulations, such as using red blood cell-derived vesicles or nanoparticles. Improved medication delivery and birthing to particular tissues or containers may be possible with these techniques.

Body tissue optimization and refinement:

Ongoing efforts are made to enhance the safety and effectiveness of handling and storing red blood cells, with a particular emphasis on lowering the risk of pathogen transmission and restoring the stability and jutting growth of output derived from red blood cells.

Investigation of plasma-drug interactions:

To improve drug formulations and anticipate possible drug-drug interactions, researchers are looking into the intricate relationships that exist between drugs and plasma components.

Personalized medicine:

Drug formulations based on plasma have the potential to enable personalized medicine, in which prescriptions are made specifically for each patient based on their unique needs and characteristics. This strategy might result in fewer side effects and more effective, targeted treatments.

Plasma Potency: A Key Player in The Therapeutic Arsenal Against Diseases ¹⁷

Transfusions of Blood:

Because it contains vital proteins, clotting factors, and antibodies, plasma is an important component of blood transfusions. When treating ailments like trauma, surgeries, and anemia, it is essential.

Conditions of Coagulation:

Because plasma contains clotting factors, it is essential for treating coagulation disorders. Products made from plasma may help patients with hemophilia or other clotting disorders.

Immunodeficiency Disorders:

Immunoglobulins derived from plasma are used to treat immunodeficiency diseases. These immunoglobulins contain antibodies that, in those with compromised immune responses, can strengthen the immune system.

Autoimmune Disorders:

Plasma exchange, also known as plasmapheresis, is the process of removing plasma from blood cells and substituting it with another substance. Guillain-Barre syndrome and myasthenia gravis are two autoimmune diseases that are treated with this technique.

Liver Conditions:

Liver diseases such as albumin and clotting factors are treated with products derived from plasma. For example, albumin infusions can aid in preserving blood volume and avoiding fluid buildup.

Patients with Burns and Trauma:

Transfusions of plasma are essential for the treatment of burn and trauma patients. In addition to providing vital proteins to support the healing process, plasma aids in blood volume restoration.

Hemolytic Disorders in Infants:

When a newborn has hemolytic disease—a condition where the mother's antibodies destroy the baby's red blood cells—plasma is used as a treatment. Plasma exchange transfusions can aid in the management of this illness.

Neurological Conditions:

A few neurological conditions, such as multiple sclerosis and chronic inflammatory demyelinating polyneuropathy (CIDP), are treated with plasma exchange occasionally.

Treatments for Cancer:

Clotting factors, for example, are products derived from plasma that can be used to support cancer patients, particularly those receiving radiation or chemotherapy.

New Therapies:

The application of plasma in novel therapeutics, such as personalized medicine and regenerative medicine, is being investigated in ongoing research to treat a range of illnesses.

Plasma-Powered Pharmaceuticals: Future Avenues in Medication Dosage Forms ¹⁸

Novel plasma-based therapeutics:

Research in the future may focus on developing novel treatments for a range of infectious diseases. Plasma has been used to treat COVID-19 and other viral infections.

Responsive Drug Delivery:

Subsequent generation of plasma drug delivery systems may include stimuli-sensitive materials or smart Nano carriers responsive components that release medication in response to physiological signals or particular environmental circumstances.

Minimizing Immunogenicity:

To reduce immunogenicity and enhance the safety profile of biologic drugs thereby lowering the likelihood of adverse reactions plasma drug delivery systems could be developed.

Targeted drug delivery:

Treatments may be more successful and have fewer side effects if medications are delivered to specific tissues or cells using nanoparticles or vesicles made from plasma.

Advances in gene therapy:

Plasma-based gene treatments may offer a workable approach for the treatment of genetic illnesses because plasma contains a variety of proteins and other components that might facilitate the delivery and expression of genes.

Integration of Diagnostic and Therapeutic:

Combining therapeutic and diagnostic capabilities in plasma drug delivery systems may enable real-time tracking of medication levels and illness development, leading to more accurate and timely interventions.

Creation of novel biomaterials:

New biomaterials for tissue engineering and regenerative medicine may be created using proteins and other ingredients derived from plasma.

Conclusion

In addition to other edible drug forms, plasma is now a sought-after component of liposomes, micelles, and skin-derived nanoparticles. Medication transmittal pores positioned in plasma may reduce responses while increasing therapeutic efficacy. However, addressing skin instability and guaranteeing the safety and features of red blood cell-derived drug delivery plans are the primary obstacles that must be overcome to fully realize the potential of red blood cells as a drug component or in any consumable form. Body tissue-located medication transfer arrangements have the potential to transform medicine delivery and offer a range of unexpected conditions and scenarios with further research and development.

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Conflict of Interest

We declare no conflict of interest

References

1. Woloszyk, A, Rozanski, J, and Banasuik, R. Application of plasma technology in the pharmaceutical industry. *Acta Polniae Pharmaceutica*, 2017; 74(3):805-814.
2. Kirschner, C. M., and Brennan, A. B. Biofunctionalization of plasma-treated surfaces. *J Phys D Appl Phys*. 2012; 45(18):183001. <https://doi.org/10.1088/0022-3727/45/18/183001>
3. Luan, Y, Meng, Q, and Chen, C. Low- Low-temperature atmospheric plasma: a novel treatment for cutaneous leishmaniasis. *PloSNegl Tropical Disease*, 2020; 14(11):e0008814.
4. Laroussi, M. From killing bacteria to destroying cancer cells: 20 years of plasma medicine. *Plasma Processes Polymerization*, 2014;11(12):1138-1141. <https://doi.org/10.1002/ppap.201400152>
5. Tanaka, H., Ishikawa, K., Mizuno, M., Toyokuni, S., Kajiyama, H., Kikkawa, F., Metelmann, H.R., and Hori, M. State of the art in medical applications using non-thermal atmospheric pressure plasma. *Reviews of Modern Plasma Physics*, 2017;1(1):89. <https://doi.org/10.1007/s41614-017-0004-3>
6. Jayasree, M., Gautham Chakra, R., Venkata Lava Kumar Reddy, K., Dilshad, K., Thulasi, P., Shereen Taj, S., Vasanth, S., Lathifmunnisha, Y., and Akshitha, P. A Research on Clinical Pharmacists' Assessment of Drug-Related Problems in Patients with Chronic Kidney Disease. *International Journal of Experimental and Biomedical Research*, 2023;2(4): 139-150. <https://doi.org/10.26452/ijebbr.v2i3.540>
7. Maldonado, A. P., and Bogaerts, A. Plasma in Cancer Treatment. *Cancers (Basel)*, 2020;12(9):2617. <https://doi.org/10.3390/cancers12092617> PMID:32937802 PMCID:PMC7564655
8. Keidar, M. Plasma for cancer treatment. *Plasma Sources Science and Technology*, 2015;24(3):033001. <https://doi.org/10.1088/0963-0252/24/3/033001>
9. Li, Y., Li, Y., Li, S. Plasma techniques for enhancing drug bioavailability and efficacy: A review of recent advances. *European Journal of Pharmaceutical Sciences*, 2021; 164:105960. <https://doi.org/10.1016/j.ejps.2021.105960> PMID:34339828
10. Prapurna Chandra, Y., Yamini, M., and Naveena, B. A Review on Health Promotion and Disease Prevention in Children and Adults. *International Journal of clinical Pharmacokinetics and Medical Sciences*, 2023;3(3):87-95. <https://doi.org/10.26452/ijcpms.v3i3.537>
11. Laroussi, M., Keidar, M., and Moinuddin, M. Plasma medicine: Opportunities for nanotechnology in a digital age. *Wiley Online Library*, 2021;123(2):e4713.
12. Fridman, A., Shereshevsky, A., Gutsol, A., Vasilets, V., Stankevich, A., and Bratskaya, S. Plasma medicine for the treatment and diagnosis of COVID-19. *Plasma Processes and Polymers*, 2021;18(3):e2000233.
13. Shi, J., Votruba, A. R., Farokhzad, O. C. Plasma polymerized nanoparticles effectively deliver dual siRNA and drug therapy invivo. *Scientific Reports*, 2020;10(1):1-9. <https://doi.org/10.1038/s41598-020-69591-x> PMID:32732927 PMCID:PMC7393381
14. Chidinma, M., Ekebor Chika, J., Obonga, W. O. Is Transdermal Delivery Potential Route for Sitagliptin Phosphate: The pH Control Effect. *Future Journal of Pharmaceuticals and Health Sciences*, 2023;3(4):528-533. <https://doi.org/10.26452/fjphs.v3i4.532>
15. Zhang, Z., Chen, H., Hu, Z., Wang, H., and Wu, Z. Plasma medicine for neuroscience-an introduction. *Chinese Neurosurgical Journal*, 2019;6(6):19720.
16. Fridman, G., Friedman, A., Gutsol, A., Shekhter, A. B., Vasilets, V. N., and Fridman, G. Plasma-mediated sterilization of bacteria and drug-resistant strains. *Plasma Processes and Polymers*. 2019;16(4):e1800214.
17. Reddy J. C., Reddigari, P., Ramesh, Y., Kothapalli, C. B. A Novel Approaches On Ocular Drug Delivery System. *Journal of Drug Delivery and Therapeutics*, 2017;7(6): 117-124. <https://doi.org/10.22270/jddt.v7i6.1512>
18. Yan, D., Sherman, J. H., and Keidar, M. Cold atmospheric plasma, a novel promising anti-cancer treatment modality. *Oncotarget*, 2017; 8(9):15977-15995. <https://doi.org/10.18632/oncotarget.13304> PMID:27845910 PMCID:PMC5362540