International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 32, Issue 6, June 2026 **ijppr.humanjournals.com** ISSN: 2349-7203

Microspheres: A Promising Approach in Controlled Drug Delivery

Ms. Thakare Pooja Manohar[1], Ms. Sulbha.G.Patil[1], Dr.S.P.Pawar[1]

P.S.G.V.P.Mandals College Of Pharmacy, Shahada, Maharashtra, India.

Received: 07 May 2026 Revised: 30 May 2026 Accepted: 10 June 2026

ABSTRACT:

Microspheres are an important drug delivery system that have gained significant attention in pharmaceutical research due to their ability to provide controlled and sustained drug release. They are small, free-flowing spherical particles composed of a drug dispersed or encapsulated within a polymeric matrix. Microsphere formulations are prepared using natural or synthetic biodegradable polymers and are widely used to improve drug stability, bioavailability, and therapeutic efficacy. This review article highlights the classification, materials used, methods of preparation, and evaluation parameters of microsphere formulations. Various techniques such as solvent evaporation, spray drying, emulsion cross-linking, and coacervation are discussed. The advantages of microspheres, including prolonged drug release, reduced dosing frequency, improved patient compliance, and minimized side effects, are emphasized. In addition, recent applications of microspheres in targeted drug delivery and controlled release systems are reviewed. Overall, microsphere-based drug delivery systems represent a promising approach for improving therapeutic outcomes and overcoming the limitations associated with conventional dosage forms.

Keywords: Microspheres; Microparticles; Controlled drug delivery; Sustained release; Biodegradable polymers; Drug encapsulation; Targeted drug delivery; Novel drug delivery systems (NDDS).

INTRODUCTION:

The concept of microsphere began Between the 1940s and 1960s, microencapsulation technology emerged as an alternative approach for drug delivery. With the continued pursuit of more advanced and refined delivery systems, polymer and membrane technologies gained prominence in the 1980s. Subsequently, targeting and site-specific drug delivery with greater precision has been achieved through the attachment of bioactive molecules to liposomes, bioerodible polymers, implants, monoclonal antibodies, and various particulate carriers such as nanoparticles and microspheres. Microparticle-based delivery systems are now widely recognized as reliable and effective means for delivering drugs to specific target sites with high specificity.A notable example of such advancements is the development of microspheres designed for the treatment of vascular complications of the eye.

Microspheres, also referred to as microparticles, are small, free-flowing spherical systems composed of a drug dispersed within a polymer matrix. They are typically prepared using biodegradable natural or synthetic polymers and generally have particle sizes below 200 µm, most commonly ranging from 1 µm to 1000 µm. Microspheres have been extensively investigated as drug delivery systems due to their ability to provide controlled and sustained release of therapeutic agents. This controlled release helps maintain a consistent plasma drug concentration, thereby reducing dosing frequency, lowering the total dose required, and minimizing adverse effects.[1]

Microspheres are broadly classified into two types: **microcapsules** and **micromatrices**. Microcapsules consist of a core containing the drug that is surrounded by a distinct polymeric wall, whereas in micromatrices, the drug is uniformly dispersed throughout the polymer matrix.

Microspheres are mainly classified into two types: **reservoir type** and **matrix type**.

Reservoir-Type Microspheres

In reservoir-type microspheres, the drug is enclosed as a core inside a water-insoluble polymer coating. This polymer layer controls the release of the drug. Common polymers used in this system are **ethylcellulose** and **polyvinyl acetate**. Reservoir-type microspheres are also known as **microcapsules**.

Matrix-Type Microspheres

In matrix-type microspheres, the drug is uniformly distributed throughout the polymer matrix. The polymer controls the drug release rate. Commonly used polymers for this type include **sodium alginate** and **hydroxypropyl methylcellulose (HPMC)**. These microspheres are also called **micromatrices.** [2]

ADVANTAGES OF MICROSPHERS

1. Microspheres have a long-lasting and consistent therapeutic impact.
2. Improves patient compliance by lowering the frequency of dose.
3. Because of their smaller size and spherical shape, they may be injected into the body.
4. Improved medicine use will increase bioavailability and lessen the frequency or severity of side effects.
5. The shape of microspheres permits controlled variation in medication release and breakdown.

DISADVANTAGES OF MICROSPHERS

1. Complex manufacturing process.
2. High production cost.
3. Possible toxicity of encapsulation material.
4. Size dependence issues.[3]

Polymer used in microsphere formulation:

1. Synthetic Polymers: divided into two types:

1. Non-biodegradable:

✓ Acrolein

✓ Glycidyl methacrylate

✓ Epoxy polymers, etc.

2. Biodegradable :

✓ Polyanhydrides

✓ Lactides glycosides, and their copolymers.[4]

2. Natural materials: They are obtained from different sources like

✓ Proteins (albumin, gelatin, collagen)

✓ Carbohydrate (starch, agarose, carrageenan)

Chemically modified carbohydrates [poly (acryl dextran), Poly (acryl starch)]

Types of Microspheres

1.Bioadhesive microspheres

2.Magnetic microspheres

3.Radioactive microspheres

4.Mucoadhesive microspheres

5.Floating microspheres

6.Polymeric microspheres

TYPES OF MICROSPHERES

1. Bioadhesive Microspheres

Bioadhesive microspheres are drug delivery systems that have the ability to adhere to biological membranes using water-soluble polymers. Bioadhesion refers to the attachment of a drug delivery system to mucosal membranes such as the buccal, ocular, nasal, or rectal mucosa. Materials that can bind to biological tissues, especially mucosal membranes, are known as bioadhesive materials.

Bioadhesive microspheres help in forming close and prolonged contact with the site of administration by adhering to the mucosal tissue. This increased residence time improves drug absorption. When combined with controlled drug release, bioadhesive systems can also improve patient compliance by reducing the frequency of drug administration.

Carrier technology is an advanced drug delivery approach in which the drug is attached to carrier particles such as microspheres, nanospheres, liposomes, or nanoparticles. Among these, microspheres play an important role due to their small size and high drug-carrying capacity, which help in controlled drug release and better absorption.

2. Magnetic Microspheres

Magnetic microspheres are an important drug delivery system because they allow targeted delivery of drugs to a specific disease site. In this system, a magnetic field is applied externally to guide the drug-loaded microspheres to the desired location. As a result, a smaller dose of drug can be used compared to conventional therapy, reducing side effects.

Magnetic microspheres respond to an external magnetic field due to the presence of magnetic materials within them. Common polymers used in the preparation of magnetic microspheres include chitosan and dextran. Therapeutic magnetic microspheres are widely used to deliver chemotherapeutic agents to liver tumors. This technique is also useful for targeting drugs such as proteins and peptides.

3. Radioactive Microspheres

Radioactive microspheres are tiny spheres, usually 10–30 nm, used in radioembolization therapy. They are slightly larger than capillaries, so when injected into arteries leading to a tumor, they get trapped in the first capillary bed. This allows a high dose of radiation to reach the tumor while minimizing damage to surrounding healthy tissues.

Unlike conventional drug delivery systems, radioactive microspheres do not release the drug; instead, the radiation acts locally from the microsphere itself. Different types of radioactive microspheres are classified based on the type of emitter they contain.

4. Mucoadhesive Microspheres

Mucoadhesive microspheres have a diameter of 1–1000 μm and are made entirely of a mucoadhesive polymer or have an outer mucoadhesive coating. These microspheres stick to mucosal surfaces, such as in the eye, nasal cavity, urinary tract, or gastrointestinal tract, increasing drug absorption and bioavailability.

Key advantages:

✓ High surface-to-volume ratio allows more intimate contact with mucus.

✓ Can target drugs specifically by attaching molecules like plant lectins, bacterial adhesins, or antibodies.

✓ Can provide localized or systemic controlled drug release.

5. Floating Microspheres

Floating microspheres are designed to float in gastric fluids because their bulk density is less than that of stomach contents. They remain buoyant without affecting gastric emptying, allowing prolonged drug release at the desired rate.

Advantages:

✓ Increases gastric residence time.

✓ Reduces fluctuations in plasma drug levels.

✓ Prevents dose dumping.

✓ Produces prolonged therapeutic effect, which can reduce dosing frequency.

6. Polymeric Microspheres

Polymeric microspheres are made from polymers and can be classified into two main types:

✓ Biodegradable polymeric microspheres – break down naturally in the body over time.

✓ Synthetic polymeric microspheres – made from man-made polymers and may be non-biodegradable or slowly degradable.[7]

Methods of preparation of microsphere:

1. Single emulsion technique:

✓ Used mainly for microparticles of natural polymers like proteins and carbohydrates.

✓ Process:

o Dissolve the natural polymer in an aqueous medium.

o Add the solution to a non-aqueous phase (usually oil) to form droplets.

o Cross-link the dispersed polymer droplets using heat or chemical cross-linking agents like formaldehyde or glutaraldehyde.

o Collect microspheres by centrifugation, then clean and separate them.

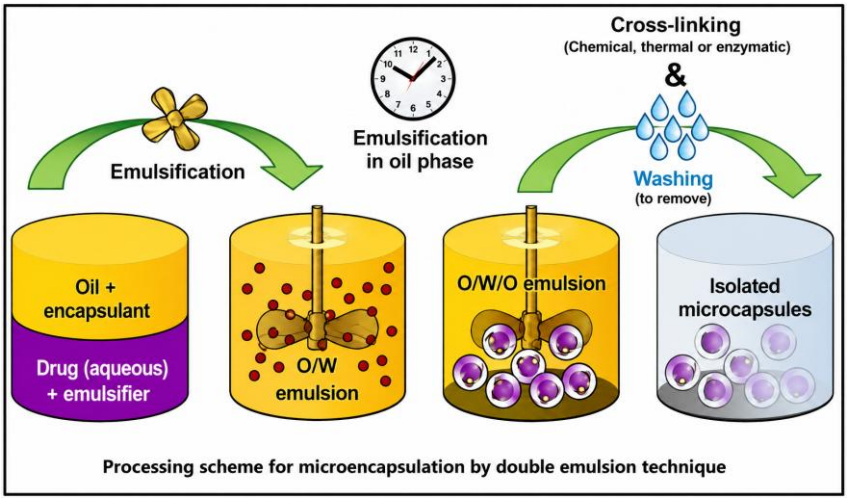
✓ Best suited for hydrophobic drugs and natural polymers.

2. Double Emulsion Technique (W/O/W)

- Ideal for **water-soluble drugs** such as proteins, peptides, and vaccines.
- Process:

1. Dissolve the drug in an **aqueous solution**.
2. Disperse it in an **organic polymer solution** to form a **primary water-in-oil (W/O) emulsion**.
3. Add this to an aqueous solution containing **polyvinyl alcohol (PVA)** and homogenize to form a **secondary W/O/W emulsion**.
4. Microspheres are then **dried and filtered**.

- Can use **both natural and synthetic polymers**.

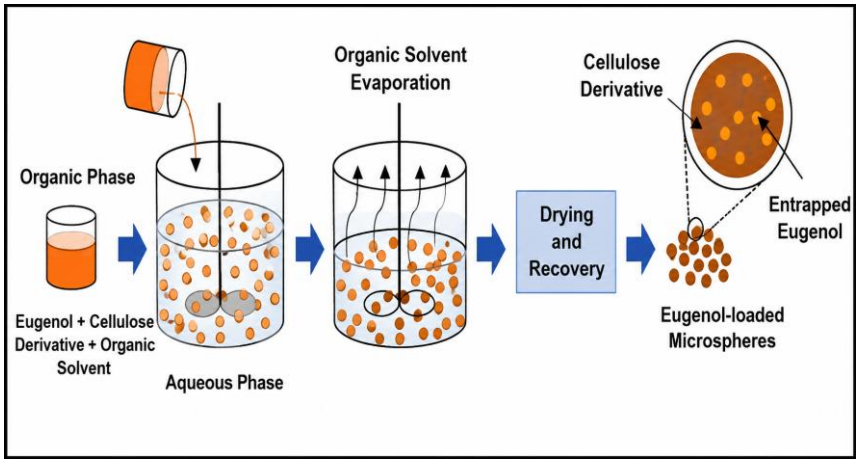


3. Solvent Evaporation Technique

- Used for both **microcapsules and matrix-type microspheres**.
- Process:

1. Dissolve or disperse the **core material** in a **polymer solution**.
2. Disperse the polymer solution in a **volatile solvent** that is immiscible with the surrounding liquid.
3. Agitate the mixture to form microspheres of desired size.
4. Evaporate the solvent using **heating**, leaving behind solidified microspheres.

- Commonly used for **synthetic polymers** and drugs requiring controlled release.



4. Spray Drying and Spray Congealing

- Both methods produce microspheres by **drying or cooling a polymer-drug solution**.

Spray Drying:

1. Dissolve the polymer in a **volatile organic solvent** (e.g., dichloromethane or acetone).

2. Mix the drug into the polymer solution.
3. Atomize the solution into a **hot air stream** to rapidly evaporate the solvent.
4. Collect microspheres (1–100 µm) using a **cyclone separator**.
5. Any residual solvent is removed under **vacuum**.

Spray Congealing:

- Instead of solvent evaporation, the polymer-drug solution is **cooled** to solidify the droplets into microspheres.

5. Quasi-Emulsion Solvent Diffusion

- Used mainly for **acrylic polymer-based controlled-release microspheres**.
- Process involves forming microspheres by **diffusing solvent out of a quasi-emulsion**, creating solid microspheres with controlled release properties.[8]

Evaluation of Microspheres

1. Determination of Percentage Yield

- After preparation, **microspheres are thoroughly dried** and weighed accurately.
- **Percentage yield** is calculated using the formula:

$$\%\text{Yield} = \frac{\text{Mass of microspheres obtained}}{\text{Total weight of drug + polymer}} \times 100$$

This indicates the efficiency of the microsphere preparation process.

2. Morphological Characterization

- The **shape and surface features** of microspheres are examined using a **Scanning Electron Microscope (SEM)** (e.g., ZEOL JSM–5610).
- Procedure:

1. Dry microspheres are mounted on a **SEM stub** using double-sided tape.
2. Coated with a thin **ion layer (~200 nm)** under reduced pressure (~0.001 torr).
3. Microspheres are photographed by **random scanning** of the stub.

3. Swelling Studies

- Used to measure how microspheres **absorb water and swell**.
- Procedure:

1. Place a known weight of microspheres in **10 mL distilled water** at 37 ± 0.5°C.
2. Shake occasionally and remove microspheres at intervals, blot dry, and weigh.
3. Continue until **equilibrium swelling** is reached (usually 24 hours).

- **Swelling ratio (SR)** is calculated as:

$$SR = \frac{e - 0}{0}$$

Where:

- $_0$= Initial weight of dry microspheres
- $_e$= Weight of swollen microspheres at equilibrium
- Studies are usually **performed in triplicate**.[9]

4. Density Determination

- The **density** of microspheres is measured using a **multivolume pycnometer**.
- Procedure:

1. Weigh the microsphere sample and place it in the pycnometer cup.
2. Introduce **helium gas** at constant pressure into the chamber.
3. Helium expansion causes a **pressure drop**, which is recorded twice at different pressures.
4. Using these readings, the **volume and density** of microspheres are calculated.

5. Isoelectric Point (pI)

- The **isoelectric point** is the pH at which microspheres carry **no net electrical charge**.
- Determination:

1. Measure the **electrophoretic mobility** of microspheres using **microelectrophoresis**.
2. Track particle movement over 1 mm at different pH values (3–10).
3. Mobility depends on **surface charge, ionizable groups, and ion adsorption**.

6. Drug Entrapment Efficiency (DEE)

- Measures how much drug is actually **encapsulated** in microspheres.
- Procedure:

1. Take a known quantity of microspheres and **break them**.
2. Dissolve in buffer solution and filter.
3. Analyze the filtrate using **UV spectrophotometry** at a specific wavelength.

- Calculated using the formula.[10]

$$\text{Drug Entrapment Efficiency (\%)} = \frac{\text{Actual drug content in microspheres}}{\text{Total drug used}} \times 100$$

Applications of Microspheres

1. Oral Drug Delivery

The oral route is the most commonly used and preferred route of drug administration due to its ease of administration, safety, and high patient compliance. Microspheres play an important role in oral drug delivery systems by improving drug solubility, stability, and permeability.

Drugs encapsulated in microspheres are protected from degradation in the gastrointestinal tract and are released in a controlled or sustained manner, leading to prolonged therapeutic action. This reduces dosing frequency and enhances patient compliance. Microspheres are particularly useful for drugs with poor bioavailability and short half-lives.

2. Ocular Drug Delivery

Microspheres are excellent carriers for ocular drug delivery because conventional eye drops are rapidly eliminated due to tear drainage and blinking. Microsphere-based ocular formulations increase drug residence time in the eye, thereby improving bioavailability. Due to their sustained release properties, microspheres allow long-lasting drug action, reduce dosing frequency, and minimize systemic side effects. They are widely used in the treatment of eye infections, glaucoma, and inflammatory conditions.

3. Microspheres in Cancer Treatment

Microspheres have significant applications in cancer therapy, especially in targeted drug delivery and radiotherapy.

Radioactive microspheres such as Yttrium-90 (Y-90) are used in the treatment of liver tumors. These microspheres (approximately 20–30 microns in diameter) are injected into the hepatic artery, where they selectively lodge in tumor vasculature. The radioactive emitters deliver localized radiation, destroying cancer cells while minimizing damage to healthy tissues. Chemotherapeutic agents like 5-fluorouracil are also incorporated into microspheres for targeted treatment of colon cancer.

4. Microspheres in Gene Delivery

Microspheres are used as carriers in gene delivery systems to transport genetic material such as DNA or RNA into target cells. Traditional viral vectors are highly efficient but can cause immune reactions and toxicity. To overcome these limitations, non-viral gene delivery systems using microspheres, polymers, liposomes, and microcapsules have been developed.

These systems offer advantages such as improved safety, controlled release, protection of genetic material, and reduced immune response. Microspheres facilitate sustained and localized gene expression in target tissues.

5. Monoclonal Antibodies

Microspheres coated with monoclonal antibodies (also known as immunomicrospheres) are used for targeted drug delivery. These antibodies selectively bind to specific antigens present on diseased cells, allowing precise localization of microspheres containing bioactive compounds. Methods of attaching monoclonal antibodies to microspheres include:

- Non-specific adsorption
- Specific adsorption
- Direct chemical coupling
- Coupling via linking agents

This approach is highly useful in cancer diagnosis, therapy, and immunoassays.

6. Other Applications

Microspheres are widely used in several other fields, including:

- Membrane technology

- Fluorescence-linked immunosorbent assays (FLISA)
- Mass spectrometry
- Cell biology research
- Microencapsulation in pharmaceutical and food industries
- Photosensitive paper production

Yttrium-based microspheres are extensively used in the treatment of hepatocellular carcinoma, while industrial applications include controlled release systems, coatings, and diagnostic tools.[11]

Conclusion:

Microspheres represent a versatile and advanced drug delivery system with significant potential to enhance therapeutic outcomes. Their ability to provide controlled and sustained release, improve bioavailability, reduce dosing frequency, and minimize side effects makes them an attractive alternative to conventional dosage forms. By utilizing both natural and synthetic biodegradable polymers, microspheres can be tailored for specific applications, including oral, ocular, and targeted drug delivery, as well as gene therapy, cancer treatment, and monoclonal antibody targeting. Various preparation techniques—such as solvent evaporation, spray drying, emulsion cross-linking, and coacervation—allow for precise control over particle size, drug loading, and release kinetics. Despite challenges such as complex manufacturing processes and potential toxicity of encapsulation materials, the advantages of microspheres outweigh these limitations. Overall, microsphere-based delivery systems continue to be a promising platform for achieving site-specific, sustained, and efficient therapeutic drug delivery, while opening new avenues in modern medicine and biotechnology.

REFERENCES

1. K A, Vineetha K, Kamath K K, Shabaraya AR. Microspheres as A Novel Drug Delivery System - A Review. Int J Pharm Sci Rev Res. 2022 July 15;160–6.
2. Raj H, Sharma S, Sharma A, Verma KK, Chaudhary A. A Novel Drug Delivery System: Review on Microspheres. J Drug Deliv Ther. 2021 Apr 15;11(2-S):156–61.
3. Sinha PK, Tiwari H, Ali MZ. Microsphere: A Review Article. Int J Pharm Res Appl. 2024 June;09(06):1122–34.
4. Khar R.K, Vyas, S.P. Targeted and Controlled Drug Delivery- Novel Carrier Systems., 1st edition. CBS Publications and Distributors, New Delhi; 2002; 417- 418.
5. Midha K, Nagpal M, Arora S. Microspheres: a recent update. International Journal of Recent Scientific Research. 2015; Jul: 5859-67.
6. Sipai AB, Vandanayadav M, Mamatha Y, Prasanth VV. Mucoadhesive Microsphere An overview. American Journal of Pharmaceutical Research. 2012; 2(1):237-58.
7. Prasanth VV, Moy AC, Mathew ST and Mathapan R: Microspheres: An overview. International Journal of Pharmaceutical and Biomedical Sciences 2011; 2(2): 332 8
8. Anusha, R., Gayathri, K., Sindhu, T., Shahi, R. R., Hassan, R., Afroz, S., & Vaishnavi, J. (2025). Formulation and characterization studies of microspheres. *International Journal of Basic & Clinical Pharmacology*, *14*(2),
9. . Shailaja AK. Biomedical applications of microspheres, J Mod Drug Dis Drug Del Res. 2015;4(2):1-5.
10. Thundimadathil J, Peptide therapeutics: strategy and tactics for chemistry manufacturing and controls. In: Srivastava V. editor. Formulations of microspheres and nanoparticles for peptide delivery. 1st edition. Cryodon: Royal Society of Chemistry; 2019: 503-30.
11. Liu W, Lee BS, Meiler WF, Kang-Meiler JJ. Biodegradable microsphere-hydrogel ocular drug delivery system for controlled and extended release of bioactive aflibercept in vitro. Curr Eye, Res. 2019;44:264-74.
12. Tomofumi Yamuda, Hiraku Onishi, Yoshiharu Machida, Sustained release kitoprofen micropartieles with ethyl cellulose and carboxymethyl ethyl cellulose. Journal of controlled Release. 2001; 75: 271-282.
13. Goodman S, Gilman A. The Pharmacological Basis of Therapeutics, New York, NY: Macmillan Publishing company; 1985.
14. Jung-Hwa lee, Tae Gwan Park and Hoo-kyan choi. Effect of formulation and processing variable on the characteristics of microspheres for water soluble drugs prepared by w/o/o double emulsion solvent diffusion method. International journal of pharmaceutics. 2000; 196:75-78.
15. Chowdary K.P.R., Koteshwara Rao N, and Malathi K. Ethyl cellulose microspheres of gliplizide: characterization, in vitro and in vivo evaluation. Indian Journal of pharmaceutical sciences. 2004; 66 (4): 412-416.
16. Pralhad T.Tayade, and Rajendra Kumar D.Kale. Encapsulation of water – insoluble Drug by a cross linking Technique: Effect

of process and formulation variables on encapsulation efficiency, particle size, and In vitro Dissolution Rate. AAPS Pharma Sci Tech. 2004; 6(1) Article 12.
17. Badri Viswanathan N, Thomas P.A, Pandit J.K, Kulkarni M.G and Mashelkar R.A. Preparation of non-porous microspheres with high entrapment of proteins by a (water-in-oil) –in –oil emulsion technique. Journal of controlled release. 1999; 58: 9-20.
18. Barkai A, Pathak V, Benita S. Polyacrylate (Eudrugit retard) microspheres for oral controlled release of nifedipine. I. Formulation design and process optimization. Drug Dev Ind Pharm. 1990; 16: 2057 2075.
19. Kawashia Y, Niwa T, Takeuchi H, Hino T, Itoh Y, Furuyamas. Characterization of polymorphs of tranilast anhydrate and tranilast monohydrate when crystallized by two solvent change spherical crystallization techniques. J Pharma Sci. 1991; 81: 472–478.
20. Costa P and Lobo J.M.S. Modeling and comparison of dissolution Profiles. European Journal of pharmaceutical Sciences. 2001; 13:123 -133. 11. Bodmeier R, Chen H. Preparation and characterization of microspheres containing the anti-inflammatory agents, Indomethacin, ibuprofen and kitoprofen. J. Controlled Release. 1989; 10: 167-175
21. S. Hazedar, B.Dortunc. Preparation and in vitro evaluation of eudragit microspheres containing acetazolamide. International journal of pharmaceutics. 2004; 269: 131-140. 12. Jones DS, Pearce KJ,
22. Investigation of the effects of some process variables on microencapsulation of propranolol HCl by solvent evaporation method. Int J Pharm. 1995; 118: 99 -2005. Trop J Pharm Res, June 2005; 4

How to cite this article:
Ms. Thakare Pooja Manohar et al. Ijppr.Human, 2026; Vol. 32 (6): 466-475

Conflict of Interest Statement: All authors have nothing else to disclose.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.