Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 11 [3]February 2022 : 192-196
©2022 Academy for Environment and Life Sciences, India
Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

REVIEW ARTICLE **OPEN ACCESS**

A Conceptual Review on Nanoparticles Loaded Matrix Tablets

Shrikrushna A. Shinde*[1], Parulben D. Mehta[1]
[1]School of Pharmacy, LNCT University, Bhopal, MP, India
For Correspondence : shindeshrikrushna@gmail.com

ABSTRACT
Polymeric nanosystems are widely used today. Nanoparticles loaded matrix tablets are one of the novel hybrid drug delivery system can be used efficiently. Suitable polymeric combination can be employed to produce effective controlled-release systems for different drugs. Various natural and physico-chemical factors affect the biopharmaceutical properties of drugs. Matrix tablet act as a drug reservoir for sustain drug release. The dual system of nanoparticles loaded matrix tablets will be more promising formulation because of increased effective surface area of particles & better stability.
Keywords: Nanoparticles, Matrix tablet, Controlled release, Drug reservoir

Received 11.11.2021 Revised 15.01.2022 Accepted 30.01.2022

INTRODUCTION

Currently, oral medications account for more than 65 percent of all marketed drugs. Because of its ease of administration, high patient compliance, non-sterile nature, cost-effectiveness, and flexibility of dose forms, the oral route of administration is the most expedient and extensively utilized for drug delivery. However, poor water-soluble drug bioavailability is a key issue. It is also unsuitable due to physicochemical and pharmacokinetic features that are undesired [1-2]. As a result, such medicines have low oral bioavailability, which leads to considerable variability and poor control of plasma levels and therapeutic effects [2]. One of the greatest contemporary issues facing the pharmaceutical business is low aqueous solubility [1]. The rate limiting criteria for oral absorption include the drug's solubility, dissolution, and permeability [1]. The problem is exacerbated by the vast number of active pharmacological components that emerge from the drug discovery process [2]. The oral bioavailability of a medicine is affected by a variety of physicochemical and physiological characteristics [3]. Medication size reduction improves oral bioavailability by increasing the effective surface area of the drug, which increases its solubility and dissolving rate [3-5]. Dissolution is the transformation of a solid substance into a liquid [2-3]. The rate limiting criteria for oral absorption include the drug's solubility, dissolution, and permeability [6]. According to the Noyes and Whitney equation and the Ostwald-Freundlich equation, as the effective surface area of a medication increases, it becomes more accessible to the dissolution media, which promotes its aqueous solubility, resulting in good bioavailability [7]. The poor water solubility and dissolution of oral dosage forms presents a barrier in their design [7]. Solubility, stability, temperature, humidity, compatibility, mixing speed, mixing time, and other process and formulation factors are all important for optimal drug formulation [7-8]. It has become necessary to develop techniques to increase the water solubility and dissolution rate of such medicines [8]. Manipulation of drug properties is a more capable strategy in pharmaceutical research than developing new drug molecules and dealing with the issues mentioned above [9-10]. The therapeutic efficiency is elicited by delivering the medicament at the right pace and quantity to its site of action [10].

Physiologic availability or bioavailability is term used to describe this property of the dose form [11]. The pharmacologic response is precisely proportional to the drug's bioavailability for the majority of medications [11]. The rate and extent to which a medicine reaches the systemic circulation is known as bioavailability. There are two types of it. a) Absolute bioavailability: This is the comparison of a drug's bioavailability after non-intravenous delivery against the same drug's bioavailability after intravenous administration. b) Relative bioavailability: This is a comparison of the bioavailability of the test drug and the reference drug when administered via the same route [12-13]. The bioavailability of medications is influenced by a variety of pharmacological and physiological factors. In the development of drugs, nanotechnology plays a crucial role. It's an interdisciplinary scientific field that's still evolving. The delivery of conventional medications, recombinant proteins, vaccines, and nucleotides is a crucial technique [14]. Nanoformulations based on polymers are frequently employed today. Researchers have been drawn to these products because of their altered physical and chemical features [15]. By retaining the medication in

its preferred crystalline state, nanoparticles can overcome the problem of poor dissolving rate and impaired oral bioavailability, as well as reducing delivery difficulties [15-16]. The Nernst-Brunner diffusion layer model predicts that the solid particle's peripheral layer breaks up fast into an adjacent thin section of solvent [16]. Stable state mass transfer into the bulk solution occurs through that saturated film [16]. It has been established that an effective medication delivery system is one that achieves and maintains therapeutic drug plasma concentrations [4-5, 17-20].

Why nanoformulations?

Nanomedicines are a somewhat new however quickly creating science where materials in the nanoscale range are utilized to convey helpful active drugs in a controlled way. One of the promising strategies for producing nanosuspension of low water soluble medicinal compounds is nanoprecipitation [21]. The following are the basic requirements for a drug's nanosuspension formulation: a) a high log P value, b) a high melting point, and c) a high dose. Drugs with a log P value of 1 to 3 have good passive absorption across lipid membranes, while those with a log P value of greater than 3 or less than 1 usually have poor transport mechanisms [3]. Nanoparticles can be isolated from nanosuspensions using high-speed centrifugation and drying. Various nanonization techniques for hydrophobic medications have been utilised to control their solubility and bioavailability difficulties throughout the last 30 years [2-3]. Efforts are currently being undertaken to expand their use in site-specific targeted medication delivery [23]. One of the disadvantages of nanosizing a medicine is that it becomes amorphous. The change is caused by the stirrer's high speed as well as the heat generated throughout the process. Because the drug's mobility in the amorphous phase is higher than in the crystalline phase, nanocrystals are more stable in nanosuspension. The XRD analysis of freeze dried nanosuspension is critical for determining how the drug molecules' crystalline state has changed.

Common problems with nanoformulations

Ostwald ripening is a thermodynamically driven spontaneous process that results in particle aggregation. The system is continually attempting to reduce its overall energy consumption. The energetics of molecules on the surface of tiny particles is unfavourable. These molecules have a tendency to separate from the surface of small particles and dissolve in solution, according to Kelvin's equation. When all particles accomplish this, the number of free molecules in the solution rises (Supersaturation). On the surface of bigger particles, unbound molecules have a tendency to condense. As a result, all smaller particles contract while larger particles expand. Overall average size will eventually increase, a phenomenon known as Ostwald ripening. Ostwald ripening is directly related to increasing drug bulk solubility and increased interfacial tension. Also, due to Ostwald ripening, a shift in Gibbs free energy causes agglomeration or crystal development, resulting in thermodynamically unstable nanosuspension.

Polymers used for nanosystems

Steric stabilisation is achieved by adsorbing polymers onto the drug particle surface, whereas electrostatic stabilisation is achieved by adsorbing charged or ionic molecules [24]. The key thermodynamic driving factor for such adsorption on the particle surface is the molecular weight of the polymer [24]. The higher the molecule weight, the slower the adsorption rate [24]. Nano-systems are made up of a variety of synthetic and natural polymers. Because of their biocompatible elimination from the body, biodegradable polymers are preferable to alternative materials for application in drug delivery systems. They can be moulded into a number of forms and sizes for a range of uses. The polymer type, molecular weight, copolymer ratio, and desired degradation/ erosion effect of the nanoparticles are all factors to consider when choosing a polymer. Natural polymers are typically considered to be safe, cost-effective, water soluble, and biocompatible with both the human body and formulation components [25]. Denaturation or cross-linking is the most common methods for converting them to nanoparticles [25-26]. One of the methods of nanoparticle production by oppositely charged counter-ions against charged groups existing in the substance is electrostatic neutralization [25-27]. Gelatin, albumin, lecithin, alginate, dextran, chitosan, agarose, and other similar polymers are widely utilized in industry. Eudragit RL100 (acrylate copolymer) is insoluble at physiological pH values and has swelling capability, making it excellent for medication controlled release dispersions [25-29]. Polymeric suspensions based on Eudragit have been shown to be a viable carrier system for the intended ocular release of a variety of medicines [25-29]. Nanoparticles retain chemical characteristics better than synthetic polymers. Various polymers, such as Polystyrene, Poly (lactic acid), and others, are used to modify medication delivery. Surfactants (SLS, SDS, Tween 80, Poloxamer 188, etc.) are useful in nanosuspension for three reasons: (1) increasing drug wettability and penetrability; (2) preventing drug precipitation; and (3) increasing apparent solubility due to micelle formation. Micelle production occurs at concentrations higher than CMC. They have an internal core with accumulated hydrophobic regions and an exterior hydrophilic shell that acts as a balancing out interface. Non-polar particles are dissolved inside the micelle centre, while polar atoms are adsorbed on the micelle surface.

Methods employed to produce nanoparticles

Nano size can be achieved by 'Bottom Up Technologies' (creation of smaller particles by precipitation at the molecular level) or 'Top Down Technologies' (fracturing larger particles into smaller particles). Media Milling, for example. For years, precipitation has been used to prepare submicron particles of weakly water soluble medicines. The medicine is usually dissolved in a solvent before being combined with miscible anti-solvent containing surfactants. Rapid addition of a drug solution results in drug supersaturation, nuclei formation, and crystal development, resulting in ultrafine drug solids. For stable nanosuspension, a small particle size with a slow growth rate is required. Crystal growth is also influenced by temperature [30].

Nanoparticles are extremely effective:

- To mediate the bio-distribution of active molecules
- To improve drug loading
- For drug targeting
- For easy transport, release and exchanges with biological barriers
- To increase the saturation solubility and dissolution velocity of drug
- For incorporation in a solid matrix

When it comes to incorporating nanoparticles into other forms, there are a variety of ways that can be used. Due to excellent patient compliance and flexibility in the production of dose forms, the oral route is the most suitable, affordable, and common method for drug delivery [1-3]. Aqueous solubility and oral bioavailability are low in many medicines [38-39].

Matrix tablets are useful for cost effective extended-release medication therapy. It is even distribution of actives through hydrophilic or hydrophobic polymers. It is a formulation for continuous drug delivery.

Advantages of matrix tablets

- Reduced drug dosing
- Better patient compliance
- Fewer systemic drug fluctuations
- Dose reduction
- Less drug accumulation
- Lessening drug toxicity
- Stabilization due to uniformity in drug levels
- Bioavailability enhancement
- Cost-effective product

Disadvantages of matrix tablets

- Continuous release
- Delayed onset time
- Dose-dumping probability
- High possibility of pre-systemic metabolism

Sustained release matrix tablets can be made in two ways: directly compressing the powder mix comprising the medication, polymer, and other additives, or granulating the powder blend before compression [40]. The qualities of the medication, polymer, and other substances influence the approach chosen. The matrix tablet is one of the most practical methods for creating sustained-release dosage forms. In practice, direct compression of the drug, retardant material, and additives results in a tablet with drug particles embedded in the retardant matrix core [41]. Diffusion, degradation, and swelling followed by diffusion are the three basic ways by which active compounds might be released from a delivery system. The development of a sustained release tablet dosage form is based on a large number of statistical studies, which are acknowledged as useful strategies for designing an optimal formulation with a suitable dissolving rate in a short amount of time and with the fewest possible trials [42].

Nanoparticles loaded matrix tablets

Stable nanoparticles stacked matrix tablets of medications can be created with adjusted biopharmaceutical characters with wanted results. Such frameworks will be gainful for upgrade of disintegration pace of BCS class II medications, stability of medication, sustains delivery and patient consistence.

Conclusion

Nanoformulations based on polymers are frequently employed today. Nanoparticles loaded matrix tablets can be used as harmless, efficient & convenient formulations. Various controlled-release systems can be designed with suitable polymeric compounds. Effective formulations rely on different natural and physico-chemical variables. The hybrid formulation (dual system) i.e. nanoparticles loaded matrix tablet will be

more promising dosage form because nano size will be able to increase effective surface area, and matrix tablet act as a drug reservoir for sustain drug release.

REFERENCES

1. Verma, S., Gokhale, R., & Burgess, D. J. (2009). A comparative study of top-down and bottom-up approaches for the preparation of micro/nanosuspensions. *International journal of pharmaceutics*, *380*(1-2), 216-222.
2. Doornbos CA, Haan PD. Encyclopedia of pharmaceutical technology. Swarbrick J, Boylan JC. Marcel Dekker, New York. 1995; 77.
3. Ahuja, B. K., Jena, S. K., Paidi, S. K., Bagri, S., & Suresh, S. (2015). Formulation, optimization and in vitro–in vivo evaluation of febuxostat nanosuspension. *International journal of pharmaceutics*, *478*(2), 540-552.
4. Shrivastava, A., Sakthivel, S., Pitchumani, B., & Rathore, A. S. (2011). A statistical approach for estimation of significant variables in wet attrition milling. *Powder technology*, *211*(1), 46-53.
5. Kassem, M. A., Rahman, A. A., Ghorab, M. M., Ahmed, M. B., & Khalil, R. M. (2007). Nanosuspension as an ophthalmic delivery system for certain glucocorticoid drugs. *International journal of pharmaceutics*, *340*(1-2), 126-133.
6. Rowland M, Thomas N, Tozer. Clinical pharmacokinetic pharmacodynamics: Concepts and applications. 4th edition, PA: Lippincott Williams & Wilkins, Philadelphia. 2010.
7. Sun, J., Wang, F., Sui, Y., She, Z., Zhai, W., Wang, C., & Deng, Y. (2012). Effect of particle size on solubility, dissolution rate, and oral bioavailability: evaluation using coenzyme Q10 as naked nanocrystals. *International journal of nanomedicine*, *7*, 5733.
8. Vyas SP, Khar RK. Targeted and controlled drug delivery: Novel carrier systems. CBS Publishers, New Delhi. 2002; 331–364.
9. Brahmankar DM, Jaiswal SB. Biopharmaceutics and pharmacokinetic a treatise. Vallabh Prakashan, New Delhi. 2015.
10. Witztum JL. Drugs used in the treatment of hyperlipoproteinemias. Goodman and Gillman's: The pharmacological basis of therapeutics. 9th edition, McGraw Hill, New York. 1996; 891–892.
11. Shargel L, Yu AB. Applied Biopharmaceutics& pharmacokinetics. 4th edition, New York: McGraw-Hill. 1999.
12. Govindarajan, R., & Nagarsenker, M. S. (2005). Formulation studies and in vivo evaluation of a flurbiprofen-hydroxypropyl β-cyclodextrin system. *Pharmaceutical development and technology*, *10*(1), 105-114.
13. Heaney, R. P. (2001). Factors influencing the measurement of bioavailability, taking calcium as a model. *The Journal of nutrition*, *131*(4), 1344S-1348S.
14. Parveen, S., Misra, R., & Sahoo, S. K. (2012). Nanoparticles: a boon to drug delivery, therapeutics, diagnostics and imaging. *Nanomedicine: Nanotechnology, Biology and Medicine*, *8*(2), 147-166.
15. Han, J., Zhao, D., Li, D., Wang, X., Jin, Z., & Zhao, K. (2018). Polymer-based nanomaterials and applications for vaccines and drugs. *Polymers*, *10*(1), 31.
16. http://www.in-adme.com/dissolution_theory.html
17. Ghosh, I., Bose, S., Vippagunta, R., & Harmon, F. (2011). Nanosuspension for improving the bioavailability of a poorly soluble drug and screening of stabilizing agents to inhibit crystal growth. *International journal of pharmaceutics*, *409*(1-2), 260-268.
18. Hu, X., Chen, X., Zhang, L., Lin, X., Zhang, Y., Tang, X., & Wang, Y. (2014). A combined bottom–up/top–down approach to prepare a sterile injectable nanosuspension. *International Journal of Pharmaceutics*, *472*(1-2), 130-139.
19. Müller, R. H., & Keck, C. M. (2012). Twenty years of drug nanocrystals: where are we, and where do we go?. *European journal of pharmaceutics and biopharmaceutics*, *80*(1), 1-3.
20. Zhang, X., Guan, J., Ni, R., Li, L. C., & Mao, S. (2014). Preparation and solidification of redispersible nanosuspensions. *Journal of Pharmaceutical Sciences*, *103*(7), 2166-2176.
21. Xia, D., Quan, P., Piao, H., Piao, H., Sun, S., Yin, Y., & Cui, F. (2010). Preparation of stable nitrendipine nanosuspensions using the precipitation–ultrasonication method for enhancement of dissolution and oral bioavailability. *European Journal of Pharmaceutical Sciences*, *40*(4), 325-334.
22. Kumar Singh, S., Vaidya, Y., Gulati, M., Bhattacharya, S., Garg, V., & Kumar Pandey, N. (2016). Nanosuspension: principles, perspectives and practices. *Current drug delivery*, *13*(8), 1222-1246.
23. Modh, N., Mehta, D., Parejiya, P., Popat, A., & Barot, B. (2014). An overview of recent patents on nanosuspension. *Recent patents on drug delivery & formulation*, *8*(2), 144-154.
24. Tuomela, A., Hirvonen, J., & Peltonen, L. (2016). Stabilizing agents for drug nanocrystals: effect on bioavailability. *Pharmaceutics*, *8*(2), 16.
25. Kocbek, P., Baumgartner, S., & Kristl, J. (2006). Preparation and evaluation of nanosuspensions for enhancing the dissolution of poorly soluble drugs. *International journal of pharmaceutics*, *312*(1-2), 179-186.
26. Krause, K. P., & Müller, R. H. (2001). Production and characterisation of highly concentrated nanosuspensions by high pressure homogenisation. *International journal of pharmaceutics*, *214*(1-2), 21-24.
27. Müller, R. H., Grau, M. J., & Hildebrand, G. E. (1999). Increase of solubility of poorly soluble drugs by transfer to Dissocubes using high pressure homogenization. In *Proc Int Symp Control Rel Bioact Mater* (Vol. 26, pp. 112-3).
28. Radtke, M. (2001). Pure drug nanoparticles for the formulation of poorly soluble drugs. *New drugs*, *3*(62-68).
29. Dearans R. Atovaquone pharmaceutical composition. US Patent, US 6018080, 2000.
30. Krishna, K. B., & Prabhakar, C. (2011). A review on nanosuspensions in drug delivery. *Int J Pharma and Bio Sci*, *2*(1), 549-58.

31. Montasser, I., Fessi, H., & Coleman, A. W. (2002). Atomic force microscopy imaging of novel type of polymeric colloidal nanostructures. *European journal of pharmaceutics and biopharmaceutics*, *54*(3), 281-284.
32. Bujňáková, Z., Dutková, E., Baláž, M., Turianicová, E., & Baláž, P. (2015). Stability studies of As4S4 nanosuspension prepared by wet milling in Poloxamer 407. *International Journal of Pharmaceutics*, *478*(1), 187-192.
33. Ravichandran R (2013). Development of an oral curcumin nanocrystal formulation. Journal of Nanotechnology in Engineering and Medicine. 3(4): 041007.
34. Khan, M. I., Madni, A., & Peltonen, L. (2016). Development and in-vitro characterization of sorbitan monolaurate and poloxamer 184 based niosomes for oral delivery of diacerein. *European Journal of Pharmaceutical Sciences*, *95*, 88-95.
35. Schöler, N., Krause, K., Kayser, O., Müller, R. H., Borner, K., Hahn, H., & Liesenfeld, O. (2001). Atovaquone nanosuspensions show excellent therapeutic effect in a new murine model of reactivated toxoplasmosis. *Antimicrobial agents and chemotherapy*, *45*(6), 1771-1779.
36. Herzberger, J., Niederer, K., Pohlit, H., Seiwert, J., Worm, M., Wurm, F. R., & Frey, H. (2016). Polymerization of ethylene oxide, propylene oxide, and other alkylene oxides: synthesis, novel polymer architectures, and bioconjugation. *Chemical reviews*, *116*(4), 2170-2243.
37. Yousif, E., & Haddad, R. (2013). Photodegradation and photostabilization of polymers, especially polystyrene. *SpringerPlus*, *2*(1), 1-32.
38. Sievens-Figueroa, L., Bhakay, A., Jerez-Rozo, J. I., Pandya, N., Romañach, R. J., Michniak-Kohn, B., ... & Davé, R. N. (2012). Preparation and characterization of hydroxypropyl methyl cellulose films containing stable BCS Class II drug nanoparticles for pharmaceutical applications. *International journal of pharmaceutics*, *423*(2), 496-508.
39. Rao, Y. M., Kumar, M. P., & Apte, S. (2008). Formulation of nanosuspensions of albendazole for oral administration. *Current Nanoscience*, *4*(1), 53-58.
40. Sastry, S. V., & Khan, M. A. (1998). Aqueous based polymeric dispersion: Plackett–Burman design for screening of formulation variables of atenolol gastrointestinal therapeutic system. *Pharmaceutica Acta Helvetiae*, *73*(2), 105-112.
41. Huang, Y. B., Tsai, Y. H., Yang, W. C., Chang, J. S., & Wu, P. C. (2004). Optimization of sustained-release propranolol dosage form using factorial design and response surface methodology. *Biological and Pharmaceutical Bulletin*, *27*(10), 1626-1629.
42. Bozič, D. Z., Vrečer, F., & Kozjek, F. (1997). Optimization of diclofenac sodium dissolution from sustained release formulations using an artificial neural network. *European journal of pharmaceutical sciences*, *5*(3), 163-169.

CITATION OF THIS ARTICLE

Shrikrushna A. Shinde, Parulben D. Mehta. A Conceptual Review On Nanoparticles Loaded Matrix Tablets. Bull. Env. Pharmacol. Life Sci., Vol 11[3] Feb 2022 : 192-196.