

Antibiotic Drug Delivery System for the Intracellular Targeting of Bacterial Pathogen

Gayatri Anil Patil¹ and Rutuja Gajanan Chaudhari²
Dr. Uttamrao Mahajan College of B. Pharmacy, Chalisgaon, India

Abstract: *Treatment of intracellular infections remains a serious pharmaceutical issue even with the introduction of a significant number of novel medicines. These specialized frequently have sub therapeutic antibiotic concentrations, necessitating the frequent administration of large antibiotic dosages. Not only is this expensive, but it could also have more systemic or localized adverse effects. Treatment for intracellular bacterial diseases is challenging due to the resistance of commonly used antimicrobial drugs such as macrolides, aminoglycosides, β -lactamases, and fluoroquinolones to enter, accumulate, or stay inside mammalian cells. The growing issue of antibiotic resistance makes treating illnesses brought on by these drugs increasingly difficult. Targeted drug delivery into the cell compartment that is the most vulnerable to effects of the appropriate drug is a difficult issue, and a proper resolution can greatly improve the therapeutic agents' delivery's effectiveness and minimize its negative effects. A drug delivery system that meets the requirements for usage in pharmaceutical and biomedical formulations should have multiple features, including antibacterial activity, biodegradability, and biocompatibility. Through this approach, outdated antibiotics rendered ineffective due to toxicity or resistance can be revived, last-line therapy antibiotics can be saved by raising the therapeutic index, the antimicrobial spectrum of antibiotic scaffolds that failed due to membrane permeability issues can be expanded, and the time between the emergence of new antibiotics and the increasingly drug-resistant pathogens can be shortened. The Purpose of this article is, to outline the key research directions for the development of drug delivery mechanisms for the intracellular release of antibiotics, as well as the limits of each class of antibiotics in targeting intracellular bacteria. This more efficient use of antibiotics may mitigate their downsides and provide the foundation for decreasing the present time required by traditional therapies. This will be concentrate on the role of DDS as a potential tool against intracellular microorganisms.*

Keywords: Intracellular targeting bacterial pathogen, Drug Delivery System, Antibiotic classes, Mechanism of cellular Targeting Antibiotic, Antibiotic Transporters for Intracellular Activity

REFERENCES

- [1]. Mariana Carmen Chifiriuc, Alina Maria Holban, Carmen Curutiu, Lia- Mara Ditu, Grigore Mihaescu, Alexandra Elena Oprea, Alexandru Mihai Grumezescu and Veronica Lazar February 2016 In book: Smart Drug Delivery System 305-344
- [2]. Antibiotic Resistance: Implications for Global Health and Novel Intervention Strategies: Workshop Summary. Washington, DC: The National Academies Press. 2010. 496 p.
- [3]. Nigat Atbiaw,² Endris Aman,² Bereket Dessalegn,² Oumer Masrie,² Demeke Debalke,² Gashaw Enbiyale,¹ Andnet Yirga,² Gebrehiwot Tekilu,² Askale Abrhaley,² Fentahun Mitku² Pharmacy & Pharmacology International Journal Volume 6 Issue 3 – 2018
- [4]. Vyas SP, Khar RK. Targeted and controlled drug delivery: Novel Carrier Systems. Int J Pharmaceut. 2003;267(Suppl 1-2):157.
- [5]. Kumari A, Yadav SK, Yadav SC. Biodegradable polymers nanoparticles based drug delivery systems. Colloids Surf B Biointerfaces. 2010;75(1):1– 18.
- [6]. J. D. Butts: Intracellular concentrations of antibacterial agents and related clinical implications. Clin Pharmacokinet 27(1), 63- 84 (1994) 2.

- [7]. A. Alonso and F. Garcia-del Portillo: Hijacking of eukaryotic functions by intracellular bacterial pathogens. *Int Microbiol* 7(3), 181-191 (2004).
- [8]. Chifiriuc MC, Lixandru M, Iordache C, Bleotu C, Larion C, Olguta D, et al. Internalization of *Staphylococcus aureus* and *Pseudomonas aeruginosa* bacterial cells by non-phagocytic, epithelial human cells. *Romanian Biotechnological Letters*. 2008;13(2).
- [9]. Bleotu C, Chifiriuc MC, Dracea, O., Iordache C, Delcaru C, Lazar V. In vitro modulation of adherence and invasion ability of enteroinvasive *Escherichia Coli* by different viruses. *International Journal of Applied Biology and Pharmaceutical Technology*. 2010:1359–63
- [10]. M. Desjardins: Biogenesis of phagolysosomes: the kiss and run hypothesis. *Trends in Cell Biology* 5(5), 183-186 (1995) 4. W. Beron, C. Alvarez-Dominguez, L. Mayorga and P. D. Stahl: Membrane trafficking along the phagocytic pathway. *Trends in Cell Biology* 5(3), 100-104 (1995) .
- [11]. M. Desjardins, L. A. Huber, R. G. Parton and G. Griffiths: Biogenesis of phagolysosomes proceeds through a sequential series of interactions with the endocytic apparatus. *J. Cell Biol.* 124(5), 677-688 (1994).
- [12]. Chifiriuc MC, Bleotu C, Pelinescu DR, Lazar V, Ditu LM, Vassu T, et al. Patterns of colonization and immune response elicited from interactions between enteropathogenic bacteria, epithelial cells and probiotic fractions. *International Journal of Medicine and Biomedical Research*. 2010;1(4):47–57.
- [13]. Madigan M, Martinko J, J. P. Brock's *Biology of Microorganisms*. 8th edition. Net Jersey: Prentice Hall. 1997. Nizet V, Esko JD. *Bacterial and Viral Infections. Essentials of Glycobiology*. CSH Press. 2009.
- [14]. Yatsuyanagi J, Saito S, Sato H, Miyajima Y, Amano K-I, Enomoto K. Characterization of enteropathogenic and enteroaggregative *Escherichia coli* isolated from diarrheal outbreaks. *Journal of Clinical Microbiology*. 2002 07/09/received 09/03/revised 10/21/accepted;40(1):294-7. PubMed PMID: PMC120118.
- [15]. Chifiriuc MC, Bleotu C, Marutescu L, Cristea D, Lazar V. The modulation of cells secretory patterns by invasive *Shigella* spp. and enteroinvasive *E. coli* bacterial cells and their soluble components. *Roumanian Archives of Microbiology and Immunology*. 2010 Jul–Sep;69(3):139–44. PubMed PMID: 21434590. Epub 2011/03/26. eng
- [16]. C. van Ooij, L. Kalman, I. van, M. Nishijima, K. Hanada, K. Mostov and J. N. Engel: Host cell-derived sphingolipids are required for the intracellular growth of *Chlamydia trachomatis*. *Cell Microbiol* 2(6), 627-637 (2000) .
- [17]. A. D. Joshi, S. Sturgill-Koszycki and M. S. Swanson: Evidence that Dot-dependent and -independent factors isolate the *Legionella pneumophila* phagosome from the endocytic network in mouse macrophages. *Cell Microbiol* 3(2), 99-114 (2001) 30.
- [18]. A. R. Roy and L. G. Tilney: The road less traveled: transport of *Legionella* to the endoplasmic reticulum. *J Cell Biol* 158(3), 415-419 (2002)
- [19]. Galan JE, Wolf-Watz H. Protein delivery into eukaryotic cells by type III secretion machines. *Nature*. 2006;444:567–73.
- [20]. Mihaescu G, Chifiriuc (Balotescu) MC. Toxins and other potentially toxic substances. Romanian Academy Publishing House. 2005;ISBN 973-27-1136-1:364.
- [21]. Mihaescu G, Chifiriuc MC, L.M. D. Antibiotics and antimicrobial chemotherapeutic substances. Romanian Academy Publishing House. 2008;ISBN 978-973-27-1573-4.:358.
- [22]. Collier L, Balows A, Sussman M. Topley and Wilson's *Microbiology and Microbial Infections*, Vol. I, II. 1998.
- [23]. Mingeot-Leclercq MP, Glupczynski Y, Tulkens PM. Aminoglycosides: activity and resistance. *Antimicrobial Agents and Chemotherapy*. 1999 Apr;43(4):727–37. PubMed PMID: 10103173. PubMed Central PMCID: PMC89199. Epub 1999/04/02. eng.
- [24]. Chopra I, Roberts M. Tetracycline antibiotics: mode of action, applications, molecular biology, and epidemiology of bacterial resistance. *Microbiology and Molecular Biology Reviews*. 2001 Jun;65(2):232–60; second page, table of contents. PubMed PMID:11381101. PubMed Central PMCID: PMC99026. Epub 2001/05/31. eng.

- [25]. Coates TD, Torres M, Harman J, Williams V. Localization of chlorotetracycline fluorescence in human polymorphonuclear neutrophils. *Blood*. 1987 Apr;69(4):1146–52. PubMed PMID: 3828534. Epub 1987/04/01. eng.
- [26]. B. Arellano-Reynoso, N. Lapaque, S. Salcedo, G. Briones, A. E. Ciocchini, R. Ugalde, E. Moreno, I. Moriyon and J.-P. Gorvel: Cyclic [beta]-1,2-glucan is a brucella virulence factor required for intracellular survival. *Nat Immunol* 6(6), 618-625 (2005)
- [27]. Carlier MB, Garcia-Luque I, Montenez JP, Tulkens PM, Piret J. Accumulation, release and subcellular localization of azithromycin in phagocytic and non-phagocytic cells in culture. *International Journal of Tissue Reactions*. 1994;16(5–6):211–20. PubMed PMID: 7558665. Epub 1994/01/01. eng.
- [28]. Gilbert P, Collier PJ, Brown MRW. Influence of growth rate on susceptibility to antimicrobial agents: biofilms, cell cycle, dormancy, and stringent response. *Antimicrob Agents Chemother*. 1990;34(10):1865–1868.
- [29]. Huh AJ, Kwon YJ. “Nanoantibiotics”: a new paradigm for treating infectious diseases using nanomaterials in the antibiotics resistant era. *Journal of Controlled Release*. 2011 Dec 10;156(2):128–45. PubMed PMID: 21763369. Epub 2011/07/19
- [30]. Jain KK. Drug delivery systems—an overview. *Methods in Molecular Biology* (Clifton, NJ). 2008;437:1–50. PubMed PMID: 18369961. Epub 2008/03/29.
- [31]. M.-P. Mingeot-Leclercq and P. M. Tulkens: Aminoglycosides: Nephrotoxicity. *Antimicrob. Agents Chemother*. 43(5), 1003- 1012 (1999)
- [32]. . H. A. Nguyen, J. Grellet, D. Paillard, V. Dubois, C. Quentin and M. C. Saux: Factors influencing the intracellular activity of fluoroquinolones: a study using levofloxacin in a *Staphylococcus aureus* THP-1 monocyte model. *J Antimicrob Chemother* 57(5), 883-890 (2006).
- [33]. P. Gilbert, P. J. Collier and M. R. Brown: Influence of growth rate on susceptibility to antimicrobial agents: biofilms, cell cycle, dormancy, and stringent response. *Antimicrob Agents Chemother* 34(10), 1865-1868 (1990).
- [34]. A. M. Cuffini, V. Tullio, N. Mandras, J. Roana, G. Banche and N. A. Carlone: The leading role of antimicrobial agents in modulating the binomial host-microorganism. *Curr. Med. Chem.-Anti-Infective Agents* 3, 1-13 (2004).
- [35]. Tiwari G, Tiwari R, Sriwastawa B, Bhati L, Pandey S, Pandey P, et al. Drug delivery systems: an updated review. *International Journal of Pharmaceutical Investigation*. 2012 Jan;2(1):2–11 PubMed PMID: 23071954. PubMed Central PMCID: PMC3465154. Epub 2012/10/17.
- [36]. Rosenholm JM, Peuhu E, Eriksson JE, et al. Targeted intracellular delivery of hydrophobic agents using mesoporous hybrid silica nanoparticles as carrier systems. *Nano Lett*. 2002;9(9):3308–3311.