World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(Review Article)

Check for updates

A review on: CRISPR-based gene therapy in pharmacy: A revolutionary approach in modern therapeutics

Vaishnavi Dattatray Shimpi *, Prachi Nandakumar Padwal and Sancheti Santaram Rode

Samartha Institute of Pharmacy, Belhe, Pune, Maharashtra, India.

World Journal of Biology Pharmacy and Health Sciences, 2026, 26(01), 286–291

Publication history: Received on 21 March 2026; revised on 28 April 2026; accepted on 30 April 2026

Article DOI: https://doi.org/10.30574/wjbphs.2026.26.1.0230

Abstract

CRISPR-Cas9 is a revolutionary genome editing tool transforming pharmaceutical sciences. It enables precise modification of DNA sequences and has applications in genetic disorders, cancer ,and infectious diseases. This review provides detailed insights into its mechanism, applications, challenges, and future scope.CRISPR-Cas9 is a revolutionary genome editing tool transforming pharmaceutical sciences. CRISPR technology's ability to precisely and flexibly edit genes has opened up new ways to find, validate, and develop drug targets. Also, it has made way for personalized gene therapies, precise gene editing, and advanced screening techniques, all of which hold great promise for treating a wide range of diseases. In this article, we look at the latest research and clinical trials that show how CRISPR could be used to treat genetic diseases, cancer, infectious diseases, and other hard-to-treat conditions. However, ethical issues and problems with regulations are also discussed in relation to CRISPR-based therapies, which shows how important it is to use them safely and responsibly. As CRISPR continues to change how drugs are made and used, this review shines a light on the amazing things that have been done and what the future might hold in this rapidly changing field.

Keywords: CRISPR-Cas9; Gene Therapy; Genome Editing; Personalized Medicine; Drug Delivery; Biotechnology

1. Introduction

CRISPR-Cas9 has emerged as a groundbreaking tool in gene therapy, offering precise, efficient, and cost-effective genome editing. This review highlights the mechanism, applications, advantages, challenges, and future prospects of CRISPR-based gene therapy in pharmaceutical sciences. It has shown promising outcomes in treating genetic disorders, cancer, and viral infections. Despite its potential, concerns regarding off-target effects, ethical issues, and delivery systems remain critical. Overall, CRISPR technology is transforming drug development and personalized medicine.

1.1. Molecular Pharmacology of CRISPR Therapeutics

CRISPR-Cas systems rely on a guide RNA (gRNA) to direct the Cas nuclease to a complementary DNA sequence within the genome. Upon recognition of the target site, the Cas nuclease introduces double-strand breaks (DSBs), which are subsequently repaired by the cell's endogenous DNA repair mechanisms. Non-homologous end joining (NHEJ) can result in gene disruption through insertions or deletions, effectively knocking out target genes 9-10. In contrast, homology-directed repair (HDR) enables precise correction of the genomic sequence when a repair template is provided, allowing for accurate restoration or modification of defective genes. This dual capability—gene disruption or precise correction—forms the molecular basis for CRISPR's therapeutic versatility.

The pharmacodynamics of CRISPR therapeutics are primarily governed by the specificity and efficiency of target recognition 11-12. The gRNA sequence, the protospacer adjacent motif (PAM) recognized by the Cas protein, and the accessibility of chromatin all influence editing outcomes. Off-target cleavage remains a critical concern, as unintended

* Corresponding author: Vaishnavi Dattatray Shimpi.

genomic modifications can have deleterious effects. Therefore, careful gRNA design, rigorous preclinical validation, and ongoing monitoring are essential to maximize therapeutic benefits while minimizing risks 13-14. The pharmacokinetic behavior of CRISPR-based therapeutics is largely determined by the intracellular persistence of the editing components, which directly impacts both editing efficiency and the likelihood of off-target activity. The choice of delivery modality—whether viral vectors, lipid nanoparticles, or other non-viral systems—affects distribution, cellular uptake, clearance, and immunogenicity 15-16. Viral vectors typically offer higher efficiency and prolonged expression but carry immunogenic risks, whereas non-viral carriers are often safer but may require repeated dosing or optimization to achieve sufficient delivery. Understanding and optimizing these pharmacokinetic parameters is critical for translating CRISPR therapeutics from the laboratory to safe and effective clinical applications 17-18.

1.2. Delivery Challenges in CRISPR Therapeutics

One of the most critical factors determining the success of CRISPR-based therapeutics is the development of an efficient and safe delivery system. Since CRISPR components—whether they are DNA, mRNA, or ribonucleoprotein (RNP) complexes—must reach specific cells and nuclei to edit target genes, the mode of delivery plays a decisive role in therapeutic efficacy, biodistribution, and safety 19-20. Traditional approaches have primarily relied on viral vectors due to their high transduction efficiency. However, non-viral platforms are increasingly gaining attention because they offer enhanced safety and flexibility. The choice of delivery strategy must balance efficiency, specificity, immune compatibility, and scalability for clinical applications. Viral vectors have long been the workhorses of gene therapy and have naturally extended their role to CRISPR delivery. Adeno-associated viruses (AAVs) are particularly popular because of their ability to achieve efficient in vivo gene transfer and their relatively low immunogenicity compared to other viral systems 21-22. wHowever, their small cargo capacity of roughly 4.7 kb poses a significant limitation, especially when delivering both the Cas nuclease and guide RNA. Lentiviruses, on the other hand, offer the advantage of stable integration into the host genome, allowing for long-term expression of CRISPR components. This makes them attractive for certain therapeutic strategies but also raises concerns about insertional mutagenesis, which can lead to genomic instability or oncogenic transformation. While viral delivery remains one of the most potent strategies for ensuring intracellular uptake, the associated safety risks, immune responses, and production challenges cannot be ignored 23-24. Non-viral delivery methods are emerging as safer and more adaptable alternatives. Lipid nanoparticles (LNPs) have gained tremendous momentum as they can encapsulate and protect nucleic acids—including CRISPR mRNA or RNP complexes—while facilitating efficient cellular uptake through membrane fusion or endocytosis. This platform was notably proven during the development of mRNA vaccines, which helped accelerate their adaptation for gene editing. Polymeric nanoparticles present another versatile option; these biodegradable carriers can be engineered to provide controlled release and reduced toxicity, making them attractive for repeated or long-term administration 25-26.

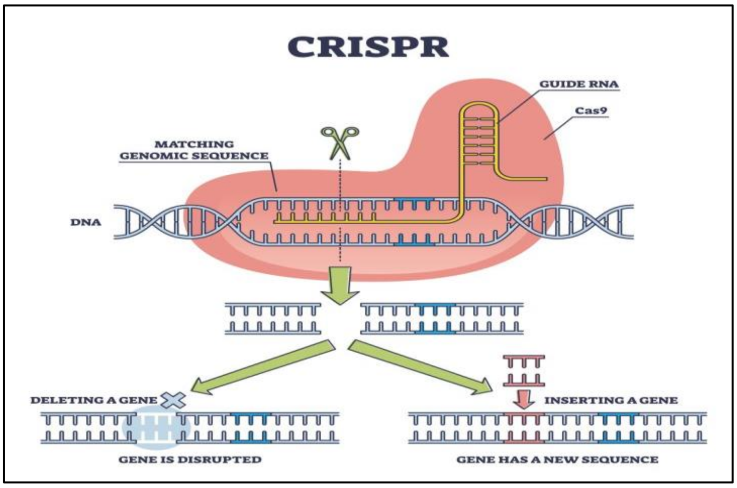

Figure 1 Mechanism of CRISPR-Cas9 Gene Editing

More recently, gold nanoparticles and exosome-based systems have emerged as novel delivery vehicles. (Table 1)These platforms offer excellent biocompatibility, tunable surface functionalization, and potential for cell-specific targeting, making them promising candidates for next-generation CRISPR delivery systems. Achieving tissue and cell-type specificity is one of the key goals in CRISPR therapeutic delivery 27. Nonspecific distribution can not only reduce efficacy but also increase the risk of off-target editing in unintended tissues. To address this, researchers are developing ligand-functionalized carriers that can selectively target specific cell populations, such as hepatocytes in the liver, neurons in the central nervous system, or immune cells for immunotherapy applications 28. This strategy improves therapeutic precision, reduces systemic exposure, and enhances safety by ensuring that CRISPR components accumulate predominantly in the desired tissues. Tissue-specific targeting, combined with controlled release and efficient cellular uptake, is expected to play a pivotal role in transforming CRISPR from a powerful lab tool into a clinically reliable therapeutic modality

2. Off-Target Effects and Safety Considerations

One of the most pressing concerns in the clinical application of CRISPR therapeutics is the risk of off-target effects. While the CRISPR-Cas system is designed for sequence specific editing, it can sometimes cleave genomic sites that are similar, but not identical, to the intended target 36. These unintended edits can lead to genotoxicity, disrupt essential genes, or cause unpredictable functional changes at the cellular level. In the context of therapeutic use, even low-frequency off-target mutations may carry significant long-term risks, especially when editing is performed in proliferative or stem cell populations 37-38. To address this challenge, multiple strategies have been developed to enhance specificity and minimize collateral damage. Optimized guide RNA (gRNA) design, using bioinformatic tools and predictive algorithms, can reduce the likelihood of binding to unintended sequences. High fidelity Cas variants such as Cas9-HF1 and eSpCas9 have been engineered to exhibit reduced nonspecific cleavage while maintaining robust on-target activity 39-40. Temporal control of nuclease activity is another powerful approach; transient delivery of CRISPR components in the form of mRNA or ribonucleoprotein (RNP) complexes limits the duration of nuclease exposure inside cells, thereby reducing the probability of off-target editing. Beyond genetic precision, immunogenicity is also a critical safety issue 41-42. Since most Cas proteins originate from bacterial species, the human immune system may recognize them as foreign, triggering an immune response. Similarly, the delivery vehicles themselves—whether viral or non-viral—can induce inflammation or immune activation. Therefore, careful monitoring of immunogenicity, both during preclinical testing and clinical translation, is essential to ensure the safety and tolerability of CRISPR therapeutics.

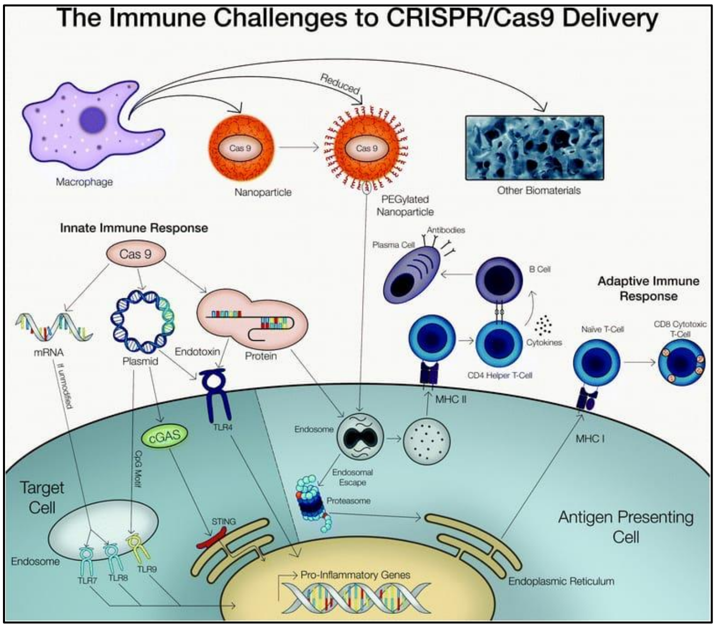

Figure 2 Pharmaceutical Delivery Strategies for CRISPR Therapeutics

3. Pharmaceutical Formulation Strategies

The formulation of CRISPR therapeutics plays a decisive role in determining their stability, bioavailability, safety, and overall clinical effectiveness. Unlike conventional small-molecule drugs, CRISPR-based therapies involve fragile biological macromolecules such as RNA and proteins, which are highly susceptible to degradation by nucleases and other environmental factors. A well-designed pharmaceutical formulation not only protects these components but also ensures their controlled delivery to the target site. Encapsulation of Cas9 mRNA and guide RNA within protective carriers is one of the most effective ways to shield them from degradation during storage, circulation, and cellular transport 45-46. By embedding these sensitive biomolecules in lipid nanoparticles, polymeric systems, or other nanocarriers, their structural integrity and functional activity are preserved. Stabilizing excipients such as sugars, amino acids, or specialized polymers are often incorporated to enhance shelf life, maintain conformational stability, and improve in vivo performance. This ensures that the therapeutic activity remains intact from formulation to target engagement. Controlled release strategies are essential for optimizing the therapeutic window of CRISPR therapeutics. Stimuli-responsive carriers can be engineered to release their payload in response to specific physiological triggers such as pH variations, redox gradients, or enzymatic activity within the target tissue microenvironment 47-48. This not only enhances local drug concentration but also minimizes systemic exposure, reducing the risk of unwanted immune activation or off-target editing. Targeted release further improves efficacy by ensuring that CRISPR components reach their intended cellular destinations in a timely and efficient manner.

3.1. Mechanism of CRISPR

CRISPR is derived from a natural defense system in bacteria. It works through:

- Guide RNA (gRNA): Identifies the target DNA sequence
- Cas9 enzyme: Acts as molecular scissors to cut DNA
- Once DNA is cut, the cell repairs it via:
- Non-Homologous End Joining (NHEJ)
- Homology Directed Repair (HDR)

This allows insertion, deletion, or correction of genes.

3.2. Applications

CRISPR is widely used in genetic disorders like sickle cell anemia, cancer therapy through CAR-T cells, infectious disease treatment, and drug discovery. It also plays a key role in pharmacogenomics.

3.3. Advantages

- CRISPR offers high precision,
- cost-effectiveness,
- faster drug development.
- potential permanent cure for genetic diseases.

3.4. Challenges and Limitations

- Off-target effects (unintended mutations)
- Ethical concerns (germline editing)
- Delivery issues (safe transport into cells)

3.5. Role in Pharmaceutical Industry

- CRISPR is transforming:
- Drug development pipelines
- Target validation
- Clinical trials
- Personalized therapy

Major pharmaceutical companies and research organizations are actively exploring CRISPR-based treatments.

3.6. Future Perspectives

Looking ahead, the future of CRISPR therapeutics is being shaped by rapid technological advancements, interdisciplinary integration, and a growing emphasis on precision and safety. AI-guided gRNA design represents a major leap forward, allowing for the selection of guide sequences with exceptional specificity and minimal off-target interactions. By leveraging massive genomic datasets, AI models can predict the optimal editing sites, improving both therapeutic precision and clinical safety 70-71. In parallel, next-generation Cas variants are being engineered to be smaller, more stable, and highly accurate, making them easier to package into delivery systems such as viral vectors, lipid nanoparticles, or polymeric carriers. Development of safer delivery systems (nanoparticles, viral vectors)Improved specificity with advanced CRISPR variants Expansion into rare and complex diseases Integration with AI and nanotechnology

4. Conclusion

CRISPR-Cas9 represents a paradigm shift in pharmaceutical sciences. Its ability to precisely edit genes offers new possibilities for treating previously incurable diseases. Although challenges remain, ongoing research and technological advancements are expected to overcome these barriers, making CRISPR a cornerstone of future medicine. CRISPR-based therapeutics represent a revolutionary leap in modern pharmacology, offering the possibility of targeted and durable interventions at the genomic level rather than merely managing symptoms. Their clinical potential spans a wide range of applications, from correcting single-gene mutations to reprogramming immune cells for targeted cancer therapy.

However, their successful translation into routine medical practice depends on the seamless integration of pharmacological insights with sophisticated pharmaceutical delivery systems that ensure precision, specificity, and minimal off-target activity. Emerging innovations in nanotechnology, AI-driven design, and next-generation Cas systems are laying the groundwork for more efficient and safer gene-editing therapeutics. At the same time, well-defined regulatory frameworks, rigorous safety monitoring, and international ethical consensus will be critical in guiding their responsible use. If these challenges are met, CRISPR technology could reshape the future of medicine, ushering in an era of precision therapeutics where genetic diseases are not just treated—but truly corrected at their source.

Compliance with ethical standards

Acknowledgement

We sincerely acknowledge the continuous guidance, motivation, and constructive feedback provided by our mentor, Prof. Prachi Padwal Their expertise and patience have been instrumental in shaping this review paper. We also extend our gratitude to Samarth Institute of Pharmacy, Belhe for providing the necessary academic environment and resources that supported this work.

References

[1] Jennifer Doudna JA, Emmanuelle Charpentier E. The new frontier of genome engineering with CRISPR-Cas9. Science. 2014;346(6213):1258096.

[2] Feng Zhang F, et al. Genome editing using CRISPR-Cas systems. Nature Biotechnology. 2014;32:347–355.

[3] Koonin EV EV, Makarova KS. CRISPR-Cas: evolution of an RNA-based adaptive immunity system. Nature Reviews Microbiology. 2019;17:67–82.

[4] Jinek M M, et al. A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity. Science. 2012;337:816–821.

[5] Barrangou R R, et al. CRISPR provides acquired resistance against viruses in prokaryotes. Science. 2007;315:1709–1712.

[6] Hsu PD PD, et al. Development and applications of CRISPR-Cas9 for genome engineering. Cell. 2014;157:1262–1278.

[7] Doudna JA JA. The promise and challenge of therapeutic genome editing. Nature. 2020;578:229–236.

[8] Ledford H H. CRISPR gene therapy shows promise against genetic diseases. Nature News. 2020.

[9] Frangoul H H, et al. CRISPR-Cas9 gene editing for sickle cell disease and beta-thalassemia. New England Journal of Medicine. 2021;384:252–260.

[10] Lino CA CA, et al. Delivering CRISPR: a review of the challenges and approaches. Drug Delivery. 2018;25:1234–1257.

[11] Wang H H, et al. CRISPR/Cas9 in genome editing and beyond. Annual Review of Biochemistry. 2016;85:227–264.

[12] Pickar-Oliver A A, Gersbach CA CA. The next generation of CRISPR–Cas technologies and applications. Nature Reviews Molecular Cell Biology. 2019;20:490–507.

[13] Kulcsár P.I., Táas A., Huszár K., et al. (2017). Crossing enhanced and high-fidelity SpCas9 nucleases to optimize specificity and cleavage. Genome Biology, 18(1), 190. https://doi.org/10.1186/s13059-017-1328-9

[14] Xu C.E., Chen G.J., Luo Y.L., et al. (2019). Advances in nucleic acid delivery systems for CRISPR/Cas9-basedgenome editing. Small, 15(46), e1901983. https://doi.org/10.1002/smll.201901983

[15] Lino C.A., Harper J.C., Carney J.P., Timlin J.A. (2018). Delivering CRISPR: a review of the challenges and approaches. Drug Delivery, 25(1), 1234–1257. https://doi.org/10.1080/10717544.2018.1474964

[16] Wang M., Zuris J.A., Meng F., et al. (2016). Efficient delivery of genome-editing proteins using bio reducible lipid nanoparticles. Proceedings of the National Academy of Sciences USA, 113(11), 2868–2873. https://doi.org/10.1073/pnas.1520244113

[17] Mout R., Ray M., Yesilbag Tonga G., et al. (2017). Direct cytosolic delivery of CRISPR/Cas9-ribonucleoprotein for efficient gene editing. ACS Nano, 11(3), 2452–2458. https://doi.org/10.1021/acsnano.6b07600

[18] Chen G., Abdeen A.A., Wang Y., et al. (2019). A biodegradable nano capsule delivers a Cas9 ribonucleoprotein complex for in vivo genome editing. Nature Nanotechnology, 14(10), 974–980. https://doi.org/10.1038/s41565-019-0544-8

[19] Wang H.X., Li M., Lee C.M., et al. (2017). CRISPR/Cas9-based genome editing for disease modeling and therapy: challenges and opportunities for nonviral delivery. Chemical Reviews, 117(15), 9874–9906. https://doi.org/10.1021/acs.chemrev.6b00799

[20] Yin H., Song C.Q., Suresh S., et al. (2016). Partial DNA-guided Cas9 enables targeted nanoparticle delivery to tumor cells. Nature Nanotechnology, 11(7), 642–650. https://doi.org/10.1038/nnano.2016.67

[21] Ledford H. (2015). CRISPR, the disruptor. Nature, 522(7554), 20–24. https://doi.org/10.1038/522020a

[22] Lee K., Conboy M., Park H.M., et al. (2017). Nanoparticle delivery of Cas9 ribonucleoprotein and donor DNA in vivo induces homology-directed DNA repair. Nature Biomedical Engineering, 1(11), 889–901. https://doi.org/10.1038/s41551-017-0137-2

[23] Wang P., Zhang L., Zheng W., Cong L., Guo Z. (2021). Nanocarriers for CRISPR delivery: design and challenges. Chemical Reviews, 121(18), 10431–10457. https://doi.org/10.1021/acs.chemrev.0c01220

[24] Liu J., Chang J., Jiang Y., et al. (2019). Fast and efficient CRISPR/Cas9 genome editing in vivo enabled by bioreducible lipid nanoparticles. Biomaterials, 208, 123–136. https://doi.org/10.1016/j.biomaterials.2019.04.022

[25] Gao X., Tao Y., Lamas V., et al. (2018). Treatment of autosomal dominant hearing loss by in vivo delivery of genome editing agents. Nature, 553(7687), 217–221. https://doi.org/10.1038/nature25164

[26] Finn J.D., Smith A.R., Patel M.C., et al. (2018). A single administration of CRISPR/Cas9 lipid nanoparticles achieves robust and persistent in vivo genome editing. Cell Reports, 22(9), 2227–2235. https://doi.org/10.1016/j.celrep.2018.02.014

[27] Zuris J.A., Thompson D.B., Shu Y., et al. (2015). Cationic lipid-mediated delivery of proteins enables efficient protein-based genome editing in vitro and in vivo. Nature Biotechnology, 33(1), 73–80. https://doi.org/10.1038/nbt.3081

[28] Glass Z., Lee M., Li Y., Xu Q. (2018). Engineering the delivery system for CRISPR-based genome editing. Trends in Biotechnology, 36(2), 173–185. https://doi.org/10.1016/j.tibtech.2017.11.006

[29] Zhang Y., Chen M., Dai C., et al. (2021). CRISPR/Cas9 genome editing system in human stem cells: current status and future perspectives. Molecular Therapy – Nucleic Acids, 23, 218–231.

[30] Qi L.S., Larson M.H., Gilbert L.A., et al. (2013). Repurposing CRISPR as an RNA-guided platform for sequence-specific control of gene expression. Cell, 152(5), 1173–1183.