DOI: https://doi.org/10.54393/fbt.v4i04.150

FUTURISTIC BIOTECHNOLOGY

https://fbtjournal.com/index.php/fbt
ISSN (E): 2959-0981, (P): 2959-0973
Volume 4, Issue 4 (Oct-Dec 2024)

Review Article

OPEN ACCESS

Biotechnological Approaches to Discovery of Drugs for Veterinary Use

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ARTICLE INFO

Keywords:
Biotechnology, Veterinary Drug Discovery, Gene Therapy, Vetinformatics, Artificial Intelligence

How to Cite:
Abdelkarim, O. F., Rehman, S. U., Samad, A., Khan, I. U., Akram, M. W., Sayeed, M. A., Yimga, F., Arshad, M. A., Rashid, A., & Basit, A. (2024). Biotechnological Approaches to Discovery of Drugs for Veterinary Use: Discovery of Drugs for Veterinary Use. Futuristic Biotechnology, 4(04), 21-28. https://doi.org /10.54393/fbt. v4i04.150

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Received date: 5th November, 2024
Accepted date: 25th December, 2024
Published date: 31st December, 2024

ABSTRACT

This review examined the application of biotechnology to veterinary drug discovery, highlighting its efficiency and potential for creating novel therapies for a wide range of animal diseases. Compared to conventional methods, biotechnological models offer several advantages, such as reduced time and cost. These models also allowed for an abysmal empathetic of disease mechanisms, facilitating the development of highly targeted treatments. Gene therapy is a significant area of research, demonstrating considerable potential in addressing various veterinary conditions. Its successful application includes the management of ocular disorders in dogs, cardiovascular and renal issues in cats, osteoarthritis in horses, and metabolic disorders like diabetes in dogs. Advances in genome sequencing and proteomics have enabled researchers to understand animal proteomes better, leading to the documentation of potential drug targets and the development of more precise therapies. vetinformatics, which uses computational tools and big data analysis, is vital for accelerating research and development in veterinary science. The convergence of biotechnology and Artificial Intelligence (AI) presents considerable promise for the future of veterinary drug discovery. AI-powered algorithms can analyses large datasets, identify patterns, and predict drug efficacy, thus expediting the drug development process and creating more effective treatments. Continued investment in these areas is essential to realize the transformative potential of biotechnology for improving animal health and advancing veterinary science.

INTRODUCTION

The ability to employ live things or substances to enhance or rebuild an artefact, develop floras or faunas, or evolve microorganisms for specific uses is a broad definition of biotechnology [1]. An excellent example of a well-established use of biotechnology is traditional animal breeding, which involves the collecting and breeding of phenotypically desired individuals [2]. The most modern biotechnology, however, is derived from new discoveries like recombinant DNA, which is a genetic material found in all existing belongings, from microbes to elephants, and which limits and controls every function of living things [3]. Through genetic operations by means of microorganisms and vector hosts, DNA machinery and related methods, monoclonal antibody methods, embryo manipulation technology, and Polymerase Chain Reaction (PCR) have highlighted the feasibility of modifying biological systems for the benefit of humankind [4]. Despite the fact that biotechnology appears to have benefited human medicine the most, affluent countries have largely been the only ones to successfully implement veterinary biotechnology. In particular, there are very few examples of biotechnology being successfully applied to advance animal farming and

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health in underdeveloped countries. Therefore, the tenacity of this study is to evaluate readily obtainable biotechnologies that may be used in the diagnosis and treatment of diseases, identify those that have been or may be used in Africa specifically, and in other countries. The description of each portion is not given much weight, given the breadth of the subject matter. In contrast, an attempt is completed to highlight the skills that are thought to have present or future use in the veterinary medical profession. This review study ends with a brief summary of the challenges relating to the potential environmental risks of inherited engineering and other biotechnologies, which call for their moral assessment for a worldwide regulatory framework [5]. Gene Therapy in Veterinary Medicine: Gene therapy's use in veterinary medicine One of the outcomes of developments in molecular biology is gene therapy, a beneficial approach in which a functional gene is introduced into a cell to treat a metabolic defect or to add a new function [6]. In both human and veterinary medicine, gene therapy holds promise for treating cancer and other hereditary illnesses [7]. Combining chemotherapy and cytotoxicity with immunomodulatory therapy's anti-tumor immune responses inhibits the growth of tumors in a variety of cancer types, and Electroporation (EP) seems like a feasible way to carefully and effectively combine these treatments [8]. Therefore, electroporation is a legitimate method for introducing substances into host cells, including plasmid DNA (pDNA) and chemotherapeutics. Since EP is a safe and effective way to deliver a range of materials (such as ions, cytotoxic medicines, and nucleic acids) into target cells and tissues without endangering them, it is being employed more and more in the scientific and medical professions [9]. In EP, the agents are transported into the cytosol by short electric pulses that open temporary holes in the cell membrane. Numerous veterinary clinical trials have shown the protection and effectiveness of Electro Chemotherapy (ECT), chemotherapy administered using EP, since EP frequently does not result in any serious negative side effects [10]. Gene therapy has also demonstrated efficacy in large animal models of X-linked retinitis pigmentosa, potentially leading to its eventual translation into human treatments: Aden associated virus-functional coagulation factor VIII (AAV-FVIII) liver gene therapy was successful in two outbred, privately owned dogs with severe Hemophilia A (HA) involved; they prevented 90% of expected bleeding episodes and demonstrated persistent expression of 1-2 percent of normal FVIII levels [11]. Aden associated virus-functional coagulation factor VIII (AAV-FVIII) liver gene therapy demonstrated that coexpression of Glucokinase (GCK) and insulin can create a "glucose sensor" in skeletal sway, improving glucose absorption and reversing hyperglycemia in diabetic mice.

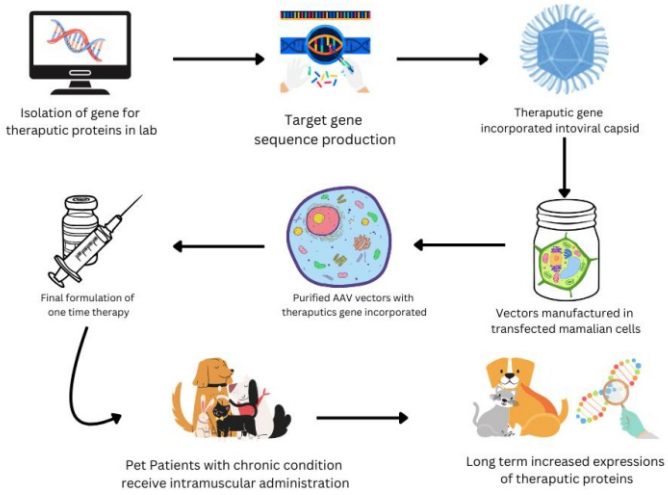

Figure 1: Development Process of Gene Therapy for Pets with Chronic Conditions

This diagram outlined the process of developing a gene therapy for pets with chronic conditions. It begins with isolating and producing a target therapeutic gene, which is incorporated into viral capsids to create viral vectors. These vectors are manufactured in mammalian cells, purified, and formulated into a one-time treatment. The therapy is administered via intramuscular injection, leading to long-term expression of the therapeutic protein to manage the condition effectively. Animal Ocular Conditions: The treatment of eye disorders is some of the primary applications of gene analysis in internal faunas. Many writers believe that keratitis of different etiologies will benefit from the application of gene therapy. Furthermore, it may help with glaucoma in dogs as well as disorders like neoplasia, corneal dystrophy, desmoids, chemical tingles, cuts, and corneal deterioration [12]. Adenovirus (AV), Lentivirus (LV), and the Adeno-Associated Viral Vector (AAV) containing the target genes are among the methods that have been suggested for the transmission of inherited material for the therapy of this condition [13]. Most hereditary retinal disorders are currently treatable. Researchers are particularly interested in gene therapy for degenerative diseases because some of them might also be natural models of these conditions [14]. A recessive modification in the RPE65 genetic factor causes congenital night blindness in Braid dogs, and Leber's congenital amaurosis type 2 is thought to be the human counterpart of this condition. A genetic factor builder based on AAV encompassing the beneficial gene was injected subrationally into 26 dogs in order to correct this condition. Of the 26 eyes that established gene therapy, 23 had positive results, and the treatment's effects persisted for at least five years. Throughout their lives, the canines showed no signs of negative effects from the genetic therapy. In RPE65-mutant dogs, another study showed that ocular

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administration of a therapeutic dose of AAV-2/2. RPE65 did not result in systemic or retinal toxicological effects [15]. Gene Therapy for Cardiovascular System Disorders: In the United States, almost 2 million domestic cats suffer from Chronic Renal Failure (CRF) and the related erythropoietin tin-sensitive anemia [16]. Using viral vectors to transfer the erythropoietin gene to cats is one of the possible gene therapy uses that is presently being investigated. The kidneys generate the hormone erythropoietin, which controls the bone marrow's erythrocyte production. Insufficient levels of hormone are frequently produced when a cat's kidneys are injured. As a result, anemia affects many cats with renal disease, which can lead to lethargy and decreased appetite [17]. Currently, human erythropoietin injections are used for treatment. Many cats' immune systems, however, view this erythropoietin as alien. We can prevent frequent injections of foreign protein by creating methods to transfer feline erythropoietin genes to cats lacking this hormone. Physiologically active feline erythropoietin can be synthesized in vitro using a replication-defective delivery method, according to in vitro research on the transfer of the erythropoietin gene to cells [18]. AAV was not employed as a viral vector by the creators of this genetic factor analysis technique. This was because earlier studies on gene therapy using AAV, which expresses recombinant feline erythropoietin, demonstrated that when given intramuscularly, it raised the hematocrit levels of healthy cats for seven weeks. Conditions Affecting the Skeletal System: Since the produced therapeutic proteins in gene therapy target the specific area without affecting the body as a whole, it may be the perfect way to treat joint problems. The necessity for frequent intra-articular injections of conventional medicinal medicines is also eliminated by gene therapy, which offers transgenes long-term expression [19]. In Osteoarthritis (OA), a chronic inflammatory disease, the pro-inflammatory cytokines interleukin 1(IL-1) and tumor necrosis factor α play a critical role. By limiting the combination and activity of IL-1, a gene therapy based on an adenovirus vector was used to treat OA in horses. The results of this gene treatment in vivo included significant improvements in experimental parameters, a reduction in pain compassion, and the preservation of articular cartilage in horses [20]. Moss and associates expected gene therapy to be used in a different way to treat OA. Since there are now no effective medications that may stop or reverse the progression of OA, the researchers referred to this as courtesy. The proposed strategy is based on the characteristics of interleukin-10 (IL-10). The suggested approach is predicated on interleukin-10's (IL-10) features. Moss and co-researchers created a gene research grounded on the AAV vector with the beneficial equine species particular gene IL-10. It is a cytokine with a strong anti-inflammatory consequence that is predominantly molded by immune cells. In vitro, IL-10 has also been shown to have an apoptotic effect on chondrocytes [21] and to maintain connective tissue homeostasis by inhibiting matrix metalloproteinase movement. By delivering the genetic component via the AAV vector in a mouse model of inflammatory soreness, in vitro revisions have demonstrated a flagging of the seditious cataract and chondroprotective capabilities related with overexpression of IL-10 [22]. It was feasible to caricature the inflammatory responses in the joints of OA-affected horses by administering this medication intra-articularly, which stopped cartilage degradation and improved osteoarthritis symptoms. The feasibility of administering the suggested gene preparation intra-articularly is demonstrated by its chondroprotective potentials [23]. Conditions Linked to Metabolic Disorders: There is presently no cure for diabetes, a chronic illness. Diabetes onset is highly correlated with increasing dog age. According to research by Heeley and associates, dogs older than eight years old are considered to be at risk. However, there was no correlation between this sickness and the animals' sex, which was consistent with prior research [24]. Achieving normoglycemia and preventing hypoglycemia are the objectives of any treatment for insulin-dependent diabetes. Exogenous insulin treatment is unable to completely prevent the illness's consequences, which result in substantial morbidity, a decreased quality of life, and fatality [25]. In canine diabetes studies, AAV serotype 1 vectors containing insulin and glucokinase transgenes have been used as a single intramuscular injection for gene therapy. The enzyme glucosidase, which activates glucose phosphorylation, is the part of this system that reacts to elevated intracellular glucose levels, and the creation of low, consistent levels of insulin has other positive effects on metabolism [26]. The improvement of insulin and gluco-kinase in muscle tissue did not have any adverse effects on the muscles or the rest of the body, allowing for long-term observations (more than two years) of dogs that had established the gene medication inoculations [27]. At the same time, histology investigations showed that a significant amount of the injected AAV vector was found inside the muscle. Even with intense physical activity, studies have shown that this method works well for treating diabetes when consuming large amounts of glucose raises the risk of hypoglycemia episodes. Genome Sequence-Based Modern Drug Discovery: It is impossible to overstate the significance of whole genome sequencing for contemporary drug development methodologies. The majority of human proteins can be categorized into structurally and

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mechanistically related groups based on sequence homology, and researchers now know the whole complement of proteins encoded by the human genome. Using bioinformatics data combining techniques, gene purpose analysis from high throughput investigations of protein-protein connections can be separated into networks and pathways [28]. A thorough components list of all the proteins found in the human body has been provided by the genome's sequence, and high throughput screening methods allow podia to expose these proteins to millions of tiny chemicals [29]. Therefore, it is impossible to overstate the importance of protein and genome sequences in today's drug discovery process. Using Proteomics in Drug Development: Although the number of proteome studies in veterinary medication and animal well-being has grown recently, they still make up a small portion of the extensive corpus of findings in the proteomics canon. In veterinary medicine, the proteomes of animal tissue and biological solutions may be examined for health and disease; in this context, there are similarities to human disease research. Nevertheless, there are other characteristics of comparative proteomics that contribute to the scientific value of proteomics in species like fish, cattle, dogs, poultry, cats, pigs, and horses [30]. These include: Animal proteomics is a separate field of study that applies to the biology and pathology of native species, offering important insights into the basic characteristics of each species. Comparative proteomics provides intriguing insight into the evolution of species' proteomes by comparing the similarities and differences between proteomes in health and sickness across species. Compared to using rodents, investigational proteomics in internal animals has intrinsic rewards. For example, time series studies can employ multiple sampling more frequently, and noninvasive (milk, slobber, urine) or slightly invasive (serum, plasma) samples can be obtained in large enough quantities for multiple analyses. In contrast to human disease research, which can merely be conducted on persistent samples from usual disease, proteomics can be used to study both investigational and natural disease progressions in the same animal [31]. As new medications get closer to controlling approval, species other than rats are frequently better matched as mockups for human bodily processes. For instance, pigs and dogs are needed for drug safety testing. Understanding the populace heredities of species where periods of recognized breeding provide a priceless reserve on proteome–genome interactions can help to facilitate the communication among the proteomic phenotype and inheritances in domestic faunas.

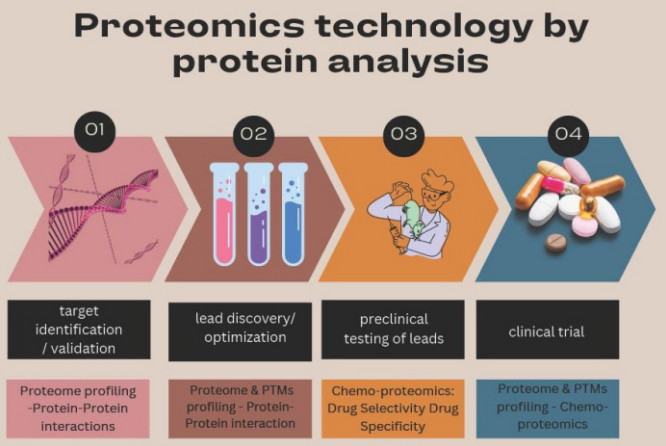

Figure 2: Proteomics and Vetinformatics in Drug Discovery for Animal Health

Proteomics technology used protein analysis to support different phases of the drug discovery process (global protein profiling, protein-protein interaction profiling, PTMs profiling, and chemo-proteomics). Vetinformatics for Drug Discovery: Animals used for livestock are vital to the existence. Public health depends on science-ran revolution in veterinary exploration that helps humans and animals as folks and populations [32-33]. This includes studies on the basic biology and welfare of animals as well as the prevention, diagnosis, and treatment of disease. Numerous chances to enhance both human and animal wellness are presented by this innovation. In addition to the challenges posed by a rapidly expanding human population that needs proper food and nutrition, veterinarians currently face a number of issues made worse by climate change, such as the emergence of new diseases. To decipher the intricate molecular mechanisms of cattle systems, interdisciplinary techniques and veterinary science must be integrated immediately [34, 35]. Research on the operation of livestock systems is vigorous and continuous. Biologists may now learn about biological systems both statistically and qualitatively because to developments in computer science, statistical methodologies, mathematical science, and information technology [36, 37]. Computers play a key role in these scientific advances because they are essential to the research and development industries and have become an important tool for researchers. Although computers can handle big data easily in the "omics" age, the term "bioinformatics" was not coined until the early 1970s by Hogeweg and Ben Hesper, when DNA sequencing was still in its infancy [38]. Prior to 1952, there was a great deal of debate regarding the role of DNA as genetic material, specifically how pure DNA from a virulent bacterial strain may be absorbed by a non-virulent strain to confer virulence. However, their findings were not immediately accepted by the scientific community, as many scientists

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believed that proteins carried genetic information instead of DNA [39]. In 1952, Hershey and Chase established that bacteriophage-infected bacterial cells eat and transmit DNA, demonstrating the role of DNA as a molecule that encodes genetic information. Although the fundamental function of DNA was established at this time, nothing was known about the structure of the DNA molecule. It was only known that its monomers, or nucleotides, were present proportionately [40]. Watson and Crick were ultimately responsible for discovering the double-helix structure of DNA. Despite this achievement, it would take another 25 years to develop the first DNA sequencing techniques and another 13 years to interpret the genetic code. Therefore, the investigation of proteins, whose chemical composition was already better understood than that of DNA, surpassed DNA analysis using computational techniques by around 20 years [41]. Protein analysis served as the foundation for bioinformatics in (Beall CJ *et al.*,) due to notable advancements in the crystallographic determination of protein structures. The first protein sequence to be published was that of insulin, or the arrangement of its amino acids [42, 43].

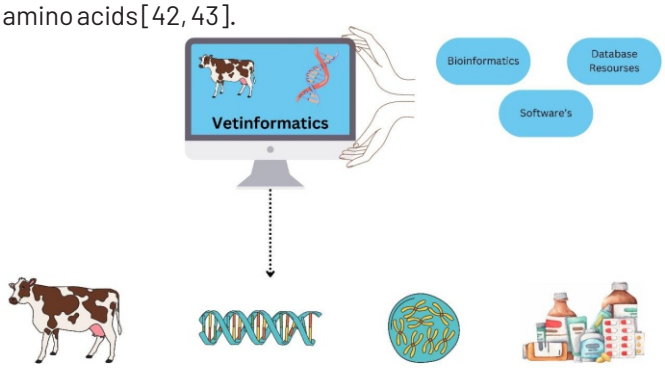

Figure 3: Role of Vetinformatics In Understanding And Improving Livestock Systems

This diagram highlighted the role of Vetinformatics in understanding and improving livestock systems. Vetinformatics combines bioinformatics, database resources, and specialized software tools to analyze genetic information of animals. The diagram illustrates how the genes of livestock, represented by DNA and microorganisms, are studied and modified to develop products such as medicines and other biotechnological advancements. This approach enhances the use of animal genetics for health, productivity, and medical purposes, showcasing the integration of technology in veterinary sciences. Biotechnological Approach in Drug Delivery: Medication distribution is one of the most important components of a drug discovery and development program. The distribution of drug molecules at a certain place and speed may be the goal of the drug-delivery system's design. Targeting medications through a delivery system allows for the development of the capacity to guide a drug to a cellular target area of interest for its efficient use. Giving drug carriers activity by including groups or ligands that are specifically recognized by receptors on the surfaces of the cells of interest is known as active targeting of drug molecules [44, 45]. Numerous drug-carrying systems, including liposomes, dendrimers, nanotubes, polymeric micelles, polymeric conjugates, chitosan-based polymers, lipid crystals, nanoparticles, and drug lead molecules, phytochemicals, and derivatives, are included in an effective drug-delivery system based on biotechnology. When it comes to medicine distribution, these systems are crucial. These systems are better options for drug delivery because of their low toxicity, biodegradability, biocompatibility, derivatization, and immunomodulatory effects. The effectiveness of a medication is also significantly influenced by how it must be taken. Drug delivery and targeting have advanced significantly as a result of academics' increased efforts over the past ten or so years to create drug delivery systems [46]. Using Bacteria to Deliver Drugs: New technologies for manipulating cellular genetic information have proliferated in recent years. Thanks to the engineering skills, we can create cells with synthetic genomes [47, 48], which could lead to the development of therapeutic or drug-producing bacteria. It may be able to give "synthetic" organisms only the genetic information they need to function, leaving out any potentially harmful and interfering genetic and metabolic material. Modular genetic components might be logically added to these cells to produce an organism with the appropriate phenotype. In the future, organisms like robots could be programmed by combining genetic devices. Initial efforts resulted in newly linked genetic circuits with newly combined biosensor modules [49]. For instance, an E. coli strain that responds to light was created by fusing a cyanobacteria phytochrome's chimeric sensor domain with an E. coli signal transduction domain [50]. It is possible to develop additional sensors and rewire downstream signaling at will by extending the engineering of novel bacterial sensors that control genes in response to novel environmental conditions. For instance, promoters could be designed to integrate (many) distinct signals [51, 52]. This strategy can be expanded to create live bacteria as probiotics, anti-tumor medicines, and tailored delivery methods for live immunization. Numerous bacteria infiltrate tumors and are designed to destroy them by secreting cytokines and TNFα, which is a chemotherapeutic prodrug.

CONCLUSIONS

The conclusion of the article is that biotechnology has made significant progress in veterinary drug discovery. The use of biotechnological models is a powerful way to identify

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and develop new therapies for a wide range of animal diseases. These models offer several advantages over traditional methods, including reduced time and cost, a deeper understanding of disease mechanisms, and the development of highly targeted treatments. With significant promise for treating a range of veterinary ailments, gene therapy has become a particularly exciting field of study. Gene therapy's transformational potential in veterinary medicine is demonstrated by its effective use in treating ophthalmic illnesses in dogs, cardiovascular and renal problems in cats, osteoarthritis in horses, and metabolic disorders including diabetes in dogs. Researchers now have a thorough understanding of animal proteomes thanks to developments in genome sequencing and proteomics, which has helped them identify possible drug targets and create more targeted treatments. Utilizing big data analysis and computational tools, the integration of vetinformatics is essential for boosting veterinary science research and development. Overall, the conclusion emphasizes that biotechnology holds great promise for improving animal health and advancing veterinary science as a whole.

Authors Contribution

Conceptualization: OFA, SUR, AS, IUK, MWA, MAS, FGTY, MAA, AR, AB
Methodology: OFA, SUR, AS, IUK, MWA, MAS, FGTY, MAA, AR, AB
Formal analysis: OFA, SUR, AS, IUK, MWA, MAS, FGTY, MAA, AR, AB
Writing, review and editing: OFA, SUR, AS, IUK, MWA, MAS, FGTY, MAA, AR, AB

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

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