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The Revival of Herbal Antivirals: A Pharmacognostic Perspective in the Post-Pandemic Era

Srikumar Chakravarthi[1*], John Paul Judson[2], Barani Karikalan[3], Vetriselvan Subramaniyan[4], Mohammad Nazmul Hasan Maziz[5]

[1*]Faculty of Medicine, Nursing and Health Sciences, SEGi University, Selangor, Malaysia

[2]Faculty of Medicine and Health Sciences, Universiti Tunku Abdul Rahman, Selangor, Malaysia

3Faculty of Medicine, MAHSA University, Selangor, Malaysia

[4]Sir Jeffrey Cheah Sunway Medical School, Faculty of Medical and Life Sciences, Sunway University, Malaysia.
[5]Graduate School of Medicine, Perdana University, Kuala Lumpur, Malaysia

***Corresponding Author E-mail: srikumarc@segi.edu.my**

ABSTRACT

The revival of herbal antivirals in the veterinary pharmacognosy is a sustainable approach to antiviral control among livestock and poultry, and its economic costs are an added advantage. Phytochemicals such as flavonoids, alkaloids, tannins, and terpenoids have been shown to potently inhibit viral replication, regulate and/or activate the immune system, and provide a pharmacological effect on viral enzymes. The use of varied animal models, such as poultry, rodent, and ruminants, enables efficacy, toxicity, and species differences assessment, in order to translate it into the practice of veterinary medicine. Combination of conventional ethnoveterinary medicine with contemporary instruments and techniques such as LC-MS/MS, molecular docking, and metabolomics allows the identification of bioactive substances and clarification of the molecular basis, converting traditional folk medicine into scientific medicine. Although there are limitations to consider in intrinsic variability of dose, inadequate pharmacokinetic information, and ethical limitations, standardized formulations, and sophisticated analytical methods together with alternative pharmacological models can maximise translation utility. This review highlights the need of herbal antivirals that are low toxicity and broad spectrum with minimal to no adverse effects, in lieu of synthetic drugs to maintain animal health and sustainable livestock management, as well as preparedness against any new viral pandemic.

Key Words:

Herbal Antivirals, Veterinary Pharmacognosy, Phytochemicals, Animal Models, Ethnoveterinary Knowledge, LC-MS/MS, Molecular Docking, Sustainable Livestock Management

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1. INTRODUCTION

Another field that has gained primary importance in the use of herbal pharmacognosy is animal health, which is specifically aids in the rising epidemics of viral infections in the animals and birds. Animal-focused studies are essential to veterinary application because there is no human medicine analog with species-specific physiology, immune responses, and disease manifestation[1]. Herbs like Azadirachta indica (Neem) and Ocimum sanctum (Tulsi) are already used as viral and bacterial animal infection controlling ethnoveterinary remedies that were practiced across many generations in Asia and Africaetc. One benefit of such practices is that it forms an abundant source of literature that leads to current scientific research.

Figure 1: Antivirals Herbal Plants[2]

Combining the animal-based herbal research methods with the contemporary pharmacognostic methods enables systematic assessment to be done in terms of efficacy, mechanisms of action and safety. Poultry, rodents and ruminants are the most widely used animals to explore antiviral, immune modulation, and toxicity of the plant-origin compounds. The integration of ethnopharmacology/ethnobotany with advanced analytical tools such as LC-MS/MS, molecular docking and metabolomics allow researchers to find bioactive phytoconstituents and determine their molecular targets. Not only do such studies contribute to veterinary medicine they also help further sustainable low-toxicity substitutes to synthetic antivirus medications in livestock management[3].

1.1 Background Information and Context

Herbal pharmacognosy which had been focused more towards human medicine is directly being adopted to animal health due to the emerging number of zoonotic ailments and the viral infections in farm animals. The worldwide spread of the COVID-19 pandemic also increased the necessity of broad-spectrum antiviral agents and showed the boundary of just 'synthetic drugs as a solution. Modern pharmacognostic studies can easily ascribe to such form of knowledge that has a long history of herb use in managing animal diseases, namely ethnoveterinary practices. These folk

remedies are currently being backed up by science in the form of molecular docking, metabolomics and in vivo animal studies, with the potential in the fight with antiviral effects[4].

1.2 Objectives of the Review

The main objective of this review is to critically examine the role of herbal pharmacognosy in addressing viral infections in animals.

- To evaluate the antiviral potential of herbal phytochemicals in animal models, including poultry, rodents, and ruminants.
- To identify key bioactive constituents (flavonoids, alkaloids, terpenoids, tannins) responsible for antiviral activity and elucidate their mechanisms of action.
- To examine the integration of traditional ethnoveterinary knowledge with modern pharmacognostic tools such as LC-MS/MS, metabolomics, and molecular docking.
- To assess the strengths, limitations, and challenges of animal-based herbal antiviral research, including dosage variability, pharmacokinetics, and ethical considerations.
- To provide future research directions for standardizing herbal formulations, enhancing translational applicability, and developing sustainable, low-toxicity antiviral therapies in veterinary medicine.

1.3 Importance of the Topic

Herbal antivirals in animal health Because viral diseases of livestock and poultry decrease productivity and animal health as well as major economic and public health costs, research in herbal antivirals in this area is of great importance. Outlining the production of antiviral agents based on natural products (plants) will support the reduction of reliance on artificial medicine and reduce the risk of toxicity, as well as offer cost-effective and sustainable solutions to farmers. Furthermore, a combination of traditional knowledge and current validation will contribute to the efficacy of herbal pharmacognosy furthermore leading to food security in the world, maintaining the health of animals, and being prepared against the rising viruses and their threats[5].

2. EVALUATING HERBAL ANTIVIRALS THROUGH ANIMAL MODELS: METHODOLOGIES, EFFICACY, AND LIMITATIONS

Pharmacological studies in animals have demonstrated good antiviral effect of herbal preparations, flavonoid rich extracts of Andrographis paniculata have been shown to ensure poultry protection against Newcastle Disease Virus, and glycyrrhizin of Glycyrrhiza glabra has been shown to prevent bovine herpesvirus in bovines. Through in vitro assays (such as Vero cell, chicken embryo fibroblast), in vivo (mice, poultry, swine), and phytochemical screening, investigators have found important phytochemicals, namely flavonoids, alkaloids, tannins and terpenoids, that cause a reduction of viral titres, immune stimulation, and amelioration of survival. Their natural production, low toxicity and broad-spectrum activity are advantages, although the absence of dosage consistency, low pharmacokinetic information and inter-phytochemical variability limit reproducibility of translation to veterinary and clinical applications[6].

2.1 Key Research Studies

The antiviral potential of herbal plant formulations has been found in significant amount of research by using animal model based pharmacological systems. As an example, flavonoid containing extracts of Andrographis paniculata was found to offer protective effect against Newcastle Disease Virus in avian species emphasising the possible role of flavonoid rich extracts in boosting immune strength in birds. Equally, it has also been shown that glycyrrhizin, a triterpenoid saponin of Glycyrrhiza glabra, can inhibit the replication of bovine herpesvirus in cattle with promising results as application in veterinary virology. In addition to the above, there has been extensive use of animal models (mouse, poultry and swine) as a way of testing the effects of plant-derived compounds against common virulent pathogens like influenza, rotavirus, adenovirus among others. Such studies emphasize the possibility of bioactive phytochemicals, not only in prevention of diseases but also as an intervention in therapeutics[7].

2.2 Methodologies and Findings

A large number of methodologies have been used in determining the antiviral effectiveness of herbal agents. In vitro First line screening of antiviral activity and cytotoxicity patterns are tested by in vitro methods, usually involving cell culture e.g. chicken embryo fibroblasts and Vero cells. Such conclusions are further substantiated through in vivo testing in which poultry and mice testing are the most frequently used models in the investigation of drug efficacy as well as toxicity in physiological conditions[8]. Composition Analysis It is worth noting that phytochemical screening always indicates the presence of the following primary majors: alkaloids, flavonoids, tannins, and terpenoids as the major compounds related to the observation of antiviral impact. Recent computational strategies such as network pharmacology, and molecular docking, have also clarified these relationships on the interactions of these phytochemicals with viral molecular targets, namely proteases and polymerases, important to viral replication. Taken together, results derived by these methods have shown consistently that viral titers are greatly reduced, immune response is modulated, morbidity is reduced and the survival rates of treated animals are increased[9].

2.3 Strengths and Weaknesses

The core strength of the herbal antivirals is its natural origin and in most cases lower than synthetic drugs. Broad-spectrum activity is also found in many plant-based extracts and are active against a variety of virus classes. Moreover, phytochemicals demonstrate the prospect of synergy when used together with standard antiviral therapy, indicating that the integrated treatment regimens have a potential to improve the patient outcome[10]. Nevertheless, they have a few shortcomings that limit their translational ability. Lack of standard dosage is still a huge obstacle since extracting methods differ, and plants used provide differences in the number of bioactive compounds. Pharmacoeconomic studies in animals are poorly represented and ADME profiles of the compounds are poorly understood. Moreover, the phytochemical composition can differ greatly in geographically, season and environment-related reasons; this is also a difficulty in the way of replicating studies. These challenges will be critical to transition experimental validation to clinical and veterinary uses of herbal antivirals[11].

Table 1: Key Literature on Plant-Based Remedies and COVID-19 Education[12]

Author(s)	Study	Focus Area	Methodology	Key Finding
Garcia, S. (2020)[13]	Pandemics and traditional plant-based remedies: A historical-botanical review in the era of COVID-19	Use of traditional medicinal plants during pandemics	Historical-botanical literature review	Ethnobotanical knowledge highlighted medicinal plants with potential therapeutic value during global health crises
Gautam, S et al. (2022)[14]	Immunity against COVID-19: potential role of Ayush Kwath	Immunomodulatory effects of traditional herbal formulation	Experimental and literature-based analysis of bioactive compounds	Ayush Kwath supported host immunity and could potentially reduce susceptibility to COVID-19
Gezici and Sekeroglu. (2020)[15]	Novel SARS-CoV-2 and COVID-2019 outbreak: Current perspectives on plant-based antiviral agents and complementary therapy	Plant-based antivirals against SARS-CoV-2	Literature review of phytochemicals and antiviral properties	Phytochemicals like flavonoids, alkaloids, and terpenoids showed in vitro antiviral activity, suggesting complementary therapy potential
Hussain et al. (2024)[16]	Video Lecture Capture in Pharmacy Education: Insights from the Pandemic Experience	Remote learning in pharmacy education during COVID-19	Observational study on video lecture implementation	Video lectures-maintained education continuity, enhanced accessibility, and supported student engagement during the pandemic

3. PHYTOCONSTITUENTS, ANIMAL MODELS, AND THE INTEGRATION OF TRADITIONAL KNOWLEDGE IN VETERINARY ANTIVIRAL RESEARCH

Flavonoids, alkaloids, terpenoids are phytochemicals with a high potential of preventing the spread of viruses in animals through interference with the replication of the virus, immunomodulatory effects, and viral enzyme inhibition hence excellent prospects as therapeutic agents in veterinary medicine[17]. Considering animal models such as poultry, rodents, and ruminants helps to determine the efficacy of such compounds, toxicity, and host-specific effect, as well as to fill the gap between laboratory experiments and practical use. Moreover, the combination of ethnoveterinary knowledge with the new technologies such as LC-MS/MS, metabolomics, and molecular docking can be used to identify and confirm that bioactive compounds retrospectively turn traditional herbal medication into scientifically accepted antiviral drugs in animal health.

3.1 Phytoconstituents with Antiviral Potential in Animals

The major phytochemical agent of herbal antivirals is through a variety of classes of compounds which exhibit a strong antiviral activity against animal viral organisms. Some flavonoids (including quercetin and luteolin) have been suggested to have inhibitory effects against avian

influenza through interference with viral entry and replication as well as immune response modulation of the host[18]. Alkaloids especially berberine, have been found to have great antiviral properties against porcine reproductive and respiratory syndrome virus (PRRSV), which has also implicated them to prevent the viral RNA replication stages and limit the oxidative stress damage in pathological sites. Herpes in livestock has been demonstrated to be inhibited using terpenoids, e.g. ursolic acid, which may act by disturbing the membrane integrity of the virus and by down-regulating the viral enzyme activities. A combination of these phytoconstituents underscores the therapeutic value of the naturally derived compounds in veterinary virology in addition to supporting the potential application as alternative/adjuvant to conventional antiviral agents[19].

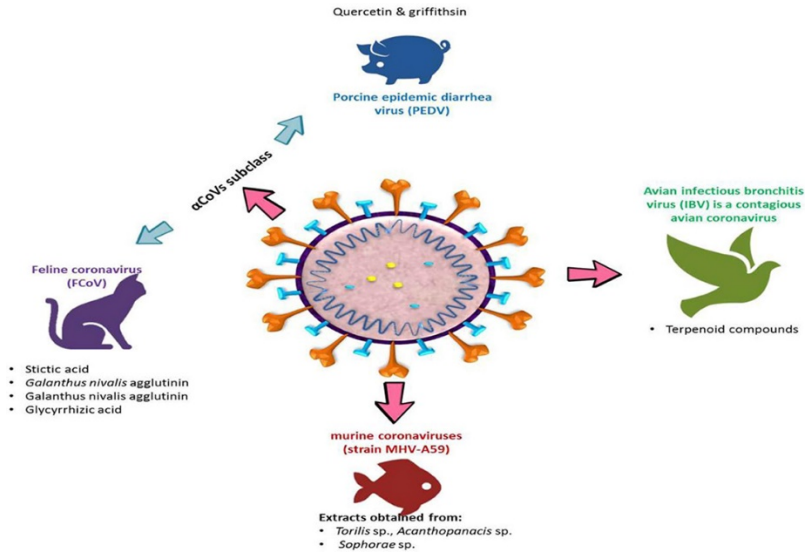

Figure 2: Phytoconstituents Targeting Animal Coronaviruses[20]

3.2 Animal Models in Pharmacognostic Research

The use of animal models in testing the antiviral potentials of phytochemicals forms a necessary tool since researchers can determine the treatment effects in a physiological environment. Chickens and ducks among the poultry can be used as subject models of avian viral infections like the Newcastle Disease Virus and avian influenza. Small rodents, mice and rats are often used in immunological and mechanistic investigations, and with the careful examination of viral-host interactions and the effects of herbal extract on the immune system of rodents, it is possible to have a vast field of immunological and mechanistic studies. Direct veterinary trial is done in ruminants (cattle and goats) particularly in the treatment of bovine herpesvirus infection and rotavirus[21]. These models can be used not only to give information about the efficacy of plant-derived compounds, but also to assess toxicity, pharmacokinetics, and to assess host-specific responses, hence crucial to the transference of preclinical research to applications in animal health.

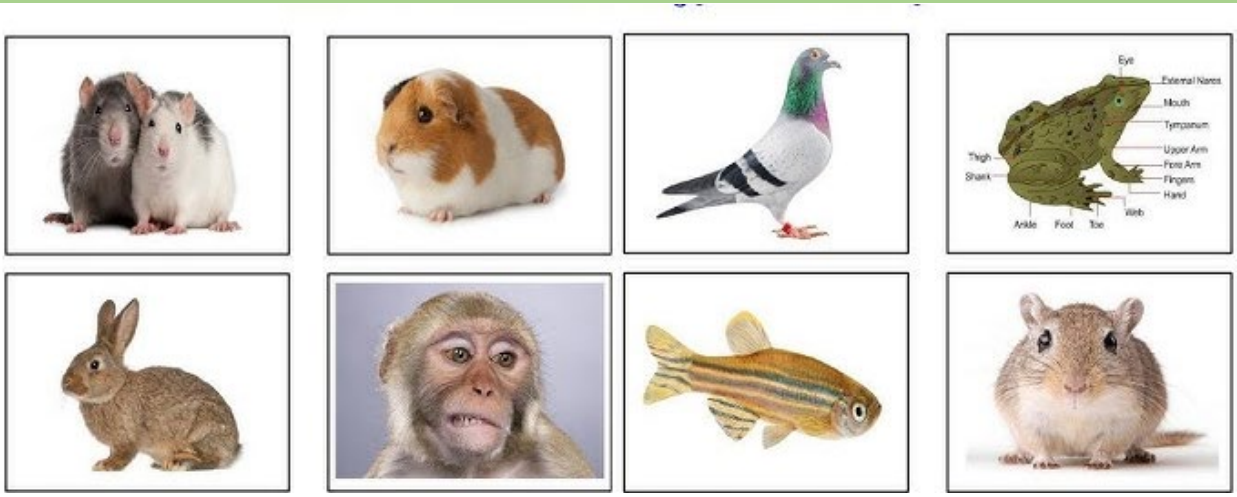

Figure 3: Animal Models in Pharmacognostic Research[22]

3.3 Integration of Traditional Knowledge with Modern Tools

Combining of ethnoveterinary knowledge with modern pharmacognostic methodology has proved to be very promising ways of finding and confirming herbal antivirals. In Asian and African countries, the more traditional systems of animal care have described the use of herbs, like Azadirachta indica (Neem) and Ocimum sanctum (Tulsi) in controlling viral infections in cattle and fowl. The practices, many of them based on centuries of empirical experience, offer a good starting point of the scientific investigations[23]. The concept of active constituents' identification, assessment of molecular targets and mechanistic enlightenment is now being achieved by modern pharmacognostic methods, including liquid chromatography-mass spectrometry (LC-MS/MS), molecular docking and metabolomics. Integrating ancient knowledge and state-of-the-art scientific endorsement, researchers will be able to establish a comprehensive picture of phytochemicals, thus speeding their way towards documentation of efficacy by science as antiviral agents in veterinary medicine[24].

4. CHALLENGES AND LIMITATIONS IN ANIMAL-BASED HERBAL ANTIVIRAL RESEARCH

Some of the implications on animal-based herbal antiviral research are that it suffers no standardized doses because of the variability of plant composition and limited pharmacokinetic/toxicological data across animal species and the multi-component nature of herbal extracts makes the analysis of mechanism complex[25]. There is also the limitation of ethical and logistical issues, especially in large animals, which add authenomore to the research, as well as fail to scale up the studies, a necessary aspect that should be addressed using uniform protocols, other models, and high-tech analysis tools to enhance reproducibility and relevancy to veterinary practice.

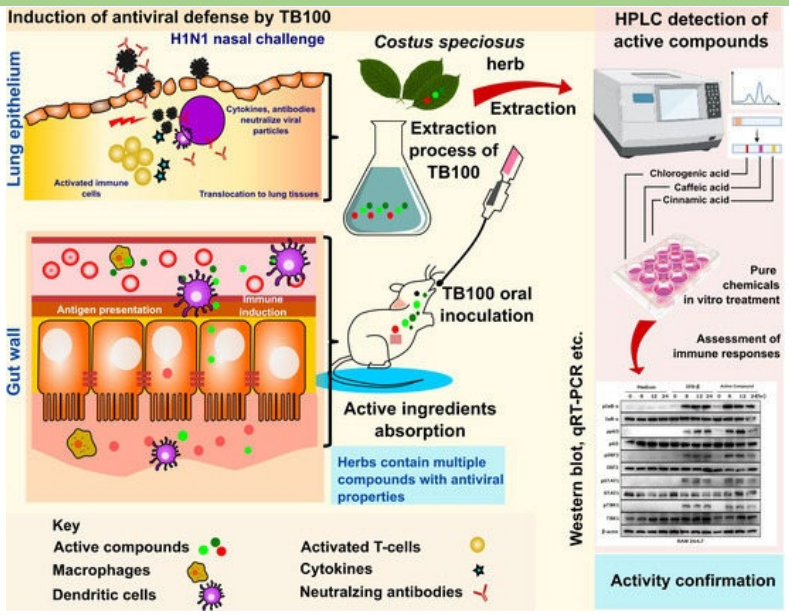

Figure 4: Mechanism of Herbal Antiviral Action of TB100 in Animal Models[26]

Standardization and Dosage Variability

Lack of standardized doses and preparations are one of the major problems of animal based research on herbal antivirals. Bioactive compound levels in plant extracts also differ greatly depending on wwhere they are grown as well as when, and on the quality of the soil and harvesting practices. This heterogeneity complicates recapitulation of experimental data and it is problematic to determine specific doses of therapy in various animal species. Without standard formulations, it is almost impossible to compare results between studies and so there is little impact of the experimental results into realistic veterinary procedures[27].

Limited Pharmacokinetic and Toxicological Data

Little data exist on pharmacokinetics and toxicology of herb antiviral medication in animals. Awareness of the absorption, distribution, metabolism and excretion (ADME) of phytochemicals is vital in measuring safety and effectiveness[28]. A large number of plant-based products might exhibit species-dependent effects, and due to the absence of formal pharmacokinetic research, it is not possible to predict adequate bioavailability, half-life, and possible side effects. This is a barrier to the advancement of herbal antivirals to preclinical research into actually using the agents in the field in livestock and poultry[29].

Complexity of Multi-Component Herbal Extracts

It is frequently the case that different bioactive compounds, which are present in herbal formulations, may have synergetic or antagonistic interactions. Whereas these multi-component interactions could be a beneficial approach of improving antiviral action, they also complicate the analysis of action mechanisms[30]. It is hard to determine the single compounds that exhibit antiviral effects and their molecular targets. More advanced methods, such as LC-MS/MS, metabolomics as well as molecular docking are useful, but need expertise, specific equipment and an extensive resource base which might not be present in every research laboratory[31].

Ethical and Logistical Constraints in Animal Studies

The research using animals prohibits both logistical and ethical factors, especially in cases where the researchers use higher-order animal species like ruminants to carry out the virus studies. Keeping large animal numbers, biosecurity and adherence to ethical standards cost extra and become cumbersome[32]. Also, immune responses and metabolism may differ in the various species, which constrains the transferability of results. Such difficulties point to the need to develop well-planned study design, strong ethical governance and to ensure alternative or complementary in vitro models are developed to ensure that live animal testing is as minimal as we can make it possible and have a meaningful foundation to understanding antiviral efficacy[33].

5. DISCUSSION

Pharmacognostic investigations on animals have elucidated the fact that herbal preparations, which abound in flavonoids, alkaloids, tannins and terpenoids, have high potent antiviral therapeutic activity against viruses that transmit to the poultry and livestock[34]. These natural antivirals are non-expensive, less toxic, able to supplement traditional knowledge, yet still standardization, pharmacokinetics, and the isolation of the active compounds are challenging. In future, research should be aimed at achieving consistency in the formulations, use of cross-species to determine the safety data, and application to higher order analysis equipment to authenticate the mechanisms and provide the convenience of application in veterinary practice[35].

5.1 Interpretation and Analysis of Findings

Pharmacognostic studies in animals have indicated extensive antiviral effect on herbal preparations. Active agents against the viruses, including Newcastle Disease Virus, bovine herpesvirus, and porcine reproductive and respiratory syndrome virus (PRRSV), were flavonoids, alkaloids, tannins, and terpenoids, and their inhibitory effect was consistently obtained[36]. In vitro tests (chicken embryo fibroblasts, Vero cells) as well as in vivo, in poultry, and rodents and ruminants, showed reduction in viral titers, enhanced immune response, and survival rate increases. Combination of ethnoveterinary traditional wisdom with modern technologies, such as LC-MS/MS, metabolomics and moleculardocking, also contributed to clarifying molecular mechanisms underpinning the antiviral effect, confirming the experimental effect of herbs such as Azadirachta indica and Ocimum sanctum.

5.2 Implications and Significance

The results have significant implications to veterinary practice and livestock. Herbal antivirals would offer a potentially renewable and affordable alternative to debilitating synthetic drug, provide an alternate to the reliance on conventional antivirals, and limit the negative side effects of such drug[37]. They may have clear potential including the capability to control several viral infections at once particularly of interest in poultry and livestock industries that have to deal with repeated viral outbreaks. Moreover, the utilization of traditional wisdom has the potential to not only validate cultural practices, but also to expedite the discovery of new bioactive molecules in order to fill the gap that exists between folk remedies and science-based veterinary medicine.

5.3 Gaps and Limitations

Although the results are quite encouraging, there are areas that have not been filled. The absence of standard dosages and methods of preparation results in inconsistency of the outcome, which inhibits the reproducibility. There is also a limited amount of pharmacokinetic and toxicological data between species, limiting dosing and apparent safety assessments. Complexity of multi-component herbal extracts hinders isolation of the precise compound involved in antiviral effect and the ability to comprehend interactions[38]. There are also limits to scalability and generalizability that is posed by ethical and logistical limitations, particularly in research with large animals. Such limitations highlight the necessity of additional well-organized, controlled and inter-specimen researches.

5.4 Future Research Directions

Future studies are to focus on standardizing herbal formulations, as well as uniformity in extracting them and measurement of active components[39]. In order to define safe and availing dosing regimen, the pharmacokinetic and toxicological studies in multiple animal species should be expanded. Future integration of advanced analytical tools like metabolomics, network pharmacology and molecular docking principles should be considered in order to obtain a deconstruction of the mechanisms of multi-component herbal extracts. Alternative and ethical in vitro models should also be generated to decrease the use of living animals, in refusing to provide translational relevance. In general, there will be a need to bridge the gap between traditional knowledge and more stringent scientific checking to translate the herbal antivirals under experimental studies into practical veterinary uses[40].

6. CONCLUSION

The recent rediscovery of herbal antivirals in veterinary pharmacognosy is a renewed and sustainable strategy against viral diseases in livestock and poultry both in terms of health and finances. There is substantial evidence from animal studies that suggest the antiviral activity of animal-based extracts, flavonoids, alkaloids, tannins and terpenoids have the potential to interact with antiviral mechanisms, including inhibition of viral replications, immune modulator and inhibiting viral essential enzymes. The application of various animal models, of poultry, rodents and ruminants, has given valuable information on efficacy of the drugs, toxicity, and species-specific reaction, and filled the gap between the laboratory data and veterinary practice. Combining the ancient ethnoveterinary wisdom with the contemporary pharmacognostic methods such as LC-MS/MS, molecular docking, and metabolomics, has facilitated the discovery of antiviral agents, mechanisms of action of known medicines and have opened the door to converting the traditional remedies to scientific evidence-based remedies. Notwithstanding its obvious benefits, the variability in plant composition and nonstandard dosages, the paucity of pharmacokinetic and toxicological information, and the ethical issues related to animal research in large animals persist as major obstacles to translation. These gaps can be only solved by use of standardized preparations, interspecies pharmacological data, sophisticated analysis methods and other in vitro models all to help maximize the therapeutic potential herbal antivirals have to offer. On balance, exploitation of the synergism of traditional medicine and modern scientific validation can not only yield low-toxicity, low-cost and broad-spectrum options to synthetic drugs but also reinforce veteran patient care, contribute to sustainable animal management and enrich epidemic

prevention of rising virIDes underlining the essential role of herbal pharmacognosy in the post-pandemic world.

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