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REVIEW ARTICLE

Traditional Herbal Medicines and their Therapeutic Effect on Rabies Disease

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ABSTRACT

Introduction: One of the ancient medical practice in the form of traditional medicine (based on beliefs and experience) which exists already with in the communities before the advent of modern health services. Several countries including India have realized the importance of these medicinal plant products in order to develop improved traditional medicines from native and endemic plants that are traditionally used at various places for various ailments.

Methods: Rabies is a fatal zoonosis disease which causes encephalitis in all warm blooded animals and humans. In this study, we collect information about natural products including medicinal plants in order to reduce the burden of rabies disease. **Results:** In view of this, some of these medicinal plants against rabies were evaluated and showed inhibition with modern pharmaceutical practices by various researches within or outside the country.

Conclusion: In short, these medicinal plant products played a crucial role in eliminating harmful as well as dreadful pathogens.

Keywords: Traditional, medicine, rabies disease, pathogens.

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1. Introduction

Medicinal plants have been continuously used for the last so many decades especially in healthcare sector. Numerous immunopharmacological studies were conducted and carried out globally pertaining to verify or determined their efficacy related to its primary and secondary metabolites [1-

3] that may be applied for the production of plant-based medicines. In this paper, we discuss about therapeutic action of medicinal plants against rabies disease. In view of this, various medicinal plants played a vital role in disease prevention as mentioned in the literature. However, efforts

were made by various researchers in order to identify and recognize its action against various pathogens. In this regard, our group focused on medicinal plants and studied its immunological as well as virological properties against rabies disease.

Rabies is caused by a virus that is transmitted to humans through the infected saliva of a range of animals. It is prevalent in all continents including India, with over 60% of human deaths occurring in Asia. But most of the human deaths due to bite or exposure to an infected dog [4, 5]. Between 30- 60% of the victims of dog bites are children under the age of 15 in countries where rabies is endemic. The numbers of global partners i.e. University of California, Davis; Council for Scientific and Industrial Research, South Africa; Institute for Allergy and Clinical Immunology of Bangladesh; One World Health South Asia, New Delhi, India etc are committed to sharing knowledge, technology and resources to help reduce the burden of rabies in the developing world.

The main constraint to rabies elimination in India is the lack of coordination and the lack of a comprehensive national programme. Since India shares borders with six countries that are all rabies affecting regions, it is essential that India's rabies control efforts are coordinated regionally. According to government statistical analysis, India is currently producing just under 15 million doses of human rabies vaccine and just over half a million vials of equine rabies immunoglobulin annually, the quantities of these vaccines that meet the national requirement. Meanwhile, the government is doing more to promote rabies awareness with initiatives such as a pilot project to prevent human rabies deaths launched by the National Centre for Disease Control (formerly called National Institute of Communicable Disease) in 2008 in five Indian cities. Few years back, global health care company, Schering Plough Corporation sponsored two projects in 10 villages surrounding Bangalore and Pune focused on educational awareness and the mass vaccination of dogs.

Rabies, a fatal viral disease, is endemic in India [4, 5] and this virus infects the central nervous system causing disease in the brain (Fig.1). As the disease progresses, more specific symptoms appear and may include anxiety, hypersalivation, paralysis, difficulty in swallowing and hydrophobia. Due to rabies, death usually occurs within days of the onset of these symptoms [6-8]. In contrast, human rabies due to dog and wild animal bites is quite common in developing and less-developed countries. Vaccination against rabies is used in two distinct situations i.e. pre-exposure vaccination and post-exposure prophylaxis. In general, vaccines for rabies used for pre-exposure and post-exposure vaccination are the same, but the immunization schedule differs [9-11]. Out of these, only rabies immunoglobulin is used for post exposure prophylaxis. According to the World Health Organization, more than 7.7 million people undergo post-exposure prophylaxis treatment for rabies globally, while an estimated 55,000 individuals/year die from rabies in Asia

and Africa alone. The vaccines currently available are too expensive for developing countries [6-11].



Figure 1: Rabies disease

There is no successful treatment for clinical rabies. Interferon, ribavirin and other drugs have shown no beneficial effects. Symptomatic treatment of rabies may prolong life but the outcome is almost always fatal. Historically, several key events have contributed to the control of human rabies: the development of a human rabies vaccine (1885) [6-11], the discovery of the diagnostic Negri body (1903) [12], the use of rabies vaccines for dogs (1940s) [13], the addition of rabies immune globulin to human post exposure vaccination treatments (1954) [8-11], the growth of rabies virus in cultured cells (1958) and the development of diagnostic fluorescent antibody tests (1959) [14].

The incubation period for the disease depends on the site of the bite, injury and the amount of infecting virus at the time of exposure. The use of these medicinal plant products with respect to vaccine production which is included as one of the important applications in the modern medicine. Most of the medicinal plant species have been used as well as exploited to accumulate number of vaccine antigens that are used for human infectious diseases. Now a day, plants have also provided new and promising aspects in the process of developing inexpensive, effective and safe production and delivery systems for the next generation of vaccines for rabies [15, 16].

This new approach are promising and addresses the concern of cost, safety and accessibility of plant produced formulation from various medicinal plants as vaccine antigen for the future control of rabies virus. Therefore, we focused on new rabies vaccines, that are safe as well as inexpensive and, if possible, that require several administrations by an oral/intraperitoneally/subcutaneously route must be developed. In this regard, plant produced glycoproteins can lead to immunogenicity and affecting its pharmacokinetic properties and certain regulatory issues [17-21]. Recent advances made in genetic modification of glycosylating enzymes in plants have made it possible to add or remove desired sugars and make protein with desired glycosylation pattern similar to human [21, 22]. It has been

suggested that plant derived recombinant proteins or antibodies may have increased immunogenicity or allergenicity as compared to mammalian counterparts [17, 23]. Few years before Bharat Bio-tech International Ltd has announced the launch of a new anti-rabies vaccine, with its brand name Rabirix, in the Indian market. It can be used for both prophylactic (vaccine before bite) or therapeutic (post bite) treatment. Rabirix, manufactured in BBIL company internationally approved facilities near Hyderabad. In contrast, two anti-rabies vaccines are also available i.e. Verorab of Sanofi Aventis (marketed by Ranbaxy) and Rabipur (marketed by Sanofi). In the global scenario of rabies disease, new type of vaccine has been found to be as effective as the existing human diploid cell rabies vaccine, which was introduced in 1967 and considered the gold standard for rabies vaccines.

The key issues for human diploid cell rabies vaccine have been its limited production capacities and high costs. In view of this, one of the products of BBIL's i.e. Rabirix, purified vero cell vaccine is now in clinical trials and has been proved and showed similar response with respect to efficacy in comparison with human diploid cell rabies vaccine, while being more significantly economical. In other words, rabies is considered as an incurable disease but still no diagnostic tests are available till yet to detect it early. In addition, there is severe shortage of rabies vaccine in the country as well. Recently, one of the drugs i.e. rabies human monoclonal antibody (RMAb), has been developed by Pune-based Serum Institute of India and US-based Mass Biologics of the University of Massachusetts Medical School and showed significant results as well. This drug is considered to be safe and effective during various phases of human clinical trials. In short, Rabishield first rabies human monoclonal antibody in the world and has been developed in a laboratory set up using recombinant DNA technology.

Examples of Ayurvedic herbs or organic compounds that are currently under investigation for determining its antirabies activity

Phytoconstituents of these medicinal plant products are very useful in order to reduce the burden of various infectious agents and these were the only remedies available before the discovery of antibiotics (most of them are plant origin). Among infectious diseases, viral diseases in particular, remain the leading cause of death in humans globally [2, 4, 6]. In the literature, lot of information related to medicinal plant products were collected and showing anti-rabies activity. All these information from across the world may be collected and tried to use by various researchers as starting material for screening as well as identifying the active constituent. Some of the medicinal plants are listed below-

Anti-rabies activity of aqueous, chloroform and methanol extract of *Salix subserata* (leaves) and *Silene macroselen* (roots) are traditionally used in Central Ethiopia [24]. In this study, oral administration of these extracts to Pasteur Virus (PV) strain rabies virus infected mice were studied and found that chloroform and methanol (80%) extract of

Silene macroselen and chloroform as well as aqueous extract of *Salix subserata* (roots) showed antirabies activity. Further characterization of the active ingredients would reveal useful compounds.

Datura, wild plant which showed various medicinal as well as pharmacological properties. Phytochemical investigation of this medicinal plant revealed the presence of alkaloids, atropine, scopolamine, tannin, saponine, glycosides, phenol, sterols, lignins, fats, carbohydrates and proteins. In view of this, one of the species of *Datura* plant i.e. *Datura metel* showed in vitro antiviral activity against rabies virus [25]. Tobacco plant may be considered as a killer because of highly immunosuppressive and cytotoxic activity whereas infected leaves of tobacco plant may be considered as antigenic properties and this plant may prove somehow as a lifesaver for those people who are suffered with rabies disease [26]. Recently, various researchers worked on genetically modified tobacco plants in order to make humanlike versions of the antibody. The extraction of these antibodies from tobacco plant and tested them on cultured cells (infected with rabies). These studies claimed that plant-produced antibody showed better results as compared to human antibodies against several strains of rabies virus in the cell culture experiments.

One of the medicinal plants i.e. *Syzygium cumini* especially fruits/leaves is considered to be one of the potent enhancer of vitamin C [27] and reported as an effective stimulator of interferon production in humans. In other words, vitamin C is used for stimulation of an enhanced interferon response to rabies vaccine [28]. From these studies, we claimed that antibody levels against rabies virus are totally inactive but there is enormous level of interferon which provides some protective role against this disease. Leaves of *P. dodecandra* showed antirabies activity in mice model studies [29] and this effect will be observed at higher doses when monitored on their survival period (Days) compared to negative control group of mice. So, further phytochemically as well as immunobiologically investigation of active ingredients of *P. dodecandra* should be studied and reveal more useful compounds.

2. Conclusion

This review helps us a lot in order to identify the natural products including medicinal plants for the treatment of rabies disease and also provides some information regarding the use of these medicinal plant products for medicinal purpose. In view of this, researchers used these natural products as a reference pertaining to conduct their immunological as well as virological activities and also identified biomolecules which are present in a large quantity and tried to use as medicine. The survey of these natural products including medicinal plants and also collected literature about those products with its economic importance and tried to reduce the burden of rabies disease. Recently, cost effective strategy for preventing the burden of rabies in people is by eliminating rabies in dogs through animal vaccinations as well as by preventing entry of stray dogs and wild animals in close proximity to domesticated

animals to prevent contact of contaminated saliva. But the major drawback is cost so these natural products should be used in order to reduce the burden of disease and also less cost effective.

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