

Scientific Insights for Drug Development Based on Normal Habitat of Tribal Population of Manipur: An Observational Study Regarding the Implication of “*Houttuynia cordata*”

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ABSTRACT

The development of new and novel drugs starts following a path of targeting possible candidate drug, elucidation their mechanism of action, animal studies, and finally after the completion of phases I/II and III clinical trials. The fundamental raw materials of drugs may be synthetic substances or plants. Many plants are habitually used in many countries as food or for the remedy of diseases. We found that a tribal population of Bangladesh use an herbal plant regularly and this plant has been shown to have potential positive effect for management of coronavirus disease-2019 (COVID-19). The present observation assessed the incidence and fatality of this community inhabitants due to COVID-19. Although a conclusion cannot be reached due to small sample size, this approach and theological concept may be helpful for the development, discovery, and innovation of new drugs for different pathological conditions.

Keywords: Bangladesh, Coronavirus diseases-2019, *Houttuynia cordata*, Manipur tribe, SARS-CoV2.

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Entire human race that include almost 8 billion people of the world have been existing under constant threat of hunger, famine, war, local conflicts, political unrest, and several others ill-defined dangers. These situations are indirectly supporting the emergence of new endemic or epidemic or pandemic diseases. Our recent experience about pandemic indicates that almost all types of pandemics are not restricted to limited number of symptoms that involve only the target organ. Rather, it affects several organs of the body and complex pathological features are developed. For example, the recent pandemic caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) is basically a respiratory virus and infects the human mainly via nasal route. However, extrapulmonary symptoms have been detected in several patients with coronavirus diseases-2019 (COVID-19).¹⁻⁵

Once these pathological diseases suddenly emerge, there starts an active movement to develop new and novel drugs, new types of vaccines and other modes of protections to tackle the epidemic or pandemic. We are still bearing the memory of SARS-CoV-2 that devastated the entire world with the presence of 3-year long pandemic and affecting around 800 million registered patients with about 7 million deaths.⁶⁻⁸ If we analyze the 3 years experience of dealing with SARS-CoV-2 and COVID-19, the entire time period may be subdivided into three phases: (1) the emergence of SARS-CoV-2 as a virus of concern in early part of 2020 and finally COVID-19 was designated as a pandemic in March 2020,⁹ (2) several preventive measures expanding from lockdown to development of vaccines were adopted in different parts of the world with an ultimate success of developing mRNA-based vaccine, DNA-based vaccine, whole cell lysate vaccine and vector-related vaccines within 1 year,¹⁰⁻¹³ (3) development of drugs starting from repurposed drugs such as chloroquine, elusive drugs, such as ivermectin, antiviral drugs with compromised functional ability, and immune modulatory drugs.¹⁴⁻¹⁷ Standing in 2023, it seems that SARS-CoV-2

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is a partially cytopathic virus with capacities to induce unregulated host immunity leading to development of severe diseases. The official figure indicates that about 770 million people were infected by SARS-CoV-2 with a death toll of about 7 million. However, both the incidence and mortality may be several fold higher in a real-life situation than the official figures. By the way, the reality indicates that the cost of drug development and adverse effects for tackling

SARS-CoV-2 and COVID-19 will never be explored in the context of COVID-19.

If the other side of the coin is properly evaluated, there remain several leads for constant working to combat known and unknown pathogens in this world. This concept is getting momentum as the world facing the possibility of embracing another pandemic in future that has been named as "Pandemic X"¹⁸ by an infectious agent defined as "Microbe X." It has also been proposed that Pandemic X may induce a fatality of four times compared with that of COVID-19.

In this context, the preparation of public health experts as well as pharmaceutical companies with all governments and public health policy makers need to consider the pros and cons of the ensuing pandemic or other pathological conditions. In this context, we diverted our attention to a new spectrum of development of novel drug or protection procedure for the ensuing epidemic or pandemic. New real pharmacological impacts of different herbs and plants may be highlighted. Natural products have a deterrent therapeutic efficacy and many of these products are endowed with control of the metabolic disorders, cardiovascular diseases, inflammation, and viral infection. These include herbal medicines, fatty acids, and probiotics as play cardinal role in host immunity. They regulate the immune system in a pleiotropic mode, and take a part in diverse adaptive and innate immunity processes. Thus, natural products are capable of directing immune modulators, in the management of definite kinds of immunological and inflammatory diseases, such as prevention of Crohn's disease, ulcerative plaque psoriasis and rheumatoid arthritis, colitis, among other immunological and inflammatory diseases. Several herbal drugs have been used to combat the adverse effects of COVID-19 around the globe. However, the positive or negative effects of these herbal drugs could be properly substantiated due to lack of proper study design and several other flaws in clinical research.

In this context, we adopted a concept of novel identity and retrieve some initial information. Bangladesh is a country of South-East Asia with a population of an estimated 170 million people containing 495 administrative zones, called Upazila. Although the country is not so expanded in terms of area of the country (only 147,600 Km²), the country is highly heterogeneous regarding culture, food habits, and language. In order to develop insights regarding the effect of herbs and plants on COVID-19, we concentrated our attention to a special tribal population of Bangladesh, the people of Monipur tribe.

In Bangladesh, majority Manipuri's are living in Sylhet division of Bangladesh in villages named, Kamalgonj Upazila under Moulvibazar district. According to the ethnic origin, the three groups of Manipuris are Bishnupriya, Meitei, and Pangans.¹⁹ In linguistic point of view, the Manipuris are divided into two groups as the Meitei and the Bishnupriyas. Bishnupriyas are mainly Indo-Aryan, Meitei are Mongoloid, and Pangans are the admixture of both Indo-Aryan and Mongoloid ethnic groups. Pangans are also known as Muslim Manipuris. They are distinct from Meitei and Bishnupriyas in terms of religion and culture. However, they speak Meitei Manipuri language. The Bishnupriya Manipuri are the follower of Hindu Vaishnavism; therefore, sociocultural and religious life also closely connected with the cult of Bengal vaishnavism. Religion and social customs also play an important role in forming food culture in a community. Food habit has become the part of the culture of a community. The staple diet of Bishnupriya Manipuri

consists of rice, fish, pulses, milk, large varieties of seasonal leafy vegetables, seasonal fruits, and some unique aromatic herbs. Chameleon plants are unique aromatic herbs of Bishnupriya Manipuri. Chameleon plants have heart-shaped yellow and green leaves. In Bishnupriya Manipuri language known as "Takpanikon." Chameleon plant herbs are the basic and important elements in Bishnupriya Manipuri cuisine. Every Bishnupriya Manipuri household has a kitchen garden where they grow several seasonal vegetables and unique aromatic herbs.

Chameleon plant, also named as "Takpanikon" is scientifically regarded as "*Houttuynia cordata*." The pharmacological properties of "*Houttuynia cordata*" has been explored substantially regarding its immune modulatory capacities against various infectious agent including SARS-CoV-2.^{20,21} Even studies have claimed that "*Houttuynia cordata*" is able to block cytokine storm in serious patients with COVID-19.^{22,23}

In this regard, we found an excellent opportunity to assess the implication of "*Houttuynia cordata*" during COVID-19 pandemic in Manipuri population who habitually use these plants on a daily basis. The fundamental plan of this study was not of invasive purpose. Rather, it is just an observational study to assess the incidence and severity of COVID-19 in Manipuri population, which consumes one of the plants that may have a positive effect.

Our observation yielded several data that need to be properly explained to have proper insights about the role of "*Houttuynia cordata*" on COVID-19 pathogenesis and prognosis. Over the 3 years period (2020–2022), a total of 228 persons were tested for SARS-CoV-2 and 41 of them were positive for SRAS-CoV-2. Out of them, one person died of severe COVID-19 among these population. This observational study bears various unique points for further analysis. First of all, we are not sure and it is impossible to provide a conclusion if 41 infections and one death over 3 years due to COVID-19 are lower or higher or pacing with country's average. In fact, several heterogeneities have been found regarding the incidence of SARS-CoV-2 infection and severity of COVID-19 in Bangladesh.

The observation found in our study should be explained not only the figure of SARS-CoV-2 infection and COVID-19-related death, but also regarding the implication of this herb on the pathogenesis of COVID-19. If the incidence of COVID-19 among Manipuri population is not different from other parts of Bangladesh, then we should critically assess the role "*Houttuynia cordata*" in COVID-19. This should enclose a proper assessment of dose, of "*Houttuynia cordata*," mode of administration, frequency of administration and other variables of the published articles. Also, there is a need to clarify the mechanism of action of this plant on SARS-CoV-2 and other infectious agents. On the other hand, if it is found that the incidence and severity of COVID-19 was milder among Manipuri population compared with general population of Bangladesh, this will provide an impetus for more detailed research and analysis regarding "*Houttuynia cordata*." However, there is an important variable in this situation. The socioeconomic condition represents an important variable in acquisition and pathogenesis of COVID-19. Thus, a straight comparison of incidence and severity of COVID-19 may not be compared with the general population of Bangladesh. This should be compared with other tribal population of Bangladesh. Unfortunately, such studies are lacking.

There is another spectrum of this studies. COVID-19 has been associated with certain comorbidities including encompassing almost all organs of the body. The role of "*Houttuynia cordata*" should be assessed on reduction of COVID-19-related pathogenesis.

In conclusion, the study emphasizes that several plants are regularly used by various population in various corners of the world. Many of these plants have been used during COVID-19 pandemic. However, there is no study regarding the incidence, prevalence, and fatality due to SARS-CoV-2 in the population of those who traditionally used "*Houttuynia cordata*" or other so-called anti-COVID-19 plants. Proper insights about these plants would be translated to develop new and novel drugs for ensuing "Pandemic X. The presented study is an observational study with different limitations as the study is retrospective in nature and the sample size is also small. However, the concept of this study may provide insights regarding the use of plants for countering new and novel microbial infections. A well-d larger sample size may be undertaken now to develop insights for challenging other ensuing.

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