Relevance of Ayurveda Anti-viral herbal wisdom from the perspective of current researches

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ABSTRACT

Due to COVID-19 outbreaks, entire humanity across the globe is suffering from this deadly disease and searching for novel and more effective antiviral herbal drug for its complete cure. Ayurveda compendia have described herbal medicines which are said to be effective against all microorganisms. Hence in this paper attempt is made to review Krimighna drugs described in Ayurveda compendia and identify its efficacy on various viral diseases. Relevant references were searched concerning krimihar drugs described in Brihatrayee viz. Charak Samhita, Sushruta Samhita and Ashtanga Hridaya. Scientific research papers related to pre-clinical and clinical studies showing the antiviral activity of individual krimighna drugs were also searched. In all Samhitas total, 56 drugs were found having Krimighna properties. Out of these only ten drugs are found to have antiviral activity against various type of viruses such as Herpes Simplex virus (HSV type 1 & 2), Dengue virus (DNGV), Newcastle Disease virus (NDV), Sindbis virus (SINV) Measles virus, Poliovirus. Herbal medicinal drugs have great potential to treat viral diseases. Considering the global disease burden caused by COVID-19, there is an urgent need to explore the Krimighna drugs with antiviral activity and to develop novel and useful antiviral agents to combat the COVID-19 menace effectively.

INTRODUCTION

Diseases caused by viruses are increasing worldwide and are becoming a great danger to humanity, causing pandemics throughout the world. COVID-19 outbreak is the latest in this series, and scientists and researchers are searching for novel and more effective antiviral drug for its complete cure. Coronavirus disease COVID-19 is caused by the recently discovered coronavirus serotype 2, which is zoonotic (spread through animals to humans) and now spreading human to human throughout the globe. It was first reported in Wuhan city of Hubei province of China in December 2019 and soon spread across the world, causing thousands of lives (Goothy et al., 2020). Corona is an RNA virus causing respiratory morbidity like MERS-Middle East Respiratory Syndrome and SARS-CoV-2 Severe Acute Respiratory Syndrome (Rathi and Rathi, 2020).
Humans have been suffering from virus attacks since time immemorial. In recent decades, several viruses have been identified from animals to humans and triggered widespread outbreaks, resulted in thousands of deaths. There have been several significant pandemics recorded in human history, including smallpox, cholera, plague, dengue, AIDS, influenza, West Nile disease and tuberculosis. Influenza pandemics (Qiu et al., 2017). In recent years have witnessed significant pandemics such as hantavirus pulmonary syndrome (HPS), severe acute respiratory syndrome (SARS), H5N1 influenza, H1N1 influenza, Middle East respiratory syndrome (MERS), and Ebola virus disease epidemic (Gostin et al., 2016). COVID-19 is the latest pandemics in this chain. No vaccine or effective antiviral drug is yet discovered for the treatment of COVID-19 disaster. It was reported to be believed that few Ayurvedic medicines may alleviate the symptoms of COVID-19. AYUSH Department also published an advisory for the sake of public interest and advised to use culinary herbs, spices like turmeric and herbal tea with ginger to protect from the COVID-19 menace effectively (of Ayush, 2020). Ayurveda has given more emphasis on preventive care through Dincharya (daily regime) and Ritucharya (Seasonal regime) to maintain a healthy life. As there is no effective medicine discovered yet,
Table 3: Krimighna drugs described in Asthanga Hridaya

| S.N. | Reference | Name of drugs with Latin Names | Properties & Indications |
|------|-----------|--------------------------------|--------------------------|
| 1    | Aasanadi gana Su.15/19-20 | Asana (Terminalia tomentosa L.) Tinish (Ougeinia dalbergioides Benth.), Bhurja (Betula utilis D. Don.), Arjuna (Terminalia arjuna W.& A.), Karanja (Pongamia glabra Vent) Khadir (Acasia catechu Wild), Kadar (Acacia suma Buch. Ham) Shirish (Albizzia lebbeck Benth.), Shinshapa (Dalbergia sissoo Roxb) Meshshringa (Gymnema sylvestree R. Br.), Chanadan (Sanctum album L.), Daruharidra (Berberis aristata DC.), Palash (Butea frondosa Koen.), Shal (Shorea robusta Gaertn.f.), Kramuka (Areca catechu L.), Dhava (Anogeissus latifolia Wall) Indrayav (Holerrhena antidysentrica Wall), Ajakarna (Dipterocarpus turbinatus L.) | Pacify Kapha, Vitiligo, Skin diseases, worm infestation, Anaemia, Diabetes, Obesity |

In Ayurveda, Charaka Samhita has described Krimighna Gana (antimicrobial drugs) to combat with any viral infection. Later Sushruta Samhita, Astanga hridaya also described a specific group of herbal medications to tackle any bacterial, fungal or viral infectious diseases. Researches on few medicinal plants have shown potent antiviral activity without any side effects and thus facilitated to boost the individual’s immune system (Kalyani and Kamaruz, 2013). Krimighna drugs also content pharmacologically active constituents in terms of phytochemicals, but their potency against antiviral diseases is yet to be assessed. Hence in the present paper, an attempt is made to review researches done on the Krimighna drugs described in Samhitas and to know its efficacy on various viral diseases. This study may help to identify novel and more effective antiviral drugs to treat viral infections effectively.

 MATERIALS AND METHODS

Relevant references were searched concerning krimihar drugs described in Brihatrayee viz. Charak Samhita, Sushruta Samhita and Asthanga Hridaya. Published scientific research papers related to pre-clinical and clinical studies showing the antiviral activity of individual krimighna drugs were searched on Pub med, Scopus, Web of science, Medknow, Ayushdhara and google scholar by using relevant keywords regarding the antiviral activity of medicinal plants studied in last twenty-five years.

 RESULTS AND DISCUSSION

In Charaka Samhita Sutrasthana, a group of 10 drugs is described named as Krimighna Mahakashaya meant for the alleviation of Krimi (microbes). In Sushruta Samhita Krimighna drugs are found in Sursadi Gana (14 drugs) and Lakshadi Gana (11 drugs) whereas, in Astanga Hridaya, krimihar drugs are mentioned in Asanadi Gana (19 drugs) and Arkadi.
Table 4: List of Researches on Krimighna drugs and their antiviral activities.

| S.N. | Botanical name                  | Family           | Part used   | Antiviral activity                  | References                                                                 |
|------|--------------------------------|------------------|-------------|-------------------------------------|-----------------------------------------------------------------------------|
| 1.   | Achyranthus aspera L.           | Amaranthaceae    | Leaves      | Epstein-Barr virus, HSV 1 and HSV 2 | (Chakraborty et al., 2002; Mukherjee et al., 2013)                           |
| 2.   | Achorus calamus L.              | Araceae          | Tuber       | DENV                                | (Rosmalena et al., 2019)                                                   |
| 3.   | Allium sativum L.               | Liliaceae        | Tuber       | NDV, Influenza Virus                | (Arify et al., 2018)                                                        |
|      |                                 |                  |             |                                     | (Mehrbood et al., 2009)                                                     |
| 4.   | Aristolochia bracteata Retz.    | Aristolochiaceae | Leaves      | Influenza virus                      | (Mona et al., 2017)                                                        |
| 5.   | Azadirachta indica L.           | Meliaceae        | Bark, leaves| HSV1, NDV, DENV, Herpes             | (Tiwari et al., 2009)                                                       |
|      |                                 |                  |             |                                     | (Ong et al., 2014)                                                         |
|      |                                 |                  |             |                                     | (Hafidh et al., 2009)                                                       |
|      |                                 |                  |             |                                     | (Hamidi et al., 1996)                                                       |
|      |                                 |                  |             |                                     | (Balasubramanian et al., 2010)                                              |
| 6.   | Calotropis gigantea L.          | Asclepiadaceae   | Flower      | Herpes simplex type-1 (HSV-1)       | (Chen et al., 2010)                                                        |
| 7.   | Cissus quadrangularis L.        | Vitaceae         | Stem        | HSV type1 and 2                     | (Hossan et al., 2018)                                                      |
| 8.   | Curcuma longa L.                | Scitaminaceae    | Tuber       | DENV                                | (Mehrbod et al., 2009)                                                     |
|      |                                 |                  |             |                                     | (Zandi et al., 2010)                                                       |
|      |                                 |                  |             |                                     | (Mazumder et al., 1996; Kutluay et al., 2008)                                |
| 9.   | Embelia ribes Burm. f.          | Myrsinaceae      | Fruits      | Influenza virus                      | (Chen et al., 2010)                                                        |
| 10.  | Ferula assa-foetida Regel       | Umbiliferae      | Gum resin   | HSV-1                               | (Hossan et al., 2018)                                                      |
| 11.  | Magnifera indica L.             | Anacardiaceae    | Seed powder | HSV                                 | (Hafidh et al., 2009)                                                      |
| 12.  | Moringa oleifera L.             | Moringaceae      | Leaves      | HSV 1                               | (Nasr-Eldin et al., 2018)                                                   |
| 13.  | Nerium odorum Soland            | Apocynaceae      | Root powder | HSV                                 | (Hamidi et al., 2009)                                                      |
| 14.  | Ocimum sanctum L.               | Lamiaceae        | Leaves      | Polio virus, Vaccinia virus, NDV    | (Devi and Manoharan, 2009)                                                  |
| 15.  | Punica granatum L.              | Punucaceae       | Fruit bark  | HSV & SINV & Poliovirus             | (Mouhajir et al., 2001)                                                    |
| 16.  | Ricinus communis L.             | Euphorbiaceae    | Root        | HSV-1, SINV                         | (Hamidi et al., 1996; Mouhajir et al., 2001)                                |
| 17.  | Semicarpus anacardium L.        | Anacardiaceae    | Nuts        | Measles and Mumps virus             | (Pa et al., 2012)                                                          |
| 18.  | Solanum nigrum L.               | Solanaceae       | Dried plant | Hepatitis C Virus, HSV              | (Devi and Manoharan, 2009; Javed et al., 2011)                              |
Gana (11 drugs) as depicted in Tables 1, 2 and 3. In Ayurveda texts, the word Krimi is used frequently to denote worms or microbes and Drugs acting on these microbial agents have been termed as Krimighna Dravyas. According to the Shabda kalpadruma (An Encyclopedic dictionary of Sanskrit words), the word Krimi is derived from the root word “Krama” which means attacking, surpassing or overcoming (Soni et al., 2017). Acharya Charaka has described 20 varieties of Krimi which include both internal and external krimis while Acharya Vagbhata described internal and external krimis with various shape, size and colour. Krimi can be compared in modern science with microorganism and macroorganism (Jain et al., 2018) Thus Ayurveda seers were very well aware of the presence of the microorganisms, their pathogenesis, symptoms and treatment.

The Krimi is a broad term which includes all types of worms and microbes. A microbe is a term for tiny creatures that individually are too small to be seen with the unaided eye. Microbes include bacteria, viruses archaea and fungi. A virus is a significant type of microbe, responsible for many infections that can only replicate inside the living cells of other organisms. Viruses can infect all kinds of living form such as human, animals, plants, and even microorganisms (Rajeevkumar et al., 2017). These viruses can spread the infection by coughing/sneezing through droplet infection. These infections can also be spread through the use of contaminated food, water, bedsheets, utensils and ornaments, body fluids such as blood and saliva. Acharya Sushruta termed such diseases as Aupasargik Vyadhish or Infectious diseases (Kalamkar et al., 2015).

Out of the total 57 Krimighna drugs (8 drugs are repeated) mentioned as Krimighna, 10 pills (Achyanthus Aspera, Azadirachta indica, Calotropis gigantea, Curcuma longa, Embelia Ribes, Moringa oleifera, Nerium odorum, Ocimum sanctum, Solanum nigrum and Vitex nigundo) were found to have antiviral activity against various type of viruses such as Herpes Simplex virus (HSV type 1 & 2), Dengue virus (DNGV), Newcastle Disease virus (NDV), Sindbis virus(SINV) Measles virus and Poliovirus some of which are fatal to human beings. (Tables 4 and 5). Remaining 13 drugs which are antimicrobial in nature but do not include in any group of Krimighna drugs in Samhitas have also shown antiviral activities in various researches. All these medicinal plants contain a wide variety of varied phytochemicals such as alkaloids, tannins, saponins, flavonoids, terpenoids, lignans, coumarins, and many other components which are supposed to be responsible for potent antiviral activity by inhibiting the replication cycle of various types of DNA or RNA viruses (Jassim and Naji, 2003; Ojo et al., 2009).

Surprisingly, few plants which are not termed as Krimighna but have shown significant antiviral activity like Glycerrhaza glabra and Phyllanthus urinaria. Glycyrhrizic acid extracted from Glycerrhaza glabra exerts antiviral activity against Kaposi’s sarcoma-associated virus by the elimination of the inactive form of the virus via apoptosis. Glycyrhrizic acid also inhibited the replication of SARS (Severe Acute Respiratory Syndrome) (Cinatl et al., 2003). The flavonoid Ellagic acid from Phyllanthus urinaria inhibits immunotolerance of mice against the hepatitis B virus e-antigen (Kang et al., 2006). Phyllan-

### Table 5: List of Researches on Krimighna drugs and their antiviral activities.

| S.N. | Botanical name | Family | Part used | Antiviral activity | References |
|------|----------------|--------|-----------|--------------------|------------|
| 19   | Swertia chirata Roxb. | Gentianaceae | Leaves | HSV-1 | (Gopalkrishna et al., 2008) |
| 20   | Terminalia chebula Retz | Combrataceae | Fruit | Measles and Mumps viruses | (Pa et al., 2012) |
| 21   | Trachyspermum Umbellifera Ammi Sprague | Umbelliferae | Seed oil | Japanese encephalitis virus | (Roy et al., 2015) |
| 22   | Vitex nigundo L. | Verbenaceae | Leaves | HIV | (Nair, 2012) |
| 23   | Zingiber officinale Roscoe | Zingiberaceae | Rhizome | HIV, Poliovirus, Measles | (Devi and Manoharan, 2009; Kalyani and Kamaruz, 2013) |

HSV-Herpes Simplex virus, DNGV- Dengue virus, NDV- Newcastle Disease virus, SINV- Sindbis virus, HIV- Human immunodeficiency Virus
thus urinaria extract markedly repress HBV replication and expression in an HBV transient transfection mouse model (Wu et al., 2015). In clinical trials conducted by Wang MX et al. in chronic hepatitis B patients demonstrated that Phyllanthus urinaria promotes HBeAg and HBeAb seroconversion from positive to negative (Wang et al., 1995; Zhong et al., 1998). The depressing thing is that modern antibiotics are not adequate to control viral infection. Though several drugs are identified as antiviral drugs against the specific virus but still a plethora of potentially useful krimighna drugs waiting to be evaluated and exploited with their antiviral activity. Hence young researchers have an opportunity to conduct in vitro and in vivo assays to evaluate the antiviral activity of these herbal drugs. If we could find out the potential antiviral drug from these studies, it will be a boon for the entire world which can do wonder in the treatment of KOVID-19 the most dangerous pandemic of the decade.

CONCLUSIONS

The number of medicinal plants described in Ayurveda compendia as Krimighna drugs have shown remarkable antiviral activities against various viruses. However, due to the global disease burden caused by COVID-19, there is an urgent need to identify novel compounds with antiviral activity from the unexplored Krimighna drugs using modern in vitro assays. It is must involve well-established sciences such as Ayurveda, immediately into the mainstream of discovering a solution for any epidemic or pandemic situation to have all possible alternatives to discover the cure. The elucidation of active constituents in these plants may provide significant lead to the development of new and effective antiviral agents to combat the COVID-19 menace effectively.

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Conflict Of Interest

None.

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