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

Bharat Rathi^{*1}, Renu Rathi², Pramod Khobragade³

¹Department of Rasashastra and Bhaishajya Kalpana, Datta Meghe Institute of Medical Sciences (deemed to be university), Sawangi (M), Wardha, Maharashtra, India

²Department of Kaumarbhritya, Datta Meghe Institute of Medical Sciences (deemed to be university), Sawangi (M), Wardha Maharashtra, India

³Department of Dravyaguna, Datta Meghe Ayurveda College Hospital & Research Centre, Wanadongari, Nagpur (MS), Maharashtra, India

Article History:	ABSTRACT
Received on: 20 Apr 2020 Revised on: 20 May 2020 Accepted on: 26 May 2020 <i>Keywords:</i>	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. <i>Krimighna</i> drugs described in Ayurveda
Antiviral, COVID-19, Herbal drugs, Krimighna drugs	this paper attempt is made to review <i>Krimighna</i> drugs described in Ayurveda compendia and identify its efficacy on various viral diseases. Relevant references were searched concerning <i>krimihar drugs</i> described in <i>Brihatrayee</i> viz. Charak Samhita, Sushruta Samhita and Ashtanga Hridaya. Scientific research papers related to pre-clinical and clinical studies showing the antiviral activity of individual <i>krimighna</i> drugs were also searched. In all Samhitas total, 56 drugs were found having <i>Krimighna</i> 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 <i>Krimighna</i> drugs with antiviral activity and to develop novel and useful antiviral agents to combat the COVID -19 menace effectively.

*Corresponding Author

Name: Bharat Rathi Phone: 91- 9011058301 Email: bharat.rathi@dmimsu.edu.in

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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).

S.N.	Reference	Name of drugs with Latin Names	Properties & Indications
1.	Krimighna Mahakashya Su.4/11	Akshiva (Moringa oleifera L.), Maricha (Piper nigrum L.) Gandira (Euphorbia antiquorum L.), Kebuka (Costus speciosus Koen.Sm), Nir- gundi (Vitex negundo L.), Vidanga (Embelia ribes Burm.f.)), Kinihi (Achyranthes aspera L.), Swadamshtra (Tribulus terrestris L.), Vrishaparni (Ipomea variety L.) and Akhu- parni (Ipomea reniformis Chois.)	Krimighna (worm infesta- tion)

Table 1: Krimighna drugs described in Charaka Samhita

Table 2: Krimighna drugs described in Sushruta Samhita

S.N.	Reference	Name of drugs with Latin names	Properties & Indica- tions
1	Sursadi gana Su. 38/18	Shweta tulsi (Oscimum sanctum L.), Fan- injak (Randia dumentorum Lam), Arjaka (Ocimum bacillicum L.) Dronapushpa (Leu- cas cephalotes Spreng.), Rajika (Brassica juncea L.), Kasmarda (Cassia occidentalis L.), Kshawak (Achyranthus aspera L.) Vidanga (Embeli ribes Burm.F.), Kayphal (Myrica escilenta L.), Nirgundi (Vitex negundo L.) Bharangi (Clerodendron serratum spreng.), Kakjangha (Peristrophe bicalyculata Nees.), Kakmachi (Solanum nigrum L.),Vishmushti (strychnos nux-vomica L.)	Pacify Kapha, worm infestation, coryza, anorexia, dyspnoea, cough .
2.	Lakshadi gana Su.38/64	Laksha (Laccifer lacca Kerr), Amlavetas (Garcinia pendunculata Roxb), Kutaj (Holar- rhena antidysentrica Wall), Karvir (Nerium odorum Soland), Kayaphala-(Myrica esci- lenta L.), Haridra(Curcuma longa L.), Daruharidra (Berberris aristata DC), Nimba (Azadirechta indicia. A. Juss), Sapta- parna (Alstonia scholaris R. Br.), Chameli (Jasminum grandiflorum L.), Traymana (Gentiana kurroo Royle)	Pacifies Kapha & Pitta, skin diseases, worm infestation, septic ulcer

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,

S.N.	Reference	Name of drugs with LatinNames	Properties & Indica- tions	
1	Aasanadi gana Su.15/19-20	Asana (Terminalia tomentosa L.) Tinish (Ougeinia dalbergioldes Benth.), Bhurja (Betula utilis D. Don.), Arjuna (Terminalia arjuna W.& A.), Karanja (Pongamia glabra Vent) Khadir (Acasia catechu Willd), Kadar (Acacia suma Buch. Ham) Shirish (Albizzia lebbeck Benth.), Shinshapa (Dalbergia sissoo Roxb) Meshshringa (Gymnema sylestree R. Br.), Chanadan (Sanctum album L.), Daruharidra (Berberis aristata DC.), Palash (Butea frondosa Koen.),Shak (Tectona grandis L.) 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, Obecity	
2.	Arkadi gana Su. 15/28-29	 Arka (Calotropis giganticum L.), Alarka (Calotropis procera R.Br.), Nagdanti (Croton oblongifolius Roxb) Vishalya (Gloriasa superb L.), Bharngi (Clerodendron serratum spreng), Rasna (Innula racemosa Hook.f.), Meshashringa (Gymnema sylvestre R. Br.), Karanja Pongamia glabra Vent.) Apamarga (Achyranthus aspera L.), Jyotishmati (Celastrus panniculataus Willd.), Shakhotaka (Balanities roxburghii Planch.) 	Pacify Kapha, Obecity, Poisoning, worm infes- tation, Skin diseases, Ulcers	

Table 3: Krimighna drugs described in Asthanga Hridaya

it is wise to adopt preventive measures which can boost our immunity during the COVID-19 crises.

In Avurveda, 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 (Kalvani 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 Ashtanga 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*

S.N.	Botanical name	Family	Part used	Antiviral activ- ity	References
1.	Achyranthus aspera L.	Amaranthaceae	Leaves	Epstein-Barr virus, HSV 1 and HSV 2	(Chakraborty <i>et al.</i> , 2002; Mukherjee <i>et al.</i> , 2013)
2.	Achorus calamus L.	Araceae	Tuber	DENV	(Rosmalena <i>et al.</i> , 2019)
3.	Allium sativum L.	Liliaceae	Tuber	NDV Influenza Virus	(Arify <i>et al.</i> , 2018) (Mehrbod <i>et al.</i> , 2009)
				HSV 1	(Devi and Manoha- ran, 2009)
4.	Aristolochia bracteata Retz.	Aristolochiacea	eLeaves	Influenza virus	(Mona <i>et al.</i> , 2017)
5.	Azadirechta indica L.	Meliaceae	Bark, leaves	HSV1 NDV DENV Herpes	(Tiwari <i>et al.</i> , 2009) (Ong <i>et al.</i> , 2014) (Hafidh <i>et al.</i> , 2009) (Kalyani and Kamaruz, 2013)
6.	Calotropis gigantea L.	Asclepiadaceae	Flower	Herpes simplex type-1 (HSV-1)	(Hamidi <i>et al.</i> , 1996)
7.	Cissus quadrangu- laris L.	Vitaceae	Stem	HSV type1 and 2	(Balasubramanian <i>et al.</i> , 2010)
8.	Curcuma longa L.	Scitaminaceae	Tuber	DENV	(Rosmalena <i>et al.</i> , 2019)
				HSV1 and HSV2 HIV1, HIV2	(Zandi <i>et al.</i> , 2010) (Mazumder <i>et al.</i> , 1996; Kutluay <i>et al.</i> , 2008)
9.	Embelia ribes Burm. f.	Myrsinaceae	fruits	Influenza virus Influenza	(Chen <i>et al.</i> , 2010) (Hossan <i>et al.</i> , 2018)
10	Ferula assa-foetida Regel	Umbiliiferae	Gum resin	HSV-1	(Ghannadi <i>et al.</i> , 2014)
11 12	Magnifera indica L. Moringa oleifera L.	Anacardiaceae Moringaceae	Seed powder Leaves	HSV HSV 1	(Hafidh <i>et al.</i> , 2009) (Nasr-Eldin <i>et al.</i> , 2019)
13.	Nerium odorum Soland	Apocynaceae	Root powder	HSV	2018) (Hafidh <i>et al.</i> , 2009)
14	Ocimum sanctum L.	Lamiaceae	Leaves	Polio virus type 3, Vaccinia virus, NDV	(Devi and Manoha- ran, 2009)
15	Punica granatum L.	Punucaceae	Fruit bark	HSV & SINV & Poliovirus	(Mouhajir <i>et al.,</i> 2001)
16	Ricinus communis L.	Euphorbiaceae	Root	HSV-1, SINV	(Hamidi <i>et al.</i> , 1996; Mouhajir <i>et al.</i> , 2001)
17	Semicarpus anac- ardium L.	Anacardiaceae	Nuts	Measles and Mumps virus	(Pa et al., 2012)
18	Solanum nigrum L.	Solanaceae	Dried plant	Hepatitis C Virus HSV	(Devi and Manoha- ran, 2009; Javed <i>et al.</i> , 2011)

Table 4: List of Researches on Krimighna drugs and their antiviral activities

S.N.	Botanical name	Family	Part used	Antiviral activity	References
19	Swertia chi- rata 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 Ammi Sprague	Umbilliferae	Seed oil	Japanese encephalitis virus	(Roy <i>et al.</i> , 2015)
22	Vitex nigundo L.	Verbeneceae	Leaves	HIV	(Nair, 2012)
23	Zingiber offic- inale Roscoe	Zingiberaceae	Rhizome	HIV, Poliovirus, Measles	(Devi and Manoharan, 2009; Kalyani and Kamaruz, 2013)

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

HSV-Herpes Simplex virus, DNGV- Dengue virus, NDV- Newcastle Disease virus, SINV- Sindbis virus, HIV- Human immunodeficiency Virus

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 "Kramana" which means attacking, surpassing or overcoming (Soni et al., 2017). Acharva 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 eve. 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. Acharva Sushruta termed such diseases as Aupasargik Vyadhis or Infectious diseases (Kalamkar et al., 2015).

Out of the total 57 Krimighna drugs (8 drugs are repeated) mentioned as Krimighna, 10 pills (Achyranthus 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. Glycyrrhizic 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. Glycyrrhizic 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). Phyllanthus 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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