

IMMUNOLOGICAL EFFECT OF AMRITADI KWATH FOR IMPROVING IMMUNITY TO FIGHT COVID -19 PANDEMIC

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ABSTRACT

COVID -19 is a respiratory disease caused by a coronavirus (SARS Cov -2). Coronaviral roteins is responsible to disrupt the immune response pathway and breakdown the immune system. In Ayurvedic system of medicine Amritadi Kwath may be effective for immunity booster drug to healthy people for improving immunity to fight COVID -19 pandemic. But Amritadi Kwath to be used freshly prepared, and shelf life is (½ -1 day). Which is major drown back of Amritadi Kwath to the large scale production. In this perspective it is an urgent need to Randomized double blind placebo controlled trial of Amritadi Kwath formulated Ghana satva convertedin to AMRITA

Tablet form on COVID -19 positive patient for more Improving Immunity to fight COVID -19 pandemic.

KEYWORDS: Amritadi kwath, Gnana satva, Amrita Tablet, covid-19, immunomodulator.

INTRODUCTION

COVID -19 is a respiratory disease caused by a coronavirus (SARS Cov -2). Coronavirus is enveloped virus with a positive sense, single -stranded RNA genome. The coronaviral genome encode four major structural proteins, the spike (S) protein, nucleocapsid (N) protein, membrane (M) protein, and the envelope (E) protein, all of which are required to produce a structurally complete viral particle.

The coronavirus disease (COVID-19 is highly transmittable and pathogenic viral. Coronaviral Proteins is responsible to disrupt the immune response pathway and breakdown the immune system. In the absence of effective inhibition patient suffer prograssive

immunological damage and develop upper respiratory infection (URTIs). Lower respiratory tract infection (LRTIs) and severe acute respiratory syndrome (SARS). Currently there are no approved therapeutic agent available for coronavirus.

Thus there is an urgent public health need for rapid development of novel interventions.

Ayurveda is the natural system of health care all over the World. Ayurvedic medicines as the major remedy in traditional medical system, have been used in medical practice for thousands of years and have made a great contribution to maintaining human health.

Ministry of AYUSH recommended the self care guideline for prevention health measures and boosting immunity with special reference to respiratory health. In this perspective Amritdi kwath may be immunity booster drugs. Amritadi Kwath which mainly constituent of Guduchi. *Tinospora Cordifolia* willd Hook f & Thomus, Ashwagandha *Withania Somnifera* L. Dunal, Yashtimadu *Glycyrrhiza glabra* Linn, Tulshi *Ocimum sanctum* Linn, Pipali *piper longum* linn.

Guduchi *Tinospora cordifolia* has been reported to benefit the immune system and successfully immunomodulator efficiency (K. G. C. Dissanayake. et. al 2020) Extract of *T cordifolia* has also may be effective in immunodeficiency virus. (HIV) (Kaliker MV. et. al 2008) Ashwagandha *Withania Somnifera* *Withania* has been reported to benefit to immune system and immunomodulatory activity (Davis. L. et. al 2000. P. Amaravati et. Al 2012) Yashtimadhu *Glycyrrhiza glabra* has been reported that immunomodulatory activity (Papaya Mitra muzamder et. al 2012, Kashif Hussein et. al 2017) Tulsi *Ocimum sanctum* has been reported to immunomodulatory activity (C. R. jaba et. al 2011, Gayatri Nahak et. al 2014) and Pipali *Piper longum* has been reported to immunomodulatory activity (E. S. sunala et. al 2004) Satyapal Singh et. al 2015 has been reported that Guduchi leads to immunomodulator by activating the lymphocytes, Tulsi act by modulating the humoral immunity, Ashwagandha act immunomodulating cellular immunity, Pippali works via modulation of both specific and non specific immune response. Yashtimadhu also evaluated for its anti-viral activity against HIV, validating its immunomodulatory effect.

Thus prepared Amritadi Kwath to clinical trial on healthy people for talking as an immunity booster drug to protect transmittable coronaviral infection.

MATERIAL AND METHOD

Procurement and preparation of plant material

The crude drugs mentioned in Bhavaprakasha Nighantu (Indian Materia Medica). The preparation of Amritadi kwath were taken from the pharmacy of Ravindra Nath Mukharje.

Ayurveda College and Hospital Motihari, after proper authentication by the Department of pharmacognosy of the Institute. Then, the physical impurities were removed and drugs were washed with water, sorted and sun dried below 45oc. Dried drugs were stored in tightly closed containers. The crude drugs used in Amritadi Kwath with their botanical identities and parts used are given in Table -1.

Table 1: Crude drugs of amritadi kwath.

Botanical	Fam	Part	Used Name
Tinospora cordifolia	Menispermaceae	Stem.	<i>Guduchi</i>
Withania Somnifera	Solanaceae	Root.	<i>Ashwagandha</i>
Glycyrrhiza glabra	Fabaceae	Root	Yastimadhu
Ocimum sanctum	Labiatae	Leaf.	<i>Tulsi</i>
Piper longum	Piperaceae	Fruit.	<i>Pipali</i>

Preparation of amritadi kwath

Preparation of amritadi kwath to be considered flowing pharmaceutical Factors.

Vessel for Amritadi Kwatha, Proportion of water, Temperature, Particle size of Amritadi Kwath Dravyas (Drugs used for decoction), Duration of heating, and Analytical study of Amritadi Kwatha.

1. Vessel to be used for amritadi kwath

Vessel imparts a specific role in Amritadi Kwath preparation. In ancient time earthen pot was used having qualities such temp regulation, alkaline in nature, doesn't take part with chemical reaction with ingredients which are under processing. Also due to its narrow opening it can control vapors within hence the important active principles can be saved. Now a day stainless steel vessel can used due to easy availability, less costly and easy for maintenance.

2. Proportion of water

Proportion of water to be added for Amritadi kwath preparation is important factor. Different proportion of water (4, 8 and 16) mentioned in classic depends on the hardness as well as on quantity of the drug used. Some Acharya has mentioned that the proportion of water may be decided on the basis of the quantity of drug taken. However, most of the times, it is difficult

to judge the consistency of drugs, especially when the contents are poly herbal. Hence, an emergence need is required for qualitative and quantitative study to standardized quantum of heat and time duration.

3. Temperature

Regulation of temperature protects heat labile phytoconstituents. Madhyamagni is the term used to denote mild-to-moderate heat in preparation of kwath. Temperature holds the significant factor in preserving thermolabile active constituent Therefore, during the preparation of Amritadi Kwath temperature may be maintained between 85 and 90°C.

4. Particle size

In conventional method of Kwath exact particle size of raw drugs is not mentioned. Most of the scholars use powder of raw drugs as Yavkut churna (Coarse powder). Mostly 60-100 size can preferred for Amritadi Kwath purpose.

5. Duration of heating

One fourth and one eighth of original volume of water are the terms used in ancient methods of Kwath preparation. The degree of heating depends on Laghutwa (Easy to digest) and Gurutwa (Hard to digest) of Amritadi Kwath,. On the basis of above principle the authenticated crude drugs were crushed to a coarse powder separately and then mixed thoroughly with 8 parts of water in a stainless steel container and then continuous mild heat was applied until it was reduced to one-fourth of its initial quantity. During the heating process, continuous stirring was done to facilitate the evaporation and avoid any deterioration due to burning of materials. After a desirable reduction in volume was achieved, the Kwatha was filtered through single folded cotton cloth and collected in a separate Vessel.

Amritadi Kwath were subjected to various analytical parameters as Organoleptic parameters, Physico-chemical parameters and phytochemical screening parameters.

Clinical aspect

I have selected 50 healthy people for clinical trial of Amritadi Kwath .Out of 50 healthy people 40 were male and 10 people female, the age varied from 18 to 70 years. I have applied 20 ML to 40 ML Amritadi Kwath daily for 2 week.

RESULT

The Organoleptic characters of Amritadi Kwath were the following:

Rupa (color) was dark brown, Rasa (taste) was bitter, Ganda (odor) was characteristics due to the specific properties of the various ingredients and sparsha (consistency / texture) of Amritadi Kwath was liquid as given in Table -2.

Table 2: Organoleptic parameters of amritadi kwath.

Parameters	Kwath
Color	Dark brown
Taste	Bitter
Odor	Characteristic
Form	Liquid

pH of the Amrita Kwath was 4.53 ± 0.03 , loss on drying in Amrita Kwath was $3.4 \pm 0.20\%$ w/w as given in Table 3.

Table 3: Physico-chemical parameters of Amritadi Kwath.

Parameters	Kwath
PH at 5% aqueous solu	3.50 ± 0.02
Loss on drying at 110°C (% w/w)	2.4 ± 0.03
Specific gravity	5.2 ± 0.20
Total solid content (% w/w)	-
Ash value (% w/w)	-
Acid insoluble Ash (% w/w)	-
Water soluble extractive Ash (% w/v)	-
Methanol soluble extractive (% w/v)	-

The number in parentheses indicate the number of sample/determination carried out.

Preliminary phytochemical screening reveals the presence of tannins, alkaloids, saponins, glycosides and flavonoids etc. in the Amritadi Kwath. given in Table 4.

Table 4: Preliminary phytochemical screening of Amritadi Kwath.

Phytoconstituents	Test performed	Results
Tannins.	Ferric chloride test	+
Alkaloids	Dragendorff's test.	+
Flavonoids.	NaOH Solution test	+
Glycosides	Keller-Killani test	+
Steroids.	Lieberman's test	+
Terpenoids.	Salkowski's test	+
Anthraquinones.	Benzene test	-

(+) Denotes presence of Phytochemical

(-) Denotes Absence. of Phytochemical

OBSERVATION

At the end of 2 week It can be observed that the people realize the natural stamina, strength and ability of the body, mind emotions, and in some people the body weight positively increased. It can be observed that Fever, cough, difficulty breathing tiredness, Nasal congestion, runny nose, sore throat, and severe disease as Asthma, bronchitis, pneumonia. etc did not appearance after 12 week used of Amritadi kwatha.

DISCUSSION

On proper investigative search, it has been seen that Amritadi kwatha becomes base material for most of the available dosage forms among Ayurvedic medicaments. Hence, to establish our assumption, literature and research papers with probable possible dosage forms were searched where Amritadi Kwatha acts as base material and it can thoroughly explored with the advantage of these dosage forms in the context of their effectiveness and safety, but they are to used in fresh state due to less stability, inconvenience to prepare fresh Amritadi Kwath every time needed etc.

The Comparative study of Amritadi Kwath, I observed that the process of the Ghana satva is considered to be similar to the aqueous extraction of the drug. It is considered to contain all the active principle as that of the whole drug. So advantage in using Ghana satva it higher concentration, lower dosage, and longer shelf life.

Thus Amritadi Kwath formulated Ghana satva converted in to AMRITA TABLET form may be increase the self life make it higher concentration, lower dosage, better bio availability and easy to dispense for dose fixation. Prepared Amritadi Kwath formulated Ghana satva Converted into AMRITA Tablet following procedure.

Preparation of amrita tablet

The Amritadi Kwatha can be boiled again over slow fire on a gas stove, maintaining the temperature between 90°C and 95°C till a semisolid consistency is obtained. As the water evaporates, the viscosity of the extract increases, resulting in Ghana satva form. Then, the Ghana satva can be mixed with the Churna of Amritadi Kwath (up to 10% of extract) further forming a solid mass.

The solid mass (Ghana satva) can be forced through a no. 16 sieve and granules were prepared and then dried at 50°C in a hot air oven for 10 hours. The dried granules were passed again

through a no. 20 sieve. The formulation can then be compressed in a single-punch tablet press with a target weight of 500 mg.

The *Amrita Tablet* can be subjected to various analytical parameters as follows.

Organoleptic parameters, Physico-chemical parameters, Quantitative tests for tablet as Weight variation test, tablet hardness test, tablet disintegration time and friability. Qualitative tests for various functional groups.

Chromatographic analysis: Thin layer chromatography (TLC) High performance liquid chromatography (HPLC), Nuclear magnetic resonance spectroscopy (NMR), Mass Spectrometry (MS) and Heavy metal analysis, pesticide residue value, Microbial overload and fungal growth study can be carried out.

Afterwards to determine acute toxicity test and long term toxicity test on animal species for assessing the safety of AMRITA Tablet as follows.

Acute toxicity test

Animal species - Rodent species can be selected.

Sex - Male and female mice can be used

Number of Animals - Each test group can consist of at least five per sex.

Route of administration - Oral route

Dose level - A sufficient number of dose levels can be used in mice to determine the appropriate lethal dose.

Duration of study - Duration of acute toxicity test evaluation seven to fourteen days.

Observation - Toxic signs and the severity on set progression and reversibility of the signs can be observed and recorded in relation to dose and time. Mice during the observation period can be autopsied. If necessary a histopathological examination can be conducted on organ or tissue showing microscopic changes of autopsy.

Long term toxicity test

Animal species - Rodent species can be selected.

Sex - Male and female mice and rats can be used.

Number of Animals - Each test group can consist of at least five mice per sex and three rats per sex.

Route of Administration - Oral route.

Administration period - The period of administration of the test substance to mice and rats will depend on the expected period of clinical use.

Observations and examinations

Observation and examination can be performed on the following items.

1. General signs, body weight and water intake.
2. Haematological examination.
3. Renal and hepatic function tests.
4. Other Function test.
5. Animals found dead during the examination can be autopsied as soon possible. A macroscopic examination can be made of Organdy and tissues.
6. In order to maximize the amount of useful information that can be obtained during the administration period, all moribund animals can be sacrificed tether than allowed to die. period to sacrifice, clinical observation can be recorded and blood sample collected for haematological and blood chemical analysis.

Recovery from toxicity

Then evaluate the immunological efficacy of AMRITA Tablet on COVID-19 positive For improving immunity to fight COVID -19 Pandemic, as follows.

Human pharmacology (phase I)

The objective of the safety in this phase is the estimation of safety and tolerability with the initial administration of Amrita Tablet on Covid -19 Positive. In this phase can be applying Amrita Tablet in healthy volunteers and certain type of patients.

Maximum tolerated dose -- To determine the tolerability of the dose range expected to be needed for later clinical study and to determine the nature of adverse reaction can be expected

Therapeutic exploratory trial (Phase II)

Therapeutic exploratory trial (phase II) studies on a limited number of COVID -19 positive patient to determine clinical efficacy and to further confirm safety. This trial can be preferably designed as randomized, double -blind, controlled study , using for control groups either an alternative treatment or a placebo.

The objectives of phase II study can include evaluation of potential study endpoints, therapeutic regimens and target populations (mild versus severe disease) for further study.

Therapeutic confirmatory trial (phase III)

Therapeutic confirmatory trial (phase III)-A larger COVID-19 positive patient group can usually study a randomized double blind design to validate preliminary evidence of efficacy obtained in earlier study.

Study in phase-III can be designed to confirm the preliminary evidence accumulated in phase II, that Amrita tablet is safe and effective then can be used in the intended indication and recipient population.

CONCLUSION

It is my conclusion that Amritadi Kwath may be an effective immunity booster for improving immunity. Amritadi Kwath may act on improving vitality, mental faculties and promoting longevity.

Amritadi Kwath has no adverse side effect and other complications even long term use in therapeutic dose. In this conclusion I would like to say that there is an urgent need to Randomized double blind placebo controlled trial of Amritadi Kwath formulated Ghana satva converted into AMRITA Tablet form on COVID-19 positive patient for more improving immunity to fight COVID-19 pandemic.

Institutional Ethics committee has approved for conducting clinical trial of Amrita Tablet on COVID-19 positive patient. After receiving CTRI Number by Clinical Trials Registry India.

ICMR- National Institute of Medical statistics, Will be

Conducting clinical trial.

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