

COMPARISON OF THE COMPUTED DRUG EFFICACY INDICES [$Q_{(VPK)}$] OF AYUSH-64 AND CORONIL TABLETS

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ABSTRACT

The COVID-19 pandemic is still continuing as a completely unresolvable problem in front of the scientific community that needs an effective scientific solution even though some vaccines were invented and developed in a short span of research. The scientific community is keenly observing to prove those vaccines for their complete therapeutic effects. It is also worthwhile to discuss about the two major drug formulations viz. Ayush-64 and Coronil Tablets that are formulated for improving the health conditions. The respective ingredients of these herbal formulations were critically studied based on the classical texts and computed the therapeutic effects in terms of Tridoshas the three somatic humours, the very fundamental principle of Ayurveda. Finally, the Drug Efficacy Indices [$Q_{(VPK)}$] of those two formulations were computed, compared and reported.

Keywords – The Drug Efficacy Index [$Q_{(VPK)}$], CORONIL, AYUSH-64, COVID-19, Ayurveda, Herbal Formulations

1. INTRODUCTION

The Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered virus belonging to the family *Coronaviridae*, a family of enveloped, positive strand RNA viruses. The SARS Cov-2 and its various mutants have been troubling, perplexing and confusing the humans since the November 2019 and remain as challenging problem that needs a better scientific solution. Almost all the countries in this world were very badly paid for this pandemic outbreak. The entire scientific community around the globe was challenged to find a better solution to overcome the present bad situations caused by this virus and its new variants. Scientific community invented and developed certain vaccines within a short span of research time to control this pandemic and are recommended by many governments. Similarly, the researchers of the alternative medicines also proposed certain medicines that can be used to control the pandemic when used complementary. The two important herbal formulations viz. AYUSH-64 and CORONIL Tablets are much discussed among those modern proprietary herbal remedies. The present research analyses and computes the Drug Efficacy Indices [$Q_{(VPK)}$] of these two oral formulations and tries to compare the therapeutic effects of those two theoretically.

1.1 COVID-19 and Ayurveda

According to Ayurveda the health consists of an equilibrium state of the three somatic humours viz. *Vata*, *Pitta* and *Kapha* (*Tridoshas*), seven tissues viz. *Rasa* (Plasma), *Rakta* (Blood), *Mamsa* (Muscle), *Meda* (Fat), *Asthi* (Bone marrow), *Sukra/Artava*

(Reproductive tissues) collectively termed as the *Sapta Dhatus*, the three wastes viz. faeces, urine and sweat (*Malas*), and the digestive/gastric fire (*Agni*) along with the clarity and balance of the senses, mind and spirit of the individual [1]. Thus, the ancient scientists (*Rshis*) pointed that the human body can certainly acts as a thermodynamic ensemble and the health results in the equilibrium state of that particular ensemble. The proper nutrition, exercise, healthy relationships, positive emotions, and a well-regulated daily routine all contribute to a healthy life while the opposite of these are the causative factors that upset the equilibrium of the somatic humours and lead to the diseases. The Ayurvedic treatments and medicaments are based on the observed *vikrti* and permanent *prakrti* of the infected persons keeping an aim to re-establish the *prakrti* of the infected persons and giving well protection to the health of non-infected persons. There are numerous research papers on COVID-19 and Ayurveda pointing many causative factors and reasons and here I consider it as a result of *Pranjaparadha* that was triggered by the *Krtyabhisapa*. The word *Pranjaparadha* means/indicates serious offense against wisdom as mentioned in the *Astangahrdaya* and one of the three crucial causes of the diseases as mentioned in *Carakasamhita*. The word *Pranja* means Wisdom/Intellect and *Aparadha* indicates the offense/wrong deed a fault and thus the coined word means Offense against Wisdom. The *Krtyabhisapa* found mentioned in the *Sutrasthana* of the *Susrutasamhita* and well explained by *Dalhana*. The definition given for *Krtya* is *Kupita-Mantrino-Abhicarakarmajanito-Rakshasivishesha* that can be better translated as a pre-programmed bioweapon resulted from destructive research [2]. The word *Kupita-Mantrina* means pre-programmed (aimed for destruction), *Abhicarakarmajanita* means result of destructive research and *Rakshasivishesha* means a bioweapon (particular deadly poisonous viruses belong to *Heti-Praheti* class/family) that can affect all the nations (*Sarvarashtrachhedaka*) irrespective of the seasonal/climate variations. Further interesting that the name *Heti* indicates/means a weapon and *Praheti* indicates/means an excessively challenging weapon in Sanskrit. It is wonderful to compare the symptoms of the modern pandemic COVID-19 to those have been explained in *Susrutasamhita* like *Kasa* (cough), *Shwasa* (dyspnoea), *Jwara* (pyrexia), *Shiroruk* (headache), *Gandhajnana* (loss of smell) etc. in addition to the various modes of transmission as explained by the ancient *Rshi*. It is worthwhile to remember the story of *Vasurimaala* who used first bioweapon that consists of viruses of *Vasuri* (Virus that cause Pox) against her enemies during the battle of Devas and Asuras. The modern bioweapon researches were also found based on viruses that cause infectious diseases like poxes and were successfully used in wars and as a tool of bioterrorism. Thus, based on Ayurveda literatures the COVID-19 can be defined as the disease caused by the viruses of excessively challenging class (*Heti-Praheti* class) that are used for pre-programmed bioweapons originated as a result of destructive research caused by the offenses against wisdom. The literatures of Ayurveda even though very ancient found supportive to many of the latest theories of Medicinal Chemistry that have been using for drug designing and discovery processes by the modern medicinal scientists [3]. There are many reported treatment protocols for COVID-19 in Ayurveda as evident from the modern research papers with various claims and are not the subject matter of this research as the present research being purely theoretical and computational in nature. The modern proprietary medicaments viz. AYUSH-64 and CORONIL tablets those are the subject matter of this study are found polyherbal as evident from the respective labels and are further explained below.

1.2 AYUSH-64: This polyherbal, nontoxic formulation was developed by Central Council for Research in Ayurvedic Sciences (CCRAS), under the Ministry of AYUSH, Government of India for controlling the most prevalent, destructive and widely spread tropical disease called Malaria. This formulation contains aqueous extracts of *Alstonia scholaris* (*Saptaparna*) stem bark, *Picrorrhiza kurroa* (*Katuki*) root, *Swertia chirata* (*Chirayata*) whole plant and powder of *Caesalpinia crista* (*Kuberaksha*) seed in a ratio of 1:1:1:2 (100mg:100mg:100mg:200mg) [4,5,6]. The CCRAS conducted controlled clinical studies and compared Chloroquine and Primaquine the commonly prescribing antimalarial drugs. The initial treatment of COVID-19 was also using Chloroquine and Hydroxychloroquine for getting relieved from the symptoms. These symptomatic resemblances of the Malaria and COVID-19 also

suggested the use of AYUSH-64 for research trials. Later CCRAS and AYUSH department conducted controlled studies and found AYUSH-64 a promising complementary formulation to reduce the risks of COVID-19.

Alstonia scholaris (Saptaparna) [7]: This is fairly common throughout India in most of the deciduous and evergreen forests from sea level to about 2000feet. This large evergreen tree belongs to the family *Apocynaceae* mentioned in *Caraka Samhita* and found classified in *Kushthaghna* group. The *Alstonia scholaris* has been using for the treatment of various fevers including malaria and associated symptoms in traditional medicines. It is also well known in the treatment of skin diseases, diarrhoea, wounds etc. According to Ayurveda it has a property to overcome or found useful in treating ulcer, *Kapha*, *Vata*, leprosy, *Vatarakta* and parasites, promotes digestive power, cures asthma etc. and phantom tumour. The *Alstonia scholaris (Saptaparna)* is found demulcent, hot astringent in taste and laxative. The tree bark is febrifuge, antiperiodic, spasmolytic, antidyentery, uterine stimulant and hypotensive in nature. The stem bark contains indole alkaloids, echitamine etc. as chemical constituents is also found useful as a blood purifier and can be recommended for the treatment of phosphaturia.

Picrorrhiza kurroa (Katuki) [8]: This herb belongs to the family *Scrophulariaceae* has been using for the treatment of liver related diseases. According to Ayurveda it has a property of alleviating pitta considerably and found mentioned in paediatrics with prime importance. It can also advisable for related intermittent fever (*vishama jvara*). This also finds applications in dyspnoea and skin diseases. The roots contain kutkin a glycosidal bitter principle, D-mannitol, kutkiol, kutkisterol and a ketone identical with apocynin. The chemical isolated kutkin has exhibited hepatoprotective activities. Kutkin, picroside-I and kutkoside exhibit anti-inflammatory property. The isolated phenolic glycoside named andosine prevent allergen and platelet activating factor induced bronchial obstruction in guinea pigs in vitro. The glycosides isolated from the root show liver protective, tumour inhibitory and antiinflammatory activities.

Swertia chirata (Chirayata) [9]: This belongs to the family *Gentianaceae* has been using for the treatment of intermittent fever (*vishama jvara*) and wounds. It is also well known for the treatment of purifying the breast milk and hence has its own prime importance in the paediatrics. The *Chirayata* is also known as *Kiratatikta* in Sanskrit due to its bitter taste. It is a blood purifier and bitter tonic prescribed for skin diseases. It has anti-inflammatory, hypoglycaemic, astringent, stomachic, antimalarial, anthelmintic, antiasthmatic, bechic and hepatoprotective activities. The herb contains various oxygenated xanthone derivatives, alkaloids and glycosyl flavones.

Caesalpinia crista (Kuberaksha) [10, 11]: This belongs to the family *Caesalpinaceae* has been using for the treatment of *Kapha* and *Vata* related diseases like hydrocele, pains and inflammation, wounds and found useful in smallpox. It is also found useful in treating the acne and related issues. It can be advisable to use in fever related ailments. The seeds contain an alkaloid caesalpinine, bitter principle bonducin, saponins and fixed oil and have antiperiodic, antirheumatic and antidiabetic properties The plant is considered as an excellent remedy for chronic fever as per homoeopaths.

1.3 Coronil Tablet: This tri-herbal ayurvedic proprietary medicine was developed by Drug Discovery and Development Division of Patanjali Research Institute, Haridwar and contains extracts from *Tinospora cordifolia (Giloy)*, *Withania somnifera (Ashwagandha)* and *Ocimum sanctum (Tulsi)* in a ratio of 6:5:1 (300mg:250mg:50mg) [12, 13]. This formulation based on the principles of Ayurveda contains the ingredients those have been used to treat respiratory ailments with symptoms overlapping with those of COVID-19. The selected ingredients in this formulation are also strong immunomodulant in nature.

Tinospora cordifolia (Giloy, Amrt) [14]: This perennial shrubby twinner belongs to the family *Menispermaceae* has proven antipyretic, antiperiodic, anti-inflammatory, antirheumatic, spasmolytic, hypoglycaemic and hepatoprotective activities. The water extract can considerably increase the urine output. The traditional practitioners prescribe the stem juice in high fever and decoction in rheumatic and bilious fevers. The dried and powdered stem has importance in treating jaundice, anaemia, polyuria

and various skin diseases. In addition, the active principles were found capable to in vitro inhibit the growth of Mycobacterium tuberculosis. The starch from roots and stem contains a polysaccharide that has effect in chronic diarrhoea and dysentery. This plant is specially trained to grow on Neem (*Azadirachta indica*) and Mango (*Mangifera indica*) trees thereby it is supposed, increasing its medicinal values (traditional believes). According to *Bhavamisra* it is pungent, bitter, sweet on digestion, tonic, arresting, astringent, hot, light, strengthening, promotes digestive power, overcomes the three *doshas* etc. *Susruta* prescribes the cold decoction of it for all kinds of fevers. In *Saligramanighantu* the combinations of this herb with other adjuvants like sugar, jaggery, honey, oil etc. are explained with the respective curative changes on various degrees of the three somatic humours or *Tridoshas*. According to *Vagbhata* it has a property for curing *Tridoshas* considerably.

Withania somnifera (Ashwagandha) [15]: This plant belongs to family *Solanaceae* is one among the time proven and well known immunomodulators. Root has anti-inflammatory activities and found useful for swellings, tumours, scrofula and rheumatism. It has also sedative and hypnotic activities. Leaves are also found anti-inflammatory, hepatoprotective and antibacterial in nature. The fruits and seeds of the *Withania somnifera* are diuretic. The root contains several alkaloids like withanine, withaninine, withananine, pseudo-withanine, somnine, somniferine etc. while the leaves contain 12 identified withanolides including withaferin A as chemical constituents. Withanine is a sedative while Withaferine A is antibacterial, antitumour, hepatoprotectant and anti-inflammatory in nature. Ayurvedic principles support the property for curing the *Vata-Kapha* and vitiated blood related ailments.

Ocimum sanctum (Tulsi) [16]: This belongs to the family *Lamiaceae* is considered as a holy herb by Hindus and has various time-tested therapeutic effects including antistress along with influenza curing and immunostimulant capabilities. The leaves are found carminative, stomachic, antispasmodic, antiasthmatic, antirheumatic, expectorant, stimulant, hepatoprotective, antiperiodic, antipyretic and diaphoretic. The seeds are therapeutic effect over genitourinary diseases. The essential oil of the Holy basil has antibacterial and antifungal activities.

The results of certain reported controlled pilot clinical studies further pointed that following Ayurvedic treatment regime reduced the inflammation markers that suggested the less severity of SARS-CoV- 2 infection in the treatment group and found safe without any adverse effect observed with that treatment [17].

2. MATERIALS AND METHODS

This being theoretical research that wholly based on computational methods has used or required neither any tablets nor any animals for computing and predicting the properties. The combinations revealed by the inventors or the manufactures were taken as such for the studies. The drug efficacy index $Q_{(V,P,K)}$ was calculated for both the tablets and was achieved by inputting the ratios as per the label declaration using previously reported computational method.

2.1 Experimental

The combinations of the tablets understudy were collected from the available published literatures and the labels of the respective products. The properties of the individual herbs were collected from the classical Ayurvedic texts and lexicons. The therapeutic effects of the respective herbs and their cumulative therapeutic effect on the combinations understudy were theoretically calculated using the reported method and their respective Drug Efficacy Indices [$Q_{(V,P,K)}$] were computed [18].

3. RESULTS AND DISCUSSION

The computed results and discussions followed by plausible theoretical explanations for the medicaments viz. Ayush-64 and Coronil Tablets are as follows.

AYUSH-64: This polyherbal formulation contains aqueous extracts of *Alstonia scholaris* (*Saptaparna*) stem bark, *Picrorrhiza kurroa* (*Katuki*) root, *Swertia chirata* (*Chirayata*) whole plant and powder of *Caesalpinia crista* (*Kuberaksha*) seed in a ratio of 1:1:1:2 (100mg:100mg:100mg:200mg). The *Alstonia scholaris* (*Saptaparna*) stem bark is *Tikta* (Bitter) and *Tuvara* (Astringent) in taste with *Laghu* (Light), *Snigdha* (Oily) and *Ushna* (Hot) properties with a *Katu vipaka* (Pungent) has effects on *kapha*, *vata* and *vatarakta*. The computed values point to the *Pitta-Kaphaghna* property that indicates the capacity to cure ailments related with *kapha* with vitiated *rakta*. The blood clotting and related symptoms of the COVID-19 might suggest the vitiation of the blood. The *Kapha* is usually related to the *Kasa* and *Shwasa* (Cough and dyspnoea/difficulty in breathing), both are also some predominant symptoms of this pandemic COVID-19. The *Picrorrhiza kurroa* (*Katuki*) root is *Tikta* (Bitter) in taste with *Laghu* (Light), *Ruksha* (Dry) and *Seeta* (Cold) properties with a *Katu vipaka* (Pungent) has effects on *Kapha-Pitta* and *Jwara* (Fever) and also support the *Kapha-Pitta hara* nature from the computational studies. The *Swertia chirata* (*Chirayata*) whole plant is *Tikta* (Bitter) in taste with *Laghu* (Light), *Ruksha* (Dry) and *Seeta* (Cold) properties with a *Katu vipaka* (Pungent) has effects on *Kapha-Pitta* and also observed as the *Kapha-Pitta hara* in nature from the computational studies. The powder of *Caesalpinia crista* (*Kuberaksha*) seed is *Tikta* (Bitter) and *Tuvara* (Astringent) in taste with *Laghu* (Light) and *Ushna* (Hot) properties with a *Katu vipaka* (Pungent) has a property to cure *Kapha-Vata*, *jwara* (Fever) and a pain reliever. The computational studies also suggested that it has a *Kaphaghna* nature. The present computational studies also suggest that *Alstonia scholaris* (*Saptaparna*) and *Caesalpinia crista* (*Kuberaksha*) has *Pitta* diminishing properties. This might be an indication for the fevers (change in temperatures) that cause the vitiation of the blood to change the plasma properties (*pitta related*) as in various viral fevers. The combination of these in the AYUSH-64 tablets in a ratio of 1:1:1:2 (100mg:100mg:100mg:200mg) makes it *Pitta-Kaphagna* in nature with a Drug Efficacy Index [$Q_{(V, P, K)}$] of 0.38 (Table 1).

Table 1: The computed Drug Efficacy Index $Q_{(VPK)}$ of ingredients and AYUSH-64 tablets

| Herb/Tablet | Individual Component of DEI $Q_{(VPK)}$ | | | DEI $Q_{(VPK)}$ | Therapeutic Category |
|--|---|-----------------|-----------------|-----------------|------------------------------|
| | Vata $q_{(V)}$ | Pitta $q_{(P)}$ | Kapha $q_{(K)}$ | | |
| <i>Alstonia scholaris</i> (<i>Saptaparna</i>) (100mg) | 20.00 | -20.00 | -60.00 | 0.60 | <i>Pitta-Kaphagna</i> |
| <i>Picrorrhiza kurroa</i> (<i>Katuki</i>) (100mg) | 42.86 | -42.86 | -14.29 | 0.14 | <i>Kapha-Pittaghna</i> |
| <i>Swertia chirata</i> (<i>Chirayata</i>) (100mg) | 42.86 | -42.86 | -14.29 | 0.14 | <i>Kapha-Pittaghna</i> |
| <i>Caesalpinia crista</i> (<i>Kuberaksha</i>) (200mg) | 20.00 | -20.00 | -60.00 | 0.60 | <i>Pitta-Kaphagna</i> |
| AYUSH-64 (1:1:1:2) | 31.03 | -31.03 | -37.93 | 0.38 | <i>Pitta-Kaphagna</i> |

CORONIL TABLET: This tri-herbal ayurvedic proprietary medicine contains extracts from *Tinospora cordifolia* (*Giloy*), *Withania somnifera* (*Ashwagandha*) and *Ocimum sanctum* (*Tulsi*) in a ratio of 6:5:1 (300mg:250mg:50mg). The *Tinospora cordifolia* (*Giloy*) is *Tikta* (Bitter), *Tuvara* (Astringent) and *Katu* (Pungent) in taste with *Laghu* (Light) and *Ushna* (Hot) properties with a *Katu vipaka* (Pungent) has a therapeutic property to control *Pitta* and *Kapha*. The computational studies also suggest the *Pitta-Kaphaghna* nature of the *Tinospora cordifolia* (*Giloy*). The Ayurvedic literatures also suggest varying the adjuvants it can cure various degrees of the three somatic humours (*Tridoshas*). The *Withania somnifera* (*Ashwagandha*) is *Madhura* (Sweet), *Tikta* (Bitter) and *Tuvara* (Astringent) in taste with *Laghu* (Light) and *Ushna* (Hot) properties with a *Madhura vipaka* (Sweet) has a therapeutic property to

cure *Vata* related diseases. The computational studies showed it has a *Pitta-Vataghna* nature that indicates the usefulness of this in *Vata* related ailments and its tonic nature. The *Ocimum sanctum* (*Tulsi*) is *Katu* (Pungent) and *Tikta* (Bitter) in taste with *Laghu* (Light), *Ruksha* (Dry), *Theekshna* (Sharp) and *Ushna* (Hot) properties with a *Katu vipaka* (Pungent) has a therapeutic property to cure various *Kapha-Vata* diseases. The computational studies also suggest the *Kaphaghna* nature of the holy herb. The combination of these herbs in the CORONIL tablets in a ratio of 6:5:1 (300mg:250mg:50mg) makes it *Tridoshaghna* in nature with a maximum Drug Efficacy Index [$Q_{(V, P, K)}$] of 1.0 (Table 2).

Table 2: The computed Drug Efficacy Index $Q_{(VPK)}$ of ingredients and CORONIL tablets

| Herb/Tablet | Individual Component of DEI $Q_{(VPK)}$ | | | DEI $Q_{(VPK)}$ | Therapeutic Category |
|---|---|--------------|--------------|-----------------|----------------------------|
| | Vata $q(V)$ | Pitta $q(P)$ | Kapha $q(K)$ | | |
| <i>Tinospora cordifolia</i> (<i>Giloy</i>) (300mg) | 20.41 | -18.37 | -61.22 | 0.59 | <i>Pitta-Kaphagna</i> |
| <i>Withania somnifera</i> (<i>Ashwagandha</i>) (250mg) | -61.36 | -22.73 | 15.91 | 0.68 | <i>Pitta-Vatagna</i> |
| <i>Ocimum sanctum</i> (<i>Tulsi</i>) (50mg) | 20.83 | 16.67 | -62.50 | 0.25 | <i>Kaphagna</i> |
| CORONIL (6:5:1) | -19.35 | -28.57 | -52.08 | 1.00 | <i>Tridoshaghna</i> |

4. CONCLUSION

The Drug Efficacy Indices [$Q_{(V, P, K)}$] of two polyherbal proprietary medicines viz. AYUSH-64 and CORONIL tablets were computed and compared. The AYUSH-64 tablets have therapeutical effect for curing *Pitta-Kapha* related diseases and the CORONIL tablets have therapeutical effect for curing the *Tridosha* related diseases. The symptoms of COVID-19 vary person to person as we observed but with certain similarities. These differences in symptoms can be attributed to the *prakrti* of the infected person and the numerous external factors like different variants of the corona viruses that cause the *vikrti*. The ingredients of both the formulations have many known therapeutic effects that can, not only pacify the causes of various ailments but also improve the immunity and health. Thus, the present computational studies of these two polyherbal formulations suggest that they can be complementary help to improve the conditions and health of the infected when administered. The therapeutic effect of the AYUSH-64 can be considerably improved to a maximum Drug Efficacy Index of approximately 0.50 by altering the compositional ratios of AYUSH-64 but its *Pitta-Kaphagna* nature remains the same. Further the pharmacological activity can be changed to *Tridoshaghna* by altering/including the *Ashwagandha* to the formulation. The study also points the urgent need of the critical editions and translations of the ancient medical texts in a scientific manner without any prejudices. The same was happened in ancient time and we got all those literatures at least in the present form as evident from the introductions of those texts.

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