Review Article

Critical review on *Samyoga Viruddha* (combination incompatibility) with special emphasis on carcinogenic effect of combination of betel quid, areca nut and tobacco

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Abstract

Background: The system of ancient Indian medicine is contributing in the global health since the time immemorial. Fast food and different types of addictions like tobacco etc. are becoming part of new lifestyles. Concept of *Viruddha* (hostility) is one such principle under the umbrella of which many such newly adopted faulty and harmful lifestyle combination could be placed. *Samyoga Viruddha* (combination incompatibility) is the term used to denote unwholesome effects of two or more combined things. Tobacco preparations or other addictions coming under the concept of *Samyoga Viruddha* may not show any hazardous effects initially due to *Vitathatwa* (futility). *Vamana* (therapeutic vomiting), *Virechana* (therapeutic purgation), *Samshamana* (intervention to normalize vitiated body constituents and function), *Samskara* (pharmaceutical processing of a drug) and *Padamshika Krama* (gradual adoption and quitting) are some measures to deal with disorders produced by *Samyoga Viruddha*. **Aims and Objectives:** This article is aimed to elaborate the concept of *Samyoga* and *Samyoga Viruddha* with special emphasis on tobacco as an example. **Materials and Methods:** Data are collected from ancient texts and recent research articles, supported with discussion and presented. **Results:** Article concludes that betel quid, which is a mixture of areca nut, betel leaf, slaked lime and tobacco is a perfect example of *Samyoga Viruddha* and its hazardous effects can be managed with principles of *Viruddha Ahara* (mutually contraindicated food).

Keywords: *Cancer,* hostility, *Samyoga Viruddha* (combination incompatibility), tobacco preparations

Introduction

The system of ancient Indian medicine is contributing well in global health since the time immemorial. In spite of having newer and newer emerging health problems in the current era, Ayurveda is dealing with these problems effectively as it was dealing in *Vaidic* period. Although huge changes have occurred in climatic conditions, newly detected microorganisms, lifestyle, psychological stress and other so many areas of human life, Ayurveda has firmly stood on its basic principles that are constant from at least 5000 years contrary to frequently changing modern medicinal principles. Fast food and different types of addictions like tobacco are becoming part of new lifestyles, which are causes of diseases mentioned in classical texts of Ayurveda. Although these causes are not described by name directly in classics, these should be considered under one of the basic principles mentioned therein. Concept of hostility *(Viruddha)* is one such principle under which so many such new things can be placed. This article deals specially with the concept of *Samyoga Viruddha* and its application in current lifestyle.

Materials and Methods

Data are collected from *Brihattrayi* (*Charaka Samhita, Sushruta Samhita*, *Ashtanga Hridaya* and *Ashtanga Sangraha*), *Laghutrayi* (mainly *Sharangadhara Samhita*) and their main commentaries including *Ayurveda Dipika*, *Nibandha Sangraha*, *Ayurveda Rasayana* and *Sarvangasundara* manually on the basis of memory. *Uhana* (hypothesis) based conceptual study is performed under the protocols of literal research. Recently

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Access this article online

Quick Response Code:

Website: www.ayujournal.org

DOI: 10.4103/ayu.AYU_71_16

How to cite this article: Sirdeshpande MK, Kashikar VA. Critical review on *Samyoga Viruddha* (combination incompatibility) with special emphasis on carcinogenic effect of combination of betel quid, areca nut and tobacco. Ayu 2017;38:97-101.

published research articles have been thoroughly studied and analyzed to present latest information about betel quid and its *Samyoga Viruddhatwa*. These articles are searched and referred from research portals including DHARA, other search engines like Google and available research publications from institute library. Classical terms used here have been thoroughly explained on the basis of methods of understanding the classical Ayurvedic texts in Samskrit.

Ancient concept of hostility

Charaka Samhita, the text of internal medicine described the concept of hostility.[1] Using the terms *Deha Dhatu*, *Pratyanika Bhutani*, *Viruddha* and *Samyoga* which are discussed below.

Explanation of term *Dehadhatu* etc

The word *Dhatu* is formed from the verb *Dha* having meaning to hold. Thus, the substances which are responsible for holding or maintaining human body equilibrium are *Deha Dhatu* (body tissue). Human body is composed of *Dosha, Rasadi Dhatu* and *Mala* (functional materialistic and excretory normal body constituents respectively).[2] Hence, according to classical definition, these are to be considered as *Deha Dhatu*. All types of cells and tissues which are essential to maintain healthy internal environment, that is, equilibrium, namely, white blood cell, red blood cell, platelets, muscle fibers, fat cells, osteocytes, bone marrow cells, sperms, neurons, etc. are included under the term *Deha Dhatu*. Group of tissues, that is, organs are also considered under the term *Deha Dhatu* such as skin, liver, brain and heart. The secretions, hormones, fluids, enzymes, minerals and vitamins could also be considered in this term as bile, GIT secretions, endocrine and exocrine hormones, etc. Thus, *Deha Dhatu* is the comprehensive term used for all materialistic things present physiologically in the human body. Sometimes, some nonmaterialistic things such as mind and sensory organs can also be considered as *Deha Dhatu*. Hence, according to classics, *Deha Dhatu* is the term used for combination of all body structures with sense organs, mind and soul.

The term *Pratyanika-Bhutani* means the things which are opposing body cells or which became hostile toward body cells.

Viruddha is hostility which is again nature to oppose anyone.

Concept of *Viruddha*

According to *Charaka Samhita* any food or medicine which when consumed, if dislodges the *Dosha* from its seat but do not expel them out of the body, is termed as *Viruddha*. *Sushruta* on the other hand opined that for the formation of diseases due to *Viruddha*, not only dislodging of *Dosha* but also the lodging of *Dosha* in *Rasadi Dhatu* is important one.

The drugs hostile to body cells have tendency to oppose the normal body cells. On the other hand, body cells have also tendency to repel the attack provoked by hostile substances. Strong and weak immunity system plays important role in manifestation and nonmanifestation of diseases depending on the result of intaraction held among these two. Although all these mechanisms are famous and familiar to all regarding microinfections; in all cases other than infectious one, some other mechanism acts which is probably non-familiar to researchers of modern field. This article is aimed to cover explanations of such principles in ancient Indian medical science.

Consideration of new extratextual examples

Some references support to the opinion of "considering examples included here in ancient texts only" and "rejecting new examples other than that," as *Dalhana* in his commentary *Nibandha Sangraha* says.[3] In spite of this, examples other than the text have been collected for present review.[1] Hostility occurs sometimes only due to *Prabhava* (majestic efficacy) of particular substances otherwise in spite of having logically calculated oppose between two substances, hostility does not occur.

Concept of *Samyoga*

The word *Samyoga* means a physical, metaphysical and all other types of attachments between two or more things.[4] When anyone eats mixture of two or more food materials, it may be termed as *Samyoga*. *Samyoga* can also take place in two non-materialistic things. Example includes *Divaswapa* (sleeping in daytime) in which, the time factor along with sleep show unwholesome effects and *Kapha Prakopa* (aggravation of *Kapha*) occurs. Sleeping in night does not vitiate *Kapha*. Thus, *Samyoga* of time period in night and action of sleeping does not act in same way as that of day. Contrary to this, *Samyoga* of night time to *Jagarana* (awakening) vitiates *Vata* and *Pitta*. Many a time, *Samyoga* may occur between one materialistic and other nonmaterialistic thing. When we eat any drug in night time, drug will have target organ specificity for diseases of head and neck region, thus such drug acts in above said region.[5] As *Triphala* acts *Chakshushya* (nourishing eyes), when used in night times.[6] Each time *Samyoga* acts differently, that is, positively or negatively depending on properties of two or more things to be attached. But in few cases and at few occassions only, it may act as *Viruddha*.

Definition of *Samyoga Viruddha* by *Chakrapanidatta*

Samyoga Viruddha[7] is the term used to denote hostile effects of combinations only which are irrespective of dose, *Samskara* (processing), etc.[7] In other words, *Samyoga Viruddha* substances do not require any condition like dose or any *Samskara* (processing) to become hostile, only association or combination or union between two or more is necessary.

Many a times, in spite of having just combination among two, some substances have been described as *Guna Viruddha* (property incompatibility), for example, combination of fish and milk has been described as *Guna Viruddha* rather than *Samyoga Viruddha*.[7] This combination does not expect specific dose or *Samskara* to be named as *Viruddha* as like honey and ghee which requires equal dose for becoming hostile.[8]

Chakrapanidatta gives example of *Nikucha* for *Samyoga Viruddha*. However, ripened *Nikucha* is hostile with black gram, soup, jaggery and ghee. Hence, ripening is the condition mentioned by *Charaka* to be named as hostile here.[9] Ripening

can be considered as impact of time factor,[10] so in spite of expecting *Samskara*, it is *Samyoga Viruddha* which is controversial to previous definition of *Chakrapanidatta*.

Charaka provides here example of combination of fruits having sour taste with milk for *Samyoga Viruddha*.[11] Here, only pure union is expected. Milk is substance, which is said to be hostile with sour foods, which is basically attribute or quality. Thus, it can be stated that *Charaka* is also in favor of considering materialistic and nonmaterialistic things in concept of *Samyoga*. Although sour is expected as *Amla Dravya* (sour substances) here, that is, substance having sour taste, we can consider it as only attribute for sake of hypothesis. So that other examples can also be included here and concept will become more comprehensive.

Concept of *Vitatha* (futility)

In some clinical conditions, in spite of consuming *Samyoga Viruddha* drug or food material, there is no manifestation of disease. *Charaka* has mentioned concept of futility[12] for such situations. Tobacco preparations or other addictions coming under the concept of *Samyoga Viruddha* may not show any hazardous effects initially due to this *Vitathatwa*. If these substances became *Satmya* (habitual) to human body or consumed in very small doses or due to good digestive power or in young age or due to unctuousness of body or due to strength of human body or due to exercise, these substances do not show any hazardous effects soon, this is termed as *Vitathatwa*.

Treatment of *Samyoga Viruddha*

Charaka has described common treatment for all 18 types of *Viruddha*.[13] *Vamana* and *Virechana* (vomiting and purgative methods of body purification) are the first line of treatment for all. *Samshamana* (pacification) therapy is the second line of treatment, which is unique for each type of *Viruddha*. *Samshamana* is the therapy that neither provokes nor opposes the *Dosha*, but only pacifies it to its normal level. *Tinospora cordifolia*, that is, *Guduchi* is one of the *Samshamana* drug used for the treatment of *Samyoga Viruddha*.[14] *Samskara* is the third line of treatment which should actually be done as preventive aspect both before and after manifestation of diseases for preventing generation and regeneration, respectively. *Samskara* is processing the human body tissues with the help of daily and seasonal regimens and with *Rasayana* (rejuvenation) therapy and thereby producing immunity against hostile ones. Concept of *Vitatha* is also useful in preventing generation and regeneration of hostility disorders. So using unctuous foods, body massage with medicated oils, that is, *Abhyanga* (oil massage), *Vyayama* (exercise) are some good remedies preventing its generation.

When *Samyoga Viruddha Dravya* become *Satmya* or habitual to human body, it should be treated by the principles of *Padamshika Krama*;[15] a specific order to reduce the dose daily and replacing it with other good diet. It may take a week, fortnight or month even more time to replace *Samyoga Viruddha Dravya* with good one depending on chronicity and severity of hostile drug.[16]

Discussion

Tobacco is a complex plant material in view of chemical composition. No other plant material has been studied more extensively in the history of mankind.[17] Gutkha, a combination of areca nut, slaked lime, paraffin and catechu along with tobacco, is virtually poison as this mixture is a combination of 4000 chemicals of which at least 40 are carcinogenic compounds.[18] It can cause non-healing ulcerative lesions in parts of the oral cavity such as cheek, lips, tongue, hard palate, floor of the mouth and soft palate. It can also affect the esophagus, larynx and kidney.[18] People commonly develop noncancerous conditions such as bronchial asthma, hypertension, heart disease and stroke. While narrowing of the blood vessels can cause gangrene, stoppage of blood supply in extreme cases can cause stroke. In women, consumption of gutkha during pregnancy can result in low birth weight babies.[18] Thus, it produces almost all disorders mentioned by *Charaka* while enlisting hazardous effects of *Viruddha Ahara*.

Viruddhaahara taken regularly could induce inflammation at a molecular level, disturbing the eicosanoid pathway creating more arachidonic acid leading to increased prostaglandin-2 and thromboxane.[19] *Samyoga Viruddha* nature of mixture of tobacco with others is probably due to effect of combination pharmacologically active molecules present in it. Combination of polyphenols (responsible for astringent taste of nut) and free calcium hydroxide, iron and magnesium (from slaked lime) with catechu-tannic acid and acacatechin (from catechu) may be responsible for such hostile nature.[20] Such hostile effect is not observed in these constituents in such hazardous way when consumed separately. Many published researches could be produced for supporting this. 57,518 textile industry workers in Ahmedabad, India, were examined in the first phase of a study conducted in 1967–1971. Bhargava *et al.* (1975) reexamined 43,654 workers among 57,518 two years later. They diagnosed 13 new cases of oral cancer, all of which had developed among individuals chewing betel quid with tobacco and/or smoking tobacco.[21] Ahluwalia and Duguid (1966) reported on the distribution of cancers in different ethnic groups of the Malay Peninsula (Malays, Chinese and Indians), using records from the Kualalumpur Institute for Medical Research. Records of cancers developed due to betel quid and areca nut chewing with and without tobacco were analyzed. Among 912 cancers of all sites in Indians who are known to chew betel quid with tobacco, 306 (33.6%) were oral cancers. Among 776 cancers of all sites in Malays who are known to chew betel quid without tobacco, 74 (9.5%) had oral cancer.[22] Hence, combination of constituents of betel quid even without tobacco showed here effects as like as *Samyoga Viruddha*.

Many a times, *Vitathatva* plays a role in nullifying effects of *Samyoga Viruddha* as observed in this case where a case–control study conducted in 1986–1992 on 247 cases of oropharyngeal cancer (all men) registered in the population-based Bhopal Cancer Registry and 260 population controls showed a nonsignificant risk for oropharyngeal cancer associated with

chewing betel quid with tobacco. Those who chewed >10 quid with tobacco per day (odds ratio, 3.6; 95% confidence interval [CI], 1.7–7.4) and those who had chewed quid with tobacco for >30 years (odds ratio, 3.1; 95% CI, 1.6-5.7) had statistically significant risks (*Dikshit* and *Kanhere*, 2000). Hence, *Samyoga Viruddha* does not show its hazardous effect when either consumed in less quantity or consumed for less duration.[23]

Samyoga Viruddha shows organ-specific response as in case–control study on 163 male lung cancer registered at population-based Bhopal cancer registry and 260 population controls showed no association between chewing betel quid with tobacco and lung cancer. Hence, oral cavity is more prone to form cancer than other organs.[23]

Many a times, dose and duration of intake also play important role in generating effect of *Samyoga Viruddha*. A case–control study of 205 cases of invasive cervical cancer and 213 age-matched hospital controls was conducted in Chennai, India, in 1998–1999. A twofold non-significantly elevated risk was noted for chewing betel quid with and without tobacco. However, a statistically significant association was seen among those who chewed more than five quid with or without tobacco per day and the dose–response relationship was also significant ($P = 0.02$).[24]

The monograph by IRAC, from which above researches were quoted concludes that there is sufficient evidence in humans for the carcinogenicity of betel quid with tobacco. There is limited evidence in experimental animals for the carcinogenicity of arecoline found in areca nut. There is inadequate evidence in experimental animals for the carcinogenicity of arecaidine. There is evidence suggesting lack of carcinogenicity in experimental animals for betel leaf. There is evidence suggesting lack of carcinogenicity in experimental animals for slaked lime. Thus, neither areca nut alone, nor betel leaf alone, nor slaked lime alone is capable of producing carcinogenic effect which has been observed from combination of betel leaf, catechu and lime and more hazardous effects were observed from addition of tobacco with them.[25]

Mode of action of *Samyoga, Viruddha, Samyoga-Viruddha* and *Vitathatwa*

According to philosophical view, *Karma* (activity) expects *Samyoga* (combination) and *Vibhaga* (despaired) and not the *Guna* (characteristics)for producing effect.[26] Due to conjunction and disjunction of *Dravya*, effects of *Karma* obviously get changed. Based on the theory of *Karma-Viryavada* of *Nagarjuna*, it can be stated that the active principle of drug, which is responsible for action, may get affected due to combination of different drugs, in which molecular interactions may be take place.[27] Hence, as some natural combination of *Mahabhuta* behaves like *Vichitra Pratyayarabdha* (formed out of differently arranged molecular pattern) *Dravya*, in the same manner artificial combination may also behave likewise.[28] Here, combination of betel leaf, catechu, lime, nut and tobacco behaves like *Vichitra Pratyayarabdha Dravya* combination. According to *Charaka*, effect of *Dravya* having more than one *Rasa* (taste) in it could not be imagined if that drug or combination of drug is having *Vikṛiti Vishama Samavaya* arrangement of its constituents.[29] Therefore, combination of some drugs only could act as hostile and not that of all, depending on nature of its constituents either *Prakṛiti Sama Samaveta* or *Vikṛiti Vishama Samaveta*. By observing cancer-producing effects of combination of betel quid on oral cavity, *Vikṛiti Vishama* of this combination could easily be imagined.

Doctrine of *Samanya* (similarity) states that it could be the cause of increment only when there is not having any opposing factor.[30] *Snigdhatwa* (unctuous), *Bala* (body strength), *Satmyatwa* (congenial), having good digestive power and youth are some opposing factors due to which *Samyoga Viruddha* could not show its hazardous effects. When these factors lose their potential due to age, increased dose of consumption or chronicity, at that age or state, *Samyoga Viruddha* definitely shows its own potential. Hence, in spite of having visible functional similarity in betel quid and increment in mouth lesions, due to opposition of *Vitathatwa*, this combination shows null effect on some individuals and full effect on others. In the same way exercise, external oil massage, specific process of food preparation and rejuvenation etc. oppose the functions of *Samyoga Viruddha* and *Samanyatwva* could not be resulted in increment of mouth ulcers.

Conclusion

Some tobacco preparations when utilized in combination with others produce more hazardous effects than the effects observed when utilized alone. Such disorders could be managed with the help of concept of combination incompatibility. Concept of *Samskara* (specific process of food preparation) for prevention, may be used in terms of *Shodhana* (body purification therapy) and *Shamana* (palliation therapy/conservative managment') for treatment, concept of *Padamshika Krama* (gradual adoption and quitting) to avoid withdrawal effects and *Rasayana* for disease prevention could be effectively used to manage hazardous effects. Thus, with the help of eternal concepts of Ayurveda, it is possible to deal with newly emerging health problems.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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