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A Comparative Pharmaco-Clinical Study of *Arjuna* and *Manjishtha* w.s.r. to *Vyanga*

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ABSTRACT

In Ayurveda *Vyanga* is a disease which is firstly described by *Acharya Sushruta* under *Kshudra Roga*. According to *Acharya Sushruta* *Krodha* and *Shoka* are responsible for development of *Vyanga*, as these psychological factors vitiate *Pitta* and *Vata Dosha* which then travel and get localized on facial skin and leads to development of *Nirujam*, *Tanu Shyava Varna Mandala*. Ayurveda is very effective in treating skin disorders and skin is also mentioned as a route of drug administration in terms of *Bahiparimarajan Chikitsa*. *Acharya Sharangdhara* has mentioned various *Lepa* formulations for various skin diseases; among them he has quoted *Arjuna Twak Churna* and *Manjishtha Churna* for treatment of *Vyanga*. It is easy to understand about *Manjishtha* because it is a very well known established *Varnya* drug, but regarding *Arjuna* it was very much important to trail it clinically as it is an established drug for heart. From *Dravyaguna* point of view it was very important to study *Arjuna*, that how it would have broken the pathogenesis of *Vyanga*, what are the major chemicals present in *Arjuna* that work on hyper pigmentation. So a proper revalidation of *Shastrokta* quote of *Acharya Sharangdhara* was done by clinical trial and pharmacognostical and HPTLC analysis of *Arjuna* and *Manjishtha*.

Key words: *Arjuna, Manjishtha, Vyanga, Lepa.*

INTRODUCTION

Ayurveda is an ancient science which is providing its services since ancient times. Ayurveda does not have only curative properties but also focus on maintaining constitutional balance of body. According to Ayurveda, health is defined as a balance of *Tridosha, Saptadhatu* and *Trimalas,* impairment of which results in unhealthy state. Most of the times and in so many diseases these unhealthy states are reflected on skin.

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In today's lifestyle there are so many lacunas like no proper *Dinacharya*, not having time for proper meal etc. people are so busy in their modern lifestyle and work that they don't have a time to take care of their skin and health. We all are moving far away from nature because of urbanization due to which ratio of all the diseases are increasing rapidly. Skin diseases are prime among them because it compel persons to lead a miserable life due to stress caused by ugly external appearance. It gives a lot of psychological disturbances. Smooth and glowing complexion of the face increases the beauty of a person and also gives self-confidence. In Ayurveda, *Acharya Sushruta* was first to explain about disease called *Vyanga* under *Kshudra Roga.*[1] *Vyanga* is a disease which directly affects the beauty face which is mainly caused by mental stress conditions.[2] *Acharya Vagbhata* has explained that because of *Krodha, Shoka, Ayasa, Vata* and *Pitta Dosha* gets vitiated and takes *Sthansamshraya* at *Mukhgata Twacha* and cause *Dushti* of *Bhrajak Pitta* due to which painless, thin,

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Shyava Varna Mandalas get develop along with symptoms of *Daha* and *Kandu.*[4] Though it is not a serious systemic disease but has great importance in society. *Vyanga* is not painful for body but is very much painful for mind; therefore treating *Vyanga* has become a major problem. *Lepa* was selected for management of *Vyanga* to make treatment simple, effective and convenient to patients. According to classics various *Lepa* are advised in various facial problems. So, on the basis of reference given by *Acharya Sharangdhara,*[3] *Arjunatwak Churna* and *Manjishtha Churna* were selected to provide effective and safe medicine to society.

Aims and Objectives

1. To evaluate the efficacy of *Arjuna Twak* on *Vyanga* in comparison to *Manjishtha.*
2. To observe the Pharmacognostic, Phytochemical and Pharmacological study of *Arjuna Twak* and *Manjishtha*.
3. To find out the safe, effective, low-cost, easily available drug for the patient suffering from *Vyanga.*

Materials and Methods

Patients: For the clinical study patients of *Vyanga* were taken randomly from the OPD section of Kayachikitsa Department of Pt. Khushilal Sharma Govt. (Autonomous) Ayurveda College and Institute, Bhopal (M.P).

Drugs: The raw drug *Arjuna* and *Manjishtha* was obtained from the Pharmacy of Pt. Khushilal Sharma Govt. (Autonomous) Ayurveda College and prepared at Rasashastra Department of College.

Pharmacognostical Study

The *Terminalia Arjuna* bark and *Rubia cordifoila* stem and their powder had been used for macroscopic and microscopic study. This was evaluated and photographed by leica DM 3000 Microscopic in 10X, 20X, 40X with the help of Vindhya Herbal Testing and Research Laboratory, Van Parisar, Barkheda Pathani, Bhopal, (M.P.) India.

Analysis Results

Organoleptic Characters

SN	Test parameters	Results of *Arjuna*	Results of *Manjishtha*
1.	Condition	Dried	Dried
2.	Colour	Pale, externally flesh coloured	Brown to purple
3.	Odour	Indistinct	Characteristic
4.	Taste	Bitter	Indistinct

Figure 1: **T.S. section of Arjuna bark**

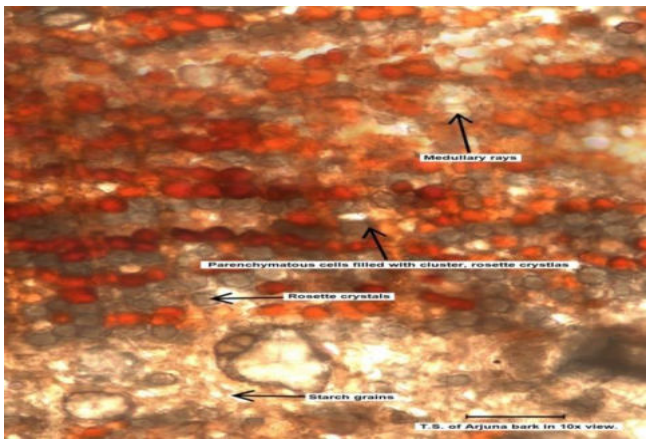
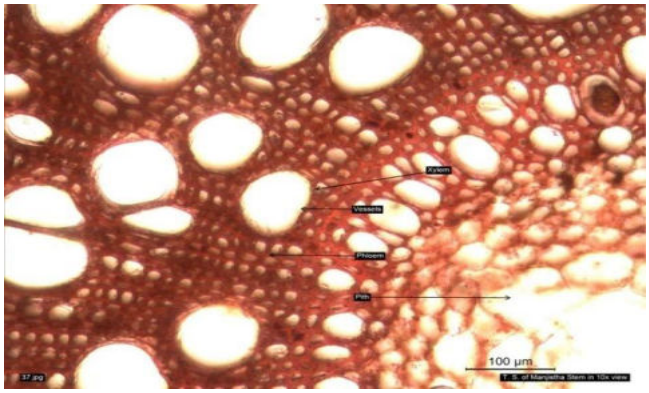


Figure 2: **T.S. section of *Manjishtha* stem**



Phytochemical Analysis

The analytical study of *Arjuna* bark and *Manjishtha* was undertaken to analyze the sample by using

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different physiochemical parameters and HPTLC profile.

Parameters	Result Arjuna	API standards	Result *Manjishtha*	API standards
Foreign matter	Nil	Not more than 2%	Nil	Not more than 2%
Loss on drying	4.65%	Not more than 12%	5.97%	-
Total ash	21.54 %	Not more than 25%	8.23%	Not more than 12%
Acid insoluble ash	0.72%	Not more than 1%	0.28%	Not more than 0.5%
Alcohol soluble extractive	22.75 %	Not less than 20%	4.43%	Not less than 3%
Water soluble extractive	21.06 %	Not less than 20%	30.03%	Not less than 17%

Figure 3: Rf value spots of *Arjuna*

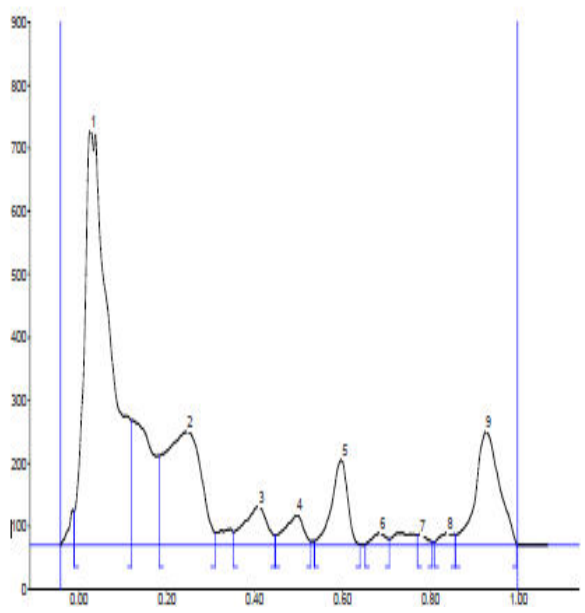
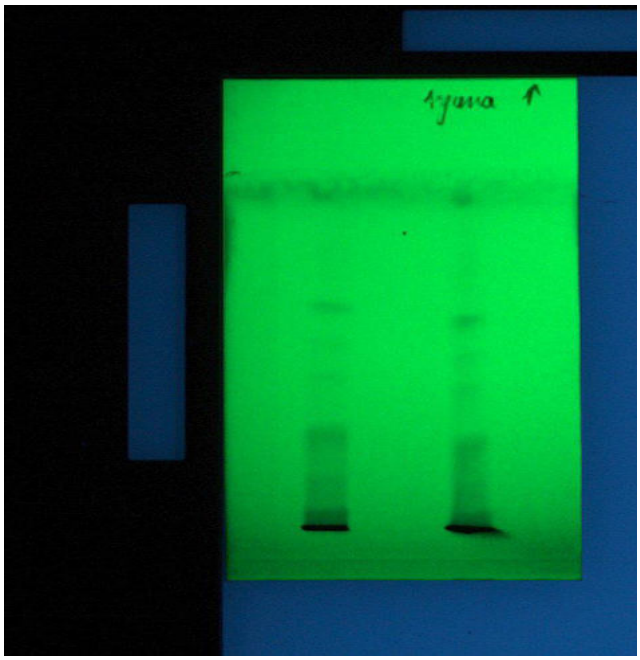


Figure 4: HTLC plate of *Arjuna*



Study design

The study was conducted on total 60 patients and all patients completed their treatment. It was a randomized control trial study of *Arjuna* in compared to *Manjishtha* on *Vyanga*. A complete proforma included all history taking points, criteria and investigations and written consent was taken from all the patients before trail.

Administration of drug with duration

SN	Title	Group A	Group B
1.	Name of Drug	*Arjuna Twak Churna*	*Manjishtha Churna*
2.	Applicable mode	*Lepa*	*Lepa*
3.	Base	*Navneeta*	*Navneeta*
4.	Application time	*Pratahkala* and *Sanyahkala* for 15-20 min.	*Pratahkala* and *Sanyahkala* for 15-20 min.
5.	Duration	8 weeks	8 weeks
6.	Follow-up	15 days	15 days

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Intercession

- All the patients were assessed before and after clinical trial.
- Written consent was taken from every patient.
- All the details regarding study was explained to every patient and was set free during the study.

Diagnostic criteria

Patients characterized with *Niruja* (painless), *Shyava* (bluish black), *Tanu Mandalas* (macules) on the face, Skin appearing rough with bluish black patches / spots, If edges are coppery red or white, Itching, Burning sensation with tingling.

Inclusive criteria

Patients fulfilling the diagnostic criteria, between the age group 16 and 60 years, irrespective of sex, religion, occupation, and chronicity were selected for the study.

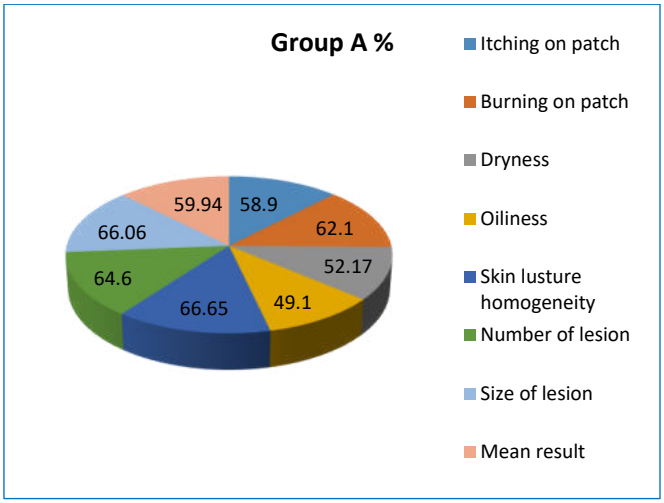
Exclusion criteria

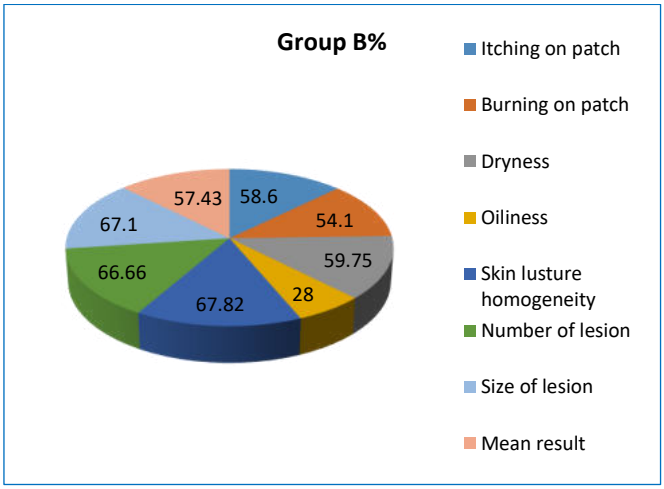
Hyperpigmentation caused due to any systemic diseases such as;

- Addison's disease,
- Cushing syndrome and
- Systemic lupus erythematosus,
- Hyperpigmentation since birth like nevus and
- Those caused by tumors such as malignant melanoma

Effect of Therapy on Cardinal Symptoms

Symptom	Group A %	Group B %
Itching on patch	58.9	58.6
Burning on patch	62.1	54.1
Dryness	52.17	59.75
Oiliness	49.1	28
Skin lusture homogeneity	66.65	67.82
Number of lesion	64.6	66.66
Size of lesion	66.06	67.10
Mean result	59.94	57.43





DISCUSSION ON EFFECT OF THERAPY

Itching: Itching is caused by vitiated *Kapha* and *Arjuna* and *Manjishtha* both possess *Kashaya Rasa* and *Ruksha Guna,* by which they subsides the vitiated *Dosha* and relief in symptom is obtained.

Burning: *Vyanga* is *Pitta Pradhan Vyadhi* and burning is a main symptom of vitiated *Pitta*. *Arjuna* possesses *Sheeta Veerya* by which it could have subsided effect of vitiated *Dosha* whereas *Manjishtha* possess *Madhura, Tikta, Kashaya Rasa* which all are *Pitta Shamaka*. According to *Acharya Sushruta Veerya* is *Pradhan* than *Rasa* therefore it can be understood on

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this basis that *Arjuna* is more effective than *Manjishtha* on this symptom.

Dryness: Dryness in *Vyanga* is caused by vitiated *Vata*. *Manjishtha* shows better results in dryness as it possess *Guru Guna, Madhura Rasa* and *Ushna Veerya*. All these inherent properties subsides vitiated *Vata.*

Oiliness: Oiliness is caused by vitiated *Kapha* and *Arjuna* possesses *Kashaya Rasa* which prominently controls oil, whereas *Manjishtha* is also *Kashaya* in *Rasa*.

Skin lusture (*Shyava Varna*): *Shyava Varna* occurs because of *Dushti* of *Bhrajak Pitta* caused by vitiated *Vata*. *Sheet Veerya* of *Arjuna* and *Guru Guna* of *Manjishtha* pacify vitiated *Dosha* and corrects *Vaivarnyata*.

Number and size of lesion: In both parameters *Arjuna* shows improvement with mean percentage of 65.33 and *Manjishtha* shows improvement with mean percentage of 66.88.

During study it was observed that results of *Manjishtha* were markedly visible within a week after trail started, whereas *Arjuna* took near about 20-25 days to make results visible. The whole study was of 8 weeks and in patients of *Manjishtha* group after completing a month, results started getting stagnate but a continuous progressive results were seen in patients of *Arjuna* group.

Probable mechanism of *Lepa*

As *Vyanga* is *Pitta Pradhana Vyadhi*, so the amount of *Sneha* i.e. base was 1/6th part of *Churna* and thickness advised to apply was of ½ *Anguli* (as described by *Acharya Sharangdhara* of *Varnya Lepa*).

Application of *Lepa* should be done opposite hair follicles due to which active principle of *Lepa* gets absorbs through hair follicle and absorption forwards through sweat vessles and capillaries and works on affected area.

Mode of action of drug on hyperpigmentation from modern point of view

Before understanding the mode of action of drug it is important to know, concept of pigmentation, mechanism of drug action, potential of plant phenolics in hyper pigmentation.

1. **Concept of pigmentation:** The primary determinant of variability in human skin colour is the density, amount as well as the distribution of melanin pigment secreted by melanocytes cells in the basal layer of the epidermis by a process known as melanogenesis.[5]

There are two types of melanin that determine skin tone viz.

- Eumelanin
- Phaeomelanin

Individuals with darker skin tone have mostly eumelanin as compared to pheomelanin and vice-versa.[6] Various physiological processes determine pigmentation in human body, few of which are controlled genetically.

Function of skin lightening agents - Skin lightening agents interfere in the,[7]

- Melanogenesis pathway or, Melanin transfer or, Desquamation of lowering pigmentation on the surface of skin, which, generally acts by any of the ways such as,[8]
- Tyrosinase inhibition,
- Mitf (micropthalmia - associated transcription factor) inhibition,
- Down regulation of MC1R (melanocortin receptor1 which is Gs- protein- coupled- receptor) activity,
- Interference with melanosome maturation and transfer and melanocyte loss.

2. **Mechanism of drug action[9]:** Drugs (except those gene based) do not impart new functions to any system, organ or cell; they only alter the pace of ongoing activity. The basic types of drug action can be broadly classed as:

Stimulation, Depression, Irritation, Replacement, Cytotoxic action

Majority of drugs produce their effects by interacting with discrete target biomolecule, which usually is a protein. Such mechanism confers selectivity of action

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to drug. Functional proteins that are targets of drug action can be grouped into four major categories, viz. Enzymes, Ion channels, Transporters, Receptors

- **Enzymes:** Enzymes are very important target of drug action. Drugs can either increase or decrease the rate of enzymatically medicated reactions.
- **Enzyme inhibition[10]:** Some chemicals (heavy metal salts, strong acids and alkalies, formaldehyde, phenol etc.) denature proteins and inhibit all enzymes non selectively. They have limited medicinal value restricted to external application only. However, selective inhibition of a particular enzyme is a common mode of drug action.

Hence by this we can understand that the drug of this study has worked on mechanism of enzyme inhibition as tyrosinase also known as polyphenol oxidase is a copper containing enzyme present in melanocytes that catalyzes two major reactions during melanogenesis, including hydroxylation of tyrosine and oxidation of the o- diphenyl product, L-DOPA which produces a highly reactive intermediate that is further oxidized to form melanin by free-radical-coupling pathway.

3. Potential of chemicals of *Arjuna* in hyperpgmentation

Aqueous extract of T. Arjuna bark was analysed for its composition and molecular weight distribution by dialysis. Compositional analysis revealed that it has 44% polyphenols and dialysis study showed that 70% of polyphenols have molecular weight greater that 3.5kDa. HPTLC confirmed that it contains flavon-3-ols such as (+)- catechin, (+)- gallocatechin and (-)-epigallocatechin.

Phenolic acids such as gallic acid, ellagic acid and its derivatives are also found in T. Arjuna extract. Triterpine glucosides are arjunetin, arjunoglucoside 1, arjunoglucoside 2, arjunoglucoside 3, arjunocide 1 and 2. Polyphenols are arjunin, arjunone and arjunotone.

- **Gallic acid -** A research study was carried out on action of gallic acid on tyrosinase inhibition. In this study the effect of Gallic acid on mushroom tyrosinase, tyrosinase inhibitory activity and melanin content were assessed in B16 melanoma cells. results indicated that gallic acid exerts antimelanogenic activity coupled with antioxidant properties by suppressing RS (reactive species) generation.[11]
- **Ellagic acid -** A research study conducted on ellagic acid on hyperpigmentation caused by UV rays. In this study conclusion was that, Ellagic acid is oxidized by tyrosinase, producing reactive o-quinones. Furthermore, ellagic acid which is a powerful antioxidant, chemically reduce the o-quinones (o- dopaquinone) and semiquinones, in this way inhibiting the melanogenesis.[12]
- **Tannin -** A research study was carried out on tannin as tyrosinase inhibitor in which results indicated that tannins were potent tyrosinase inhibitors. Results indicated that tannins were reversible and mixed type inhibitors. Fluroscence quenching, copper interacting, and molecular docking techniques were used to unravel the molecular mechanism of inhibition. The results showed that the hydroxyl group on the B ring of tannin could chelate the dicopper ions of the enzyme.[13]
- **Catechins -** A research was carried out on depigmenting effect of catechins. In this study (-) epigallocatechin-3-gallate (EGCG), (-) - epigallocatechin (EGC), (-) catechin (c), and gallic acid (GA) were used. The catechin group inhibited melanin synthesis in B16 melanoma cells. To elucidate the anti-melanogenic mechanism of catechin group, western blotting analysis was adopted for crucial melanogenesis protein name tyrosinase. The result indicated that catechin group has anti-melanogenic activity and might be effective in hyperpigmentation disorders.[14]

Mode of action of *Manjishtha* - Chemically, it contains glucoside known as manjishthin and pupurine, along with resins, lime salts and colouring agent which directly acts on melanin pigment.[15] Methanolic extract of this herb has been reported to

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show 14.80% mean inhibition of tyrosinase activity thereby acting as a skin whitening agent.[16]

Conclusion

Vayanga is a disease which is defined firstly by *Acharya Sushruta* under *Kshudra Roga* and in today's context it can be correlated with melasma on the basis of pattern of hyperpigmentation and other sign and symptoms. The trial drug *Arjuna* is widely accepted as a herbal hero of heart and its effectiveness in *Vyanga* has proved its versatility. *Vyanga* is a disease which is mainly caused by pshycological factors *Krodha, Shoka, Ayasa* and other etiological factors like *Pitta Pradhan Ahara Vihara* and in modern context mealsma is caused by hormonal changes and sun exposure. Because of stress neurons in hypothalamus secretes corticotrophin release hormone which is transported to pituitary glands where it binds with CRH1 receptor (receptor of melanocytes), which stimulates the function of melanocyte cells and increase melanin formation. In Ayurveda *Lepa* is advised to apply opposite hair follicles, the reason behind this may be that it allows the active principle of medicine to absorb through follicles and move forwards through capillaries and sweat vessels and works on affected area. In modern also the medicines of local application works on mechanism of enzyme inhibition and tyrosinase which is released from melanocyte cells and is responsible for melanin formation is also a copper containing enzyme. *Arjuna* inherits *Kashaya Rasa* and *Sheeta Veerya* by which it subsides all the symptoms of *Vyanga* i.e. *Daha, Kandu, Shyava Varna*. Gallic acid, tannins, catechin group inhibits tyrosinase activity by which excess formation of melanin gets control and reduction in hyperpigmenation is seen. Ellagic acid works on reactive agents i.e. quinines and reduce the formation of melanin. Whereas the colouring agents and main chemical of *Manjishtha* i.e. manjishthin and purpurin works directly on melanin pigment. Therefore its results are quickly visible but are stagnate after a fixed period of time, but *Arjuna* works on root of chain of melanin formation therefore visibility of results are quite slow but is very effective and progressive. And it can be used for long term. In result of subjective parameters group A showed relief of 57.78% wheras group B showed relief of 53.65%. In results of objective parameter group A showed relief of 65.33% and group B showed relief of 66.88% whereas in overall assessment the relief percentage of group A was 59.94% and in group B it was of 57.43%. Majority of the patients showed moderate results. As in this study single drug therapy in form of local application was used and results are moderate so there is a possibility that if along with this local application proper line of treatment with oral medication will be followed than better results could come out. In form of *Arjuna Twak* we have found a very effective easily available and low cost drug for *Vyanga*. Though *Vyanga* is not a serious systemic disease but possess equal importance because of its psychological effect on life. We accept it or not but somehow external beauty possess a great importance in everyone's life. So *Arjuna* could be a drug of choice for treating *Vyanga*.

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