Research article (Award paper)

A clinical study of sickle cell anemia and its management through *Kiratatikta* (*Swertia chirayata*) *Ghanvati* and *Guduchi* (*Tinospora Cordifolia*) *Ghanvati*

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ABSTRACT

Introduction and Aim: Sickle cell anemia (SCA) is a genetic condition of mutation of beta globin chain and has been acknowledged to have a global public health impact. This disease is very common among many tribal and backward populations in India. In the central part of India its prevalence varies from 10-40% and in western area of Odisha varying from 10-17%. It can be classified as two types of homozygous sickle cell disease and heterozygous sickle cell trait. In Classical Ayurveda texts word to word correlation with SCA is not found. Clinical features of SCA correspond and are in line with *Sannipataja Pandu Roga* as described in classical texts. In the present work, a scientific effort was made for management of sickle cell disease through Ayurvedic interventions.

Materials and Methods: A prospective clinical study was carried out in a total of thirty (30) patients of both sexes and randomly registered according to the clinical features of SCA from OPD and IPD of Government Ayurvedic College hospital, Bilaspur, Chhattisgarh. After assessment of subjective and objective criteria *Kiratatikta Ghanvati* and *Guduchi Ghanvati* were given 500 mg. each drug after meal with suitable fluid twice a day for a period of two months. Efficacy of therapy was inferred in 15 days interval and evaluated statistically by student's paired 't' test.

Results: The overall improvement was assessed after study. The mean score before treatment was 3.53 while the mean score after treatment was 1.52. The statistical evaluation revealed that the mean difference was ± 2.01, SD±0.85, SE± 0.22 and t value 8.803. Trial medications were statistically highly significant with $p<0.001$.

Conclusion: From the present study, it can be concluded that the trial drugs are very effective in the management of SCA; they reduce the subjective and objective parameters and its complications.

Keywords: Sickle cell anemia; *Kiratatikta Ghanvati*; *Guduchi Ghanvati*; *Sannipataja Pandu roga*.

INTRODUCTION

Human red blood cells (RBCs) have a round, biconcave shape, with the center's diameter being smaller than the outermost portion. Sickle Cell Anaemia (SCA) or sickle cell diseases are pathological situations in which circular RBCs transform into sickles as a result of faulty beta chain production in adult haemoglobin (SCD; 1). In 1910, James Herrick was the first to describe the distinctive sickle-shaped red blood cells as a Grenadan medical student. In 1949, Linus Pauling and his associates discovered that sickle haemoglobin (HbS) had a changed electrophoretic mobility, and they were the ones who initially identified it as a molecular disorder. In 1957, Vernon Ingram found that the sickle haemoglobin molecule was caused by a single amino acid change (2,3). SCA is the most severe form of anemia. This disease is confined to negroes and is also inherited as a Mendelian dominant (4). It is the most common inherited hemoglobinopathy among the black population worldwide. Data from World Health Organization and United Nations Organisation over 300,000 babies are born worldwide annually with the homozygous type, mostly in poor and progressive countries (5).

The majority of the world's tribal people reside in India. The tribal population in India makes up 8.6% of the country's overall population, or 67.8 million people, as per the 2011 Census (6). Over 83 percent of the scheduled tribe (ST) population in India lives in rural regions, with the states of Madhya Pradesh, Maharashtra, Orissa, Gujarat, Rajasthan, Jharkhand, Chhattisgarh, Andhra Pradesh, West Bengal, and Karnataka accounting for the majority. There are 461 ST communities among them, and they each have their own own cultural practises, linguistic traditions, and social structures (7). The whole subcontinent had a period of intense intermarriage several thousand years ago, which completely rearranged the genetic makeup of its population and left unmistakable remnants in the genomes of even the most remote tribes of today (8).

In 1952, indigenous tribes in the south Indian Nilgiri Hills were the first to be identified as having sickle haemoglobin in India (9). The same year, migrant labourers from tribal communities in Bihar and Odisha who worked in Upper Assam's tea gardens were revealed to have sickle haemoglobin, according to Dunlop and Mazumder (10). Since then, a large number of demographic groups have undergone

screening, and it has been shown that three socioeconomically disadvantaged ethnic groups—the scheduled tribes, scheduled castes, and other backward classes in India—are more susceptible to the sickle cell gene (11).

Morbidity and mortality of SCA has awakened a whole lot of studies for its symptomatic relief and cure. With the assistance of the most recent developments in molecular biology and genetics, modern clinical technology has started working on finding a treatment for this illness and understanding the causal genes, etc. All of these technologies are, however, still in the experimental stages right now. Therefore, until they are accessible, approachable, and affordable, reality will continue to revolve around the basic necessities of anaemia, body aches (Pain & Crisis), repeated infections, recurrent blood transfusions, recurrent jaundice, and avascular necrosis for bones. As a result, it is important to accept and effectively manage or prevent the disease's complications (12).

After keeping all these views in mind, and economical therapy and great hopes are being laid on the Ayurvedic science, which will help to prevent its complications and hazardous outcomes and function as an additional therapy in the management of SCA. Owing to Ayurveda, it's far the technological know-how that imparts all the expertise involved to existence. The essential intention being to provide hints for protection and merchandising of fitness together with prevention and remedy for this molecular disease. In different phrases Ayurveda is a technological know-how which enables in information innovative and non-innovative components of existence, happy and troubled life, useful and non-usable for life, life span, and physical dimensions.

Due to the limited number of interpretations of the disease and its problems that are available in traditional texts, current medical research has upgraded SCA to a group of disorders rather than a single sickness, which is explained as "Anukta Vyadhi" in Ayurveda. The goal of this decade's research in the field of ayurveda is to thoroughly comprehend illness and its pathological expression by meticulous study of its clinical presentation (13).

In accordance with a passage from our hidden treasure, all pathological conditions cannot be categorically named, but they can be deduced from Tridosha Vaishamya, Dhatu Dushti, etc., in the case of Sannipataja Pandu roga, Kustha, Kshudra kushtha, and Prameha because every disease is brought on by three Sharirika Doshas and two Manasika Doshas. According to Ayurveda, the diagnostic methods are based on Roga Prakriti, Adhisthana, and Samutthana (14-16).

The three doshas—*Vata, Pitta,* and *Kapha*—are the foundation of Ayurveda. Although in SCA, Ranjaka Pitta is primarily important for the development of its disease and Rakta dhatu formation is faulty (17). Therefore *Guduchi (Tinosphora Cardifolia*) and *Kiratatikta (Swertia Chirayata*) are used to treat in *Pandu Roga* and they are beneficial to reducing the symptoms in the management of SCA (18).

If two pathologies are merged, with the wellness of mankind as the first consideration, and without creating much doubt regarding the objectivity of science, a viable and effective national programme may be established for the control of SCA. The goal of the current study is to evaluate the effectiveness of the SCA treatment modalities "Kiratatikta Ghanvati (KGV) and Guduchi Ghanvati (GGV)". Due to the drug's rasayana, antiviral, antibacterial, analgesic, antispasmodic, immunomodulator, antioxidant, and hepato-spleno protecting qualities, these features have been taken into consideration (19). The major goal of this study is to use Ayurveda remedies to improve life quality, lessen problems associated with SCA, and delay the onset of more severe consequences.

MATERIALS AND METHODS

CTRI Registration Number: CTRI/2022/01/039669, Registered on: 21/01/2022
IEC Number: IEC, GAC&H Letter No.290, dated-29/2/2021.

Selection of patients

Patients were chosen from the OP and IPD of the Government Ayurveda College and Hospital in Bilaspur, Chhattisgarh, and the Department of Rognidan evam Vikriti Vigyana at the Government Ayurvedic College and Hospital in Balangir, Odisha. For randomised clinical studies, thirty people were chosen, regardless of caste, creed, language, or sexual orientation.

Criteria for selection of patients

(I) Patients were selected on the basis of sign and symptoms of SCA

a. Anemia
b. Jaundice
c. Abdominal colic
d. Palpitation
e. Hand foot syndrome
f. Loss of appetite
g. Sternal pain
h. Fever
i. Hepatomegaly
j. Splenomegaly
k. Body ache (Pain & Crisis)
l. Repeated infection
m. Blood transfusion
n. Femoral head necrosis (Pain in hip region)

(II) **Diagnostic Signs**

a. Pallor
b. Anasarca
c. Hepatomegaly
d. Splenomegaly
e. Hand foot syndrome

As per the above diagnostic criteria patients' examination proforma were prepared and patients were selected for the clinical trial.

Exclusion criteria

a. Symptoms other than sickle cell anemia were excluded from the clinical trial.
b. The patients aged below 5 years and above 50 years.
c. Pregnancy and lactations.
d. Severe illnesses like tuberculosis, cancer, cirrhosis of liver, aplastic anemia etc., also were excluded.

Dose of *Guduchi Ghanvati* and *Kiratatikta Ghanvati*

For two months, administer a child with 250 mg and an adult with 500 mg twice day with the appropriate fluids. For both experimental medicines, the dosage was the same.

Pathya-Apathya

Patients were instructed to drink as much water as possible along with their regular available diet.

Assessment criteria

The effects were demonstrated by a favourable change in the severity scores for each symptom from 1 to 5, which were determined using the Dutch-AIMS2 - HFF, symptoms severity scale technique, from 2006. (20).

Table1: Incidence of severity of grade points among the trial patients

Degree of Severity	Grade	Grade points
Very Severe	G5	5
Severe	G4	4
Moderate	G3	3
Mild	G2	2
No Sign and symptoms	G1	1

Statistical analysis

The total effect of KGV and GGV was evaluated on subjective criteria before and after treatment of study protocol as per Statistical method. (Table No.02) Comparisons were made between the Mean and Standard Deviation of each symptom and sign before and after therapy. By using the P-value from the student's paired t-test, the efficacy of the trial medication was evaluated.

Table 2: The effect of *Kiratatikta Ghanvati* and *Guduchi Ghanvati* on subjective parameters (n=30)

S. No.	Sign & Symptoms	Total No. of patients	Before Treatment Mean	After Treatment Mean	Mean Dif	% of Relief	Standard Deviation (S.D.)	Standard Error (S.E)	T-value (Paired test	P value
1.	Anemia	30	4.20	1.20	3.00	67.22	0.694	0.126	23.64	<0.001*
2.	Jaundice	30	4.23	1.40	2.83	33.09	0.698	0.127	22.20	<0.01
3.	Abdominal colic	30	4.03	1.16	2.87	71.21	0.628	0.114	24.97	<0.001*
4.	Palpitation	30	4.36	1.43	2.93	67.02	0.739	0.135	27.72	<0.10
5.	Loss of appetite	30	4.30	1.4	2.90	67.44	0.66	0.12	24.00	<0.001*
6	Hand foot syndrome	30	2.43	1.20	1.23	50.61	0.626	0.114	10.79	<0.001*
7.	Sternal Pain	30	3.40	1.83	1.56	46.17	0.626	0.114	13.70	<0.01
8.	Fever	30	3.06	1.56	1.5	49.01	0.73	0.13	11.23	<0.001*
9.	Hepatomegaly	30	2.43	1.43	1.0	41.15	0.74	0.135	7.3	<0.10
10.	Splenomegaly	30	3.13	1.66	1.46	53.03	0.73	0.11	11.73	<0.10
11.	Bodyache Pain & Crisis	30	4.6	2.03	2.56	55.86	0.56	0.09	27.89	<0.001*
12.	Repeated infection	30	3.86	1.4	2.46	63.73	0.77	0.14	17.40	<0.001*
13.	Repeated Blood transfusion	30	3.1	2.23	0.90	28.06	0.66	0.12	7.4	<0.001*
14.	Pain in hip region	30	2.3	1.4	0.86	39.13	0.43	0.07	10.93	<0.001*

*Highly significant

Table 3: Overall assessment of subjective parameters

Total no. of patients	Before treatment Mean	After treatment Mean	Mean difference	% of Relief	Standard Deviation S.D.	Standard Error S.E.	T-value (Paired test)	P value
30	3.531	1.52	2.007	57.10	0.85	0.22	8.802	<0.001*

*Highly significant

Table 4: Total effect of therapy in objective parameters (n=30)

S. No.	Investigation	Total No. of patients	Before Treatment Mean	After Treatment Mean	Mean Difference	% of Relief	Standard Deviation	Standard Error	T-value (Paired test	P value
1	Hb in gm%	30	8.487	9.513	1.027	10.79	0.816	0.1542	6.656	<0.001*
2	ESR	30	22.967	16.487	6.480	28.21	6.081	1.110	5.836	<0.001*

*Highly significant

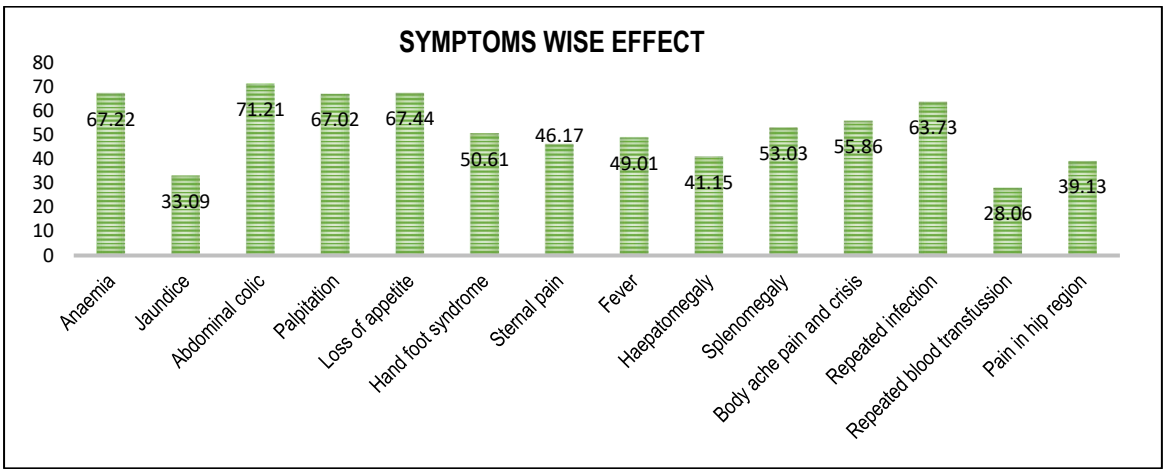

Fig. 1: Total effect of therapy in subjective parameters

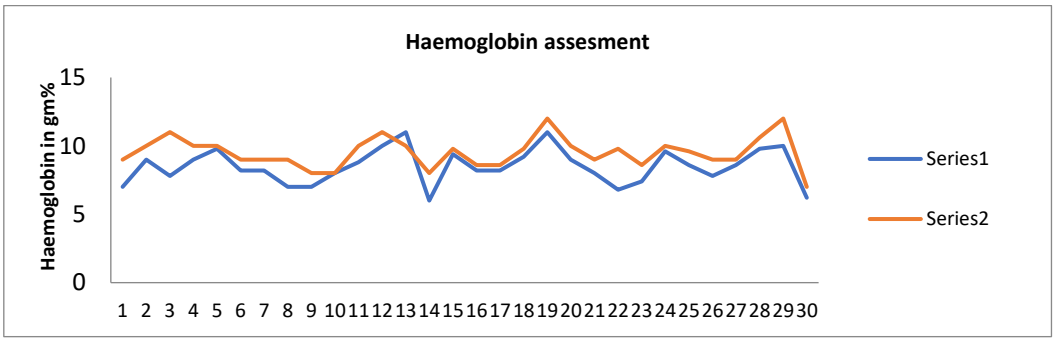

Fig. 2: Total effect of therapy in haemoglobin g%

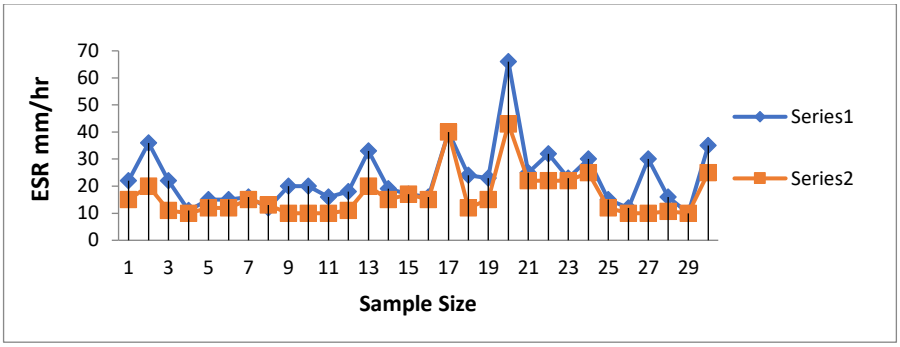

Fig. 3: Total effect of therapy in objective parameters erythrocyte sedimentation rate (ESR in mm/hr)

RESULTS

The data collected from the clinical trial was compiled and subjected for statistical evaluation. The final results of therapy were evaluated by the reduction and improvement of the signs and symptoms. In the present clinical study total thirty (30) patients were registered for the trial. The clinical study period for 30 patients was from 21-01-2022 to 03-09-2022. Within the aforementioned period the demography (Table 2) based on *Sannipatika panduroga* can be co-related with sickle cell anemia.

In Table 2, Table 3 and Fig.1, the total efficacy of KGV and GGV was observed that the symptoms like anemia was noticeably improved 67.22%, followed by 71.23% of patients exposed good response in symptom abdominal colic, 67.02% of patients markedly decreased in palpitation, 55.86% of patients exhibited decrease in body ache pain and crisis, 33.09% of patients reduced in symptoms of jaundice,

39.13% of patients showed decrease of pain in hip region, 53.03% of patients revealed in the reduction of spleen size (decreased splenomegaly), 28.06% of patients required lower incidence of repeated blood transfusion, 67.44% got better response in low appetite. Patients with symptoms like swelling and pain in hand, sternal pain and fever was symptomatically good response with reduction of symptoms with result 50.61% followed by 46.17% and 49.01%. patients observed good resistance towards repeated infections with decreased symptoms 63.73%.

The observations made before and after treatment from Table 4, Fig. 2 and Fig. 3 of objective parameters the mean of haemoglobin gm% was 8.487 which was markedly increase with mean 9.513, SD ± 0.816, SE ±0.154, t value 6.65 and $p<0.001$ which was highly significant. Trial drugs were statistically highly significant in reduction of ESR and were highly significant with $p<0.001$ where the mean before treatment was 22.96 which was reduced with mean 16.48, SD ± 6.08, SE ±1.11, and t value 5.83.

From table 3 Overall improvement in all symptoms was assessed after study the mean before treatment was 3.53 while the mean score after treatment was 1.52. The statistical evaluation revealed that the mean difference after treatment was ± 2.01, SD±0.85, SE± 0.22, and t value 8.803. From this clinical study the trial medications were statistically highly significant with $p<0.001$ and total relief observed 57.14%.

DISCUSSION

The main symptom of SCA is disease relative anemia. jaundice, abdominal colic, palpitation, loss of appetite, hand foot syndrome, sternal pain, fever, hepatosplenomegaly, body ache pain and crisis, repeated respiratory infections, repeated blood transfusion, and pain in hip region can be compared with symptoms of *Sannipatika pandu* (SP) as mentioned in Ayurvedic literature. *Nidana* of SP does not correlate with sickle cell anemia as it is autosomal and hereditary disease. The disease *samprapti* (pathogenesis) of SP can be correlated with SCA as in both the type of *Sroto dusti* is *Sanga* (Vaso occlusion found in SCA). Blood transfusion (BT) is the main procedure to maintain haemoglobin (Hb%) in individual patient and to save life of sickling patient but the use of herbal Ayurvedic medicine helps to avoid recurrent BT, reducing the clinical data and increase the haemoglobin percentage in peripheral blood. In our country these are easily available, cost effective and safer to treat SCA.

Clinical characteristics were taken into account for this study, and the aetiology, pathogenesis, clinical characteristics, and therapy outlined by current science were also followed throughout the research process. The purpose of the current study was to examine the impact of KGV and GGV on the administration of SCA, which Bhavprakash Nighantu refers to as panduhar property. *Kiratatikta* has *tikta rasa, laghu* and *ruksha guna* which clear *kapha dosha*. Owing to this quality, it has a jwaraghna and shophahara nature (21), whereas Guduchi ghana mostly contains katu, tikta, and kashaya rasa. When used, it affects the vitiated Kapha dosha. Guduchi displays the laghu and snigdha guna. Snigdha guna has the power to restore the vitiated vata dosha. This experimental medication contains ushna veerya, a dosha-relieving ingredient that balances both vata and kapha dosha. Madhura vipaka, a component of the medication, helps to balance the vata and pitta doshas. Moreover, this medication possesses deepan-pachan properties (22). As a result, the created trial medication has the capacity to rectify the agni (digestive fire), i.e., Jatharagni and Dhatwagni, which aids in the efficient management of the body metabolism and the effective treatment of the condition. *Kiratatikta* has pharmacologically antispasmodic, anti-inflammatory, antimalarial hepatoprotective, CNS depressant, antidepressant and laxative properties which decrease the symptoms of SCA, while *Guduchi* has a antimicrobial activity which is helpful in reducing repeated infections. *Guduchi* contains analgesic, antipyretic, anti-inflammatory, immunostimulant, antineoplastic and anti-inflammatory properties. Due to this it is responsible for minimising the symptoms of SCA (23).

CONCLUSION

In essence, SP roga is vyadhi being dominated by pitta pradhana tridosha. The natural colour of the body is determined by the bhrajaka pitta dosha, but owing to a few pathological factors, when it becomes vitiated, it affects the blood and causes loss of complexion or panduta (pallor). Despite the fact that vata and kapha dosha also play a significant part in the development of SP roga, pitta is the pradhana dosha in pandu roga. KGV and GGV can be provided as an efficient medication to battle SCA and its problems wherever needed with a reasoned approach, according to the analytical rationale of the study that was offered in discussion. SCA is referred as in Ayurveda parlance as Kulaja vikara janya vyadhi or beejadushtijanya vikara. The reduction of the disease's primary signs and symptoms was made possible by the use of the ayurvedic formulations KGV and GGV. Together with this, other supportive and necessary contemporary therapy may improve the quality of life for those with SCA. There is always a chance of inadequacy because the current study is in the trial phase and is a more recent one for physicians and researchers in the field of Ayurveda. A scholarly, multifaceted, and comprehensive approach to the research of this unpleasant issue may be launched in order to address this inadequacy.

CONFLICT OF INTEREST

Authors declare no conflicts of interest.

REFERENCES

1. Panigrahi, H.K. Treatment of sickle cell disorders by Ayurvedic medicine. Ancient science of life. 1997; 17(1):15-22.
2. Stuart, M.J., Nagel, R.L. Sickle cell disease. Lancet. 2004; 364: 1343-1360.
3. Rees, D.C., Williams, T.M., Gladwin, M.T. Sickle cell disease. Lancet. 2010; 376: 2018-2031.
4. Serjeant, G. R. Sickle-cell disease. Lancet. 1997; 350(9079):725-730.
5. Anie, K.A., Treadwell, M.J., Grant, A.M., Dennis-Antwi, J.A., Asafo, M.K., Lamptey, M.E., *et al.,* Community engagement to inform the development of a sickle cell counsellor training and certification program in Ghana. J Community Genet. 2016;7(3):195-202.
6. Census of India 2011. Office of the Registrar General and Census Commissioner. Ministry of Home Affairs, Govt of India. Available from: http://www.censusindia.gov.in, accessed on March 27,2015.
7. Singh, K.S. People of India: An introduction. Calcutta, India: Anthropological Survey of India; 1992.
8. Reich, D., Thangaraj, K., Patterson, N., Prince, A.L., Singh, L. Restructuring Indian population history. Nature. 2009; 461 :489-494.
9. Lehman, H., Cutbush, M. Sickle cell trait in southern India. Brit Med J 1952; 1: 404-405.
10. Dunlop, K.J., Mazumber, U.K. The occurrence of sickle cell anemia among a group of tea garden labourers in Upper Assam. Indian Med Gaz. 1952; 87: 387-391.
11. Colah, R., B., Mukharjee, M.B., Martin, S., Ghosh, K. Sickle cell disease in tribal populations in India. Indian J Med Res. May 2015; 141: 509-515.
12. Sinha, C.P., Baghel, P.K., Patra, P.K. A clinical study of sickle cell disease and its management with S-Compound, Int J Ayu Pharm Chem. 2018; 9(2): 321-333.
13. Agnivesha Charakasamhita with Ayur-veda Deepika commentary of Chakrapani-datta revised by Charaka And Dridhabala, Ayushi Hindi comentry by Vaidya H.C. Kushvaha, Chaukamba publishers, reprint 2016 Sutra sthana,Chapter 18, sloka 44,45.46 p.287.
14. Agnivesa: Caraka Samhita: Rev. by Caraka and Dradhabala with Charaka chandrika Hindi commentary by Brahmanand Tripathi: reprint (2004) Chaukhamba Surbharti Prakashan: Varanasi, Vimana sthana chapter 4, sloka 6, pg.692.
15. Agnivesha Charaka samhita with hindi Gujrati English comentry by Shri Gulab Kunverba Ayurvedic Society Jamnagar India. 1949; First edition, Vol. 2 Sutrasthan chapter 18, Sloka No. 44-46: 313-314.
16. Agnivesha Charaka samhita with hindi Gujrati English comentry by Shri Gulab Kunverba Ayurvedic Society Jamnagar India. 1949; First edition, Vol. 2, Vimana sthan chapter 4, Sloka No. 6: 301.
17. Ruchi Singh IPGT & RA Jamnagar. A study of disease thalassemia and its management with Dhatri Avaleha.2007.
18. Bhav Prakash Nighantu by shri Bhav Mishra.Vidyutini Hindi Commentry by Bramhashankar Mishra and Sri Rupalaji Vaisya,Choukhambha Sanskrit Sansthana,Varanasi, 8th edition 1997. Haritakyadi varga Sloka No: 153-155: 72 and Guduchyadi varga, Sloka No.1-10: 269.
19. Database of Indian medicinal plants used in Ayurveda Vol.1-7 By central council for research in Ayurveda and Siddha Dept. of ISM & H Ministry of health and family Welfare, Govt. of India 2005: 225 and 256.
20. Spies-Dorgelo, M.N., Terwee, C.B., Stalman, W.A.B., van der Windt, D. A.W.M. Reproducibility and responsiveness of the symptoms severity scale and the hand and finger function subscale of the Dutch arthritis impact measurement scale (Dutch-AIMS2-HFF) in primary care patients with wrist or hand problems, Health and quality of life Outcomes. 2006; 4:87.
21. Sharma, P.V. Dravyaguna Vijnana Vol. II, Chaukhambha Bharati Academy Varanasi, Reprint 2003. Pg nos. 761-763.
22. Sharma, P.V. Dravyaguna Vijnana Vol. II, Chaukhambha Bharti Academy Varanasi,Reprint 2003. Pg no.791-793.
23. Khare, C.P. Indian medicinal plants. ISBN-978-0-387-70637-5 springer-Verlag/Berlin/Delberg, Edition 2007; pp 632-633 and 662.