

**Effect of Rasayana on Complement System W.S.R. To Prameha**

<sup>1</sup>Sumana Ray Paul, Senior Ayurvedic Medical Officer, Kulai BPHC, Howrah, West Bengal

<sup>2</sup>Abichal Chattopadhyaya, Ex - Professor, Dept. of Ayurved Samhita and Siddhanta, Institute of Post Graduate Ayurvedic Education and Research, Shyamadas Vaidya Sastra Pith Hospital, Kolkata 700009, West Bengal

<sup>3</sup>Apala Sengupta, Professor, Dept. of Roga Nidan & Vikriti Vijnan, Institute of Post Graduate Ayurvedic Education and Research, Shyamadas Vaidya Sastra Pith Hospital, Kolkata 700009, West Bengal

<sup>4</sup>Gopeswar Mukherjee, Ex- guest lecturer, Dept. of Roga Nidan & Vikriti Vijnan, Institute of Post Graduate, Ayurvedic Education and Research, Shyamadas Vaidya Sastra Pith Hospital, Kolkata 700009, West Bengal

**Corresponding Author:** Sumana Ray Paul, Senior Ayurvedic Medical Officer, Kulai BPHC, Howrah, West Bengal

**Type of Publication:** Original Research Article

**Conflicts of Interest:** Nil

---

**Abstract**

**Introduction :** Rasayana has two different ways of function in our body - preventive and curative. Prameha is a disease which is characterized by Avila Mutrata ( turbidity of urine ) and Prabhuta Mutrata ( frequency of urine ) and effects all the systems. The complement system, an important soluble component of the innate immune system, is a series of plasma enzymes and regulatory proteins. The function of the complement system includes control of inflammatory reactions and chemotaxis, clearance of immune complexes, cellular activation and antimicrobial defence. Complement C3 and C4 are the major plasma proteins of the immune system complement pathways. Though Rasayana acts in multi dimension but the effect of Naimittik Rasayana in respect to complement system has not yet been carried out in the field of Ayurvedic research works.

**Aims and Objectives :** The present work has been carried out to evaluate the concept of Rasayana effect in concordance to complement system in the disease Prameha ( diabetes mellitus) along with reveal the effectiveness of Khadir (Acacia catechu Linn. ) - the Naimittik Rasayana of Prameha i.e diabetes mellitus.

**Materials and Methods :** 60 subjects comprising both patients of Prameha and healthy volunteers were selected for the study and divided in to two groups - group of patients of Prameha & group of healthy volunteers following inclusion and exclusion criteria. Khadir ( Acacia catechu Linn. ) was administered in the selected patients at a dose of one gram equivalent, orally, twice daily, with warm water for 90 consecutive days.

**Results :** The subjective and objective parameters were present in maximum number of patients. The result also reveals the significant efficacy of Khadir on relevant subjective and objective parameters with a 'p-value <0.001 in all subjective and objective parameters.

**Conclusion :** This study reveals that Khadir is very much effective to encounter the subjective manifestations of the disease Prameha and it is also effective to reduce the C3 & C4 level in specific along with blood glucose level along with

other parameters. The concomitant relation between complementary system and Prameha are well established in respect to Vikarvighatabhava through this study.

**Keywords :** Prameha, Rasayana, Vikarvighatabhava, Complementary system, Diabetes mellitus

## **Introduction**

In Ayurvedic compendium, the term Rasayana has been used in two different ways - drugs with certain preventive and curative qualities. Acharya Charak has referred Rasayana as the method of getting nourished Dhatus<sup>(1)</sup>. He has also mentioned different functions of Rasayana which includes both preventive and curative aspects<sup>(2)</sup>. Acharya Sushruta has mentioned Rasayana as anti ageing, physical and mental strength booster as well as capable of alleviate disease<sup>(3)</sup>. The commentator of Sushruta Samhita, Dalhan has classified Rasayana in to three groups – Ajasrik Rasayana , Kamyas Rasyan ( both for healthy persons) and Naimittik Rasayana (for diseased persons)<sup>(4)</sup>. Acharya Vagbhat has also mentioned Rasayana in the line of Acharya Charaka<sup>(5)</sup>. Although, he has given importance to the anti ageing property of Rasayana, that's why he has termed Rasayana Chikitsa as Jara Chikitsa. During later period, in Sharangadhar Samhita, Rasayana is defined as a method to prevent senile condition as well as to alleviate the diseased condition.<sup>(6)</sup> Prameha i.e. diabetes mellitus is a disease characterized by Avila Mutrata ( turbidity of urine) and Prabhuta Mutrata ( frequency of urine )<sup>(7)</sup> and affects almost all the systems<sup>(8)</sup>. In this disease the Dhatwagni Paka , specifically the activity of Medagni gets deranged, producing different type of complications. In the recent reports it is stated that, Prameha in term of diabetes is the eighth leading cause of death in worldwide in 2012<sup>(9)</sup> and more than 422 million people are suffering from this disease throughout the world in 2014.<sup>(10)</sup> The immune system is a system of many biological structures and processes within an organism that protects against disease. It is currently divided in to two categories – innate (non-specific) immunity and acquired (specific) immunity<sup>(11)</sup>. The innate immunity sometimes referred as in-born immunity. Major components of innate immune system are pattern recognizing receptors (PRR), antimicrobial peptides, cells, complement components and cytokines.<sup>(12)</sup> The complement system , an important soluble component of the innate immune system, is a series of plasma enzymes, regulatory proteins, and proteins that are activated in a cascading fashion, resulting in cell lysis.<sup>(13)</sup> The function of the complement system includes control of inflammatory reactions and chemotaxis, clearance of immune complexes, cellular activation and antimicrobial defence<sup>(14)</sup>. However, for more than a decade now, complement system has been implicated in a multitude of processes in the course of development, degeneration and regeneration<sup>(15)</sup>. Complement C3 and C4 are the major plasma proteins of the immune system complement pathways. The synthesis of these proteins is increased in response to inflammation and infection but at a slower rate than for traditional acute phase proteins<sup>(16)</sup>. Complement C3 and C4 are the major plasma proteins of the immune system complement pathways. The synthesis of these proteins is increased in response to inflammation and infection but at a slower rate than for traditional acute phase proteins<sup>(17)</sup>. Both C3 and C4 have shown substantial correlations with obesity<sup>(18)</sup> and high gene expression of these complement components has been reported in omental adipose tissue in obese men<sup>(19)</sup>. Normal blood level of C3 is 16- 47 mg/dl and C4 is 60-144 CAE units<sup>(20)</sup>. Both C3 and C4 have shown substantial correlations with obesity<sup>(21)</sup> and high gene expression of these complement components has been reported in omental adipose tissue in obese men<sup>(22)</sup>. High C3 levels have been reported in subjects with diabetes and insulin resistance<sup>(23)</sup>.

Though Rasayana acts in multi dimension but the effect of Naimittik Rasayana in respect to complement system has not yet been carried out in the field of Ayurvedic research works. Considering the prevalence of disease Prameha i.e. diabetes mellitus and the unexplored thoughts of the effect of Khadir as Rasayana in respect to complement system, the cost effective drug to treat the disease Prameha i.e. diabetes mellitus, has been taken to carry out the research work.

Therefore the present study was carried out with the following aims and objectives :

- (1) To clarify the concept of Rasayana mentioned in different compendiums, specifically Naimittik Rasayana.
- (2) To reveal the Rasayana effect in concordance to complement system.
- (3) To reveal the effectiveness of Khadir ( *Acacia catechu* Linn. ) - the Naimittik Rasayana of Prameha i.e diabetes mellitus.

### **Materials and Methods**

**Selection of Patient:** 60 subjects comprising both patients and healthy volunteers were selected from OPD and IPD of IPGAE&R at SVSP hospital, Kolkata irrespective of their sex, occupation and religion. The patients having the clinical feature of Prameha were selected for the study as well as healthy volunteers having Dhatu Samya Lakshans were also selected for the study. Hence, the study sample were divided in to the two group -

- (i) Group A-Patients of Prameha
- (ii) Group B-Healthy volunteers having Dhatu Samya Lakshans

### **Inclusion Criteria**

#### **(A) Criteria For Group A**

- (1) Adult subject of either sex between 16 to 60 years of age
- (2) Presence of cardinal sign and symptoms of Prameha.
- (3) Established non-insulin dependent Diabetes mellitus patients.  
(BS PP level: 180 - 400 mg/dl )
- (4) Willingness to give written inform consent for participation in the study.

#### **(B) Criteria For Group B**

- (1) Healthy volunteers, within the age limit of 16 – 60 years, having the Dhatu Samya Lakshan.
- (2) Volunteers without any minor or major pathological conditions.

### **Exclusion Criteria**

#### **(A) Criteria for Group A**

- (1) Severe diabetes mellitus ( BS PP >300mg/dl )
- (2) Insulin dependent Diabetes mellitus.
- (3) Diabetes with hepatic/renal disease/ cardiac ailments / hypertension
- (4) Co existing chronic disease.
- (5) Any concomitant serious disorders of organs
- (6) Pregnancy

#### **(B) Criteria for Group B**

- (1) Volunteers below 16 years and above 40 years of age.

- (2) Volunteers having any major or minor ailments.

### **Subjective Parameter**

#### **Group A :** <sup>(24)</sup>

- (1) Pravuta Mutrata ( increased urination in terms of frequency & quantity )
- (2) Avila Mutrata ( turbidity of urine )
- (3) Pipasa / Trishna ( excessive thirst )
- (4) Shitapriyata ( liking for cold substances )
- (5) Kara Pada Daha ( burning sensation in hand & feet )
- (6) Kara Pada Supti ( numbness in hand & feet )
- (7) Kshudhadhikyata ( polyphagia )
- (8) Sweda Pravritti ( excessive sweating )
- (9) Klama ( exertion without any activity )
- (10) Nidra & Tandra ( excessive sleep and drowsiness )
- (11) Gala Talu Mukha Sosha ( dryness of throat, palate & mouth )

#### **Group B :** <sup>(25)</sup>

- (1) Swaravarnayoga ( appearance of normal voice and complexion )
- (2) Shariropachaya ( nourishment of body )
- (3) Balavridhi ( increase in strength )
- (4) Abhyavaharyabhilasha ( desire for taking food )
- (5) Ruchiraharakaale ( appetite for food during meal time )
- (6) Abhyavaharitasya-Chaharasya Kaale Samyagjaranam ( proper digestion of the food taken )
- (7) Nidralabha Yathakaale ( getting sleep at appropriate time )
- (8) Vaikarinam Cha Swapnanamadarshanam ( absence of abnormal dreams indicating morbidity)
- (9) Sukhena Cha Pratibodhanam ( happy awakening )
- (10) Vatamutrapurisharetasam Mukti ( proper elimination of flatus, urine, stool and semen)
- (11) Sarvakaraimanobuddhindriyanam Chavyapatti ( un-impairment of mind, intellect and senses )

### **Objective Parameter**

#### **Group A**

- (1) Blood level of C3 & C4
- (2) Blood glucose (fasting and PP)
- (3) Lipid profile
- (4) Liver function test
- (5) Haematological profile.
- (6) Serum Urea & Creatinine

**Group B**

- (1) Blood level of C3, C4
- (2) Blood glucose (fasting & PP)
- (3) Hematological profile

**Adoption of Drug**

Powder of heartwood of Khadir (Acacia catechu Linn.) was administered in the selected patients (Group A) at a dose of one (1) gram equivalent, orally, twice daily, with warm water, before principal meals. Whereas, in group B subjects (healthy volunteers) no drug was administered. After 90 days, effect of the stipulated drug was evaluated.

**Dose of the Drug**

The selected drug (Khadir ) was administered in Group A patients in a dose of one gram, orally, twice daily , before principal meals with warm water for a period of 90 days.

**Study Protocol:**

**Duration of Study:** The entire clinical monitoring of the present study was completed within two years.

**Study Sample:** Among the 60 subjects who were initially selected for the study, total 20 subjects were dropped out during study course. Hence complete clinical survey was done in 40 subjects, distribute in two groups as following: (1)

Group A: 30 patients

(2) Group B - 10 volunteers.

**Statistical Analysis:** Data were compared by unpaired t-test with  $p < 0.05$  as the cut off level for statistical analysis. The obtained results were interpreted as - Insignificant -  $P > 0.05$ , Significant -  $P < 0.01$  to  $P < 0.05$ , highly significant -  $P < 0.001$

**Observations**

Distribution of subjective parameters among the 30 patients of Prameha in group A are tabulated in Table 1. Statistical analysis of subjective and objective parameters in 30 patients of Prameha before and after treatment shows that Khadir has significant efficacy on both the subjective and objective parameters with ‘p’ value  $< 0.001$  (Table 2 ). Statistical analysis ( unpaired t test ) for Prameha group ( group A ) and healthy control group ( group B ) has been shown in Table 3.

Table 1: Distribution of subjective parameters among 30 patients of Prameha

Sn.	Subjective Parameters	No. of patients	Percentage
01.	Prabhuta Mutrata - increased frequency	28	93.33 %
02.	Prabhuta Mutrata - increased volume	26	86.66 %
03.	Avila Mutrata	25	83.33 %
04.	Pipasa	29	96.66 %
05.	Shitapriyattwam	25	83.33 %
06.	Kara Pada Daha	28	93.33 %
07.	Kara Pada Supti	28	93.33 %
08.	Kshudhadhikyata	23	76.66
09.	Swedadhikyata	29	96.66
10.	Klama	29	96.66

Table 2: Statistical analysis of subjective and objective parameters in 30 patients of Prameha before and after treatment

Subjective Parameters	Mean BT	Mean AT	SD +/-	SE +/-	't' value	'p' value
Prabhutamutrata (Frequency)	2.5	1.1	0.814	0.148	9.43	<0.001
Prabhutamutrata (Quantity)	2.33	1.13	0.925	0.169	7.12	<0.001
Avilamutrata	2.3	1.57	0.977	0.178	4.11	<0.001
Pipasadhikyata	2.43	1.26	0.913	0.167	7.03	<0.001
Karapada Daha	1.86	1.23	0.999	0.182	3.47	<0.01
Sheetapriyata	1.83	1.23	0.764	0.139	4.53	<0.001
Karapada Supti	1.9	1.3	0.814	0.149	3.18	<0.01
Kshudhadhikyata	1.97	1.4	0.858	0.157	3.62	<0.01
Swedadhikyata	2.03	1.26	0.897	0.164	3.45	<0.01
Klama	1.73	1.3	0.731	0.133	3.75	<0.001
Serum C3	161.9	144.394	12.99	2.37	7.25	<0.001
Serum C4	40.697	35.913	2.424	0.442	10.865	<0.001
FBS	184.06	140.5	35.99	6.572	6.679	<0.001
PPBS	250.33	175.1	39.867	7.278	10.337	<0.001
Serum Urea	27.812	24.88	2.747	0.05	5.186	<0.001
Serum Creatinine	1.025	0.87	0.179	0.033	4.705	<0.001
Serum Cholesterol	183.466	166.5	10.01	1.828	9.268	<0.001
Serum HDL	58.166	66.6	10.63	1.941	3.81	<0.001
Serum LDL	124.4	100.5	14.94	2.728	8.758	<0.001
Serum Triglyceride	184.6	169.466	5.374	0.981	15.42	<0.001
Serum Bilirubin	0.845	0.642	0.147	0.269	6.97	<0.001
S.G.O.T.	42.67	33.1	8.159	1.489	5.820	<0.001
S.G.P.T.	28.96	22.8	5.395	0.985	6.261	<0.001
Serum Alkaline Phosphatase	195.43	182.967	10.523	1.921	8.641	<0.001
Serum Total Protein	7.804	7.1133	0.041	0.075	9.89	<0.001
Serum Albumin	4.435	4.019	0.221	0.040	10.283	<0.001
Serum Globulin	3.41	3.026	0.283	0.052	7.426	<0.001
Haemoglobin%	12.023	12.485	0.564	0.0103	4.632	<0.001

Table 3: Showing statistical analysis (unpaired t test) for Prameha group (group A ) and healthy control group ( group B )

No.	Prameha Group ( group A )	Healthy Control Group ( group B )	't' test	'p' value	C.S.
01.	C3	C3	8.131	<0.001	H.S.
02.	C4	C4	4.568	<0.001	H.S.
03.	FBS	FBS	4.318	<0.001	H.S.
04.	PPBS	PPBS	5.639	<0.001	H.S.
05.	Cholesterol	Cholesterol	4.881	<0.001	H.S.
06.	HDL	HDL	2.340	<0.05	S

07.	LDL	LDL	5.035	<0.001	H.S.
08.	Triglyceride	Triglyceride	8.544	<0.001	H.S.
09.	Bilirubin	Bilirubin	3.175	<0.05	S
10.	SGOT	SGOT	2.6	<0.05	S
11.	SGPT	SGPT	2.23	<0.05	S
12.	Alkaline Phosphatase	Alkaline Phosphatase	4.95	<0.001	H.S.
13.	Total Protein	Total Protein	4.490	<0.001	H.S.
14.	Albumin	Albumin	2.026	<0.05	S
15.	Globulin	Globulin	2.94	<0.05	S
16.	Urea	Urea	3.31	<0.05	S
17.	Creatinine	Creatinine	2.76	<0.05	S
18.	Haemoglobin%	Haemoglobin%	2.24	<0.05	S
*** H.S. = Highly significant    *** S = Significant					

### Discussions

Rasayana covers the broad ambit of adaptogenic activity, anti-ageing activity, immunomodulation activity and anti-oxidant activity. Maintenance of the function of Agni results the sustenance of body which is achieved through the action of Rasayana. The sequenced Jatharagni Paka, Bhutagni Paka and Dhatwagni Paka are responsible to quantify the Rasayana and subsequently the Rasayana effect. Meda is one of the most important Dushya in Prameha for reasons more than one: it is an Apa and Parthiva Mahabhuta dominant Dhatu. Placed in the centre of Dhatus chronological order hence can create an impact on the three previous and three later Dhatus. According to Acharya Charaka, if Meda increases all other Dhatus decrease<sup>(26)</sup>. Its function in the body is to provide Snehana i.e. Lubrication- adequate to perform any function. Its increase will also increase Snigdhdhata and in Pramehi, Dravya & Guna also increases due to increase in Apa and Prthvi. This instead of serving optimum lubrication and softness causes flaccidity hence hampers body function. The complement system, an important soluble component of the innate immune system, is a series of plasma enzymes, regulatory proteins, and proteins that are activated in cascading fashion in cell lysis. These are the consequences of Vikarvighatbhava<sup>(27)</sup> in respect to antigen/antibody immune complexes, the MBL (a serum collectin) activation pathway activate by microbes with terminal mannose groups. The series of enzymes of the complement system are the serine proteases identical to that of function entity of Oja. Oja is the supreme essence of all the Dhatus, increase the vitality of the protective force of the body. C3, C4 and helper T lymphocyte are responsible for the initiation of nearly all immunological response to pathogens. Picchil, Slakshna, Mridu, Snigdha, Shita, Guru and Sthira are the qualities of Oja<sup>(28)</sup>. Picchil is significant for its Lepana Shakti that's the ability to make cover the cellular organization by some physiological barrier. Snigdha Guna of Oja by its action make the arrangement of body fluid in different compartment and also in regulation of their volume. Certain factors possess essential role in regulation of the body fluid volume in different compartment of the body. Shita Guna signifies the conservative property of cellular content to maintain equilibrium in static and kinetic energy. Guru Guna is characterized by Brimhana Karma. The term Brimhana is applicable for synchronized function of cellular growth, cell division and increase body mass etc. Sthira Guna of Oja maintains the homeostasis. Mridu Guna affect the behaviour of miscible liquids in emulsion, helps in absorption of fat, enzyme action,



helps in penetration of various agents through the cell membrane, acts as an important factor to maintain the peripheral resistance in arterioles, helps in muscular activities and also influence ciliary movement in living tissue. This results the homeostasis of the body. Insulin is responsible for regulating carbohydrate metabolism.

This may be hypothetically considered that insulin is made of Katu, Tikta & Kashaya Rasa which regulates Madhur Rasa or carbohydrate metabolism. Madhur Rasa is predominantly composed of Kshiti and Apa Mahabhuta whereas Katu, Tikta and Kashaya Rasa are predominantly composed of Agni & Vayu, Vayu & Akash and Kshiti & Vayu Mahabhuta accordingly. Due to inhibition of Agni, Vayu and Akash receptors, Kshiti and Apa receptors get exhibited, resulting insulin resistance. Impaired function of Medagni in terms of impaired fatty acid oxidation and lipid accumulation may generate lipid peroxide or alteration of Meda-oja. The complement system, an important soluble component of the innate immune system, is a series of plasma enzymes, regulatory proteins, and proteins that are activated in cascading fashion in cell lysis. These are the consequences of Vikarvighatbhava in respect to antigen/antibody immune complexes. The series of enzymes of the complement system are the serine proteases identical to that of function entity of Oja. Rasayana therapy enhance the Vyadhivalavirodhikattva in terms of arresting the disease process by means of inhibiting the inflammation so that the C3, C4 may be regularized resulting Pramehaghna activity. Rasayana acts actively through breaking the consequence of the series of pathophysiology on specific disease as per the requirement, accelerating the action of specific receptors responsible for the causation of the disease. In Prameha, the qualitative derangement of the Akash, Vayu and Agni receptors take place therefore the drug having Tikshna & Laghu Guna and subsequently possess the Rasayana activity may breakdown the Vikarvighatabhava by restoring the Vikarbighatbhava in terms of promoting insulin secretion, inhibiting insulin resistance, correcting the excessive hepatic glucose production and fat metabolism. It boosts the immune complex in such a way so that the complementary system acts properly and the disease Prameha can be arrested in due course of time sustaining the proper function of Agni following Swabhavoparamvada. The patients who are having less Jarana Shakti and subsequently leads the most sedentary life without any exercise are likely to be affected by the disease Prameha. Their Vyadhikshamatva are also being impaired in terms of Vyadhivalavirodhikattva and Vyadhiutapadakpravandhakattva. Activation of the classic complement pathway via immune complex binding to C1q links the innate and adaptive immune systems via specific antibody in the immune complex. Rasayana therapy enhance the Vyadhivalavirodhikattva in terms of arresting the disease process by means of inhibiting the inflammation so that the C3, C4 may be regularized resulting Pramehaghna activity. Rasayana acts actively through breaking the consequence of the series of pathophysiology on specific disease as per the requirement, accelerating the action of specific receptors responsible for the causation of the disease. In Prameha, the qualitative derangement of the Akash, Vayu and Agni receptors take place therefore the drug having Tikshna & Laghu Guna and subsequently possess the Rasayana activity may breakdown the Vikarvighatabhava by restoring the Vikarbighatbhava in terms of promoting insulin secretion, inhibiting insulin resistance, correcting the excessive hepatic glucose production and fat metabolism. It boosts the immune complex in such a way so that the complementary system acts properly and the disease Prameha can be arrested in due course of time sustaining the proper function of Agni following Swabhavoparamvada. Table 2 shows - statistical analysis of patients of Prameha before and after administration of the test drug - Khadir. These analysis reveals that Khadir is very much effective to encounter the subjective manifestations of the disease Prameha and also effective to reduce the C3 & C4



level specifically along with other objective parameters like FBS, PPBS etc. These findings have well established the concomitant relation between complementary system and diabetes mellitus in respect to Vikaravighatabhava. Vikaravighatabhava is the phenomenon where Vyadhikshamatva gets reduced because altered complement system. <sup>(29)</sup>.

### Conclusion

This study reveals that Khadir is very much effective to encounter the subjective manifestations of the disease Prameha and it is also effective to reduce the C3 & C4 level in specific along with blood glucose level along with other parameters. It signifies that in diabetes mellitus, C3 & C4 level get increased along with the alteration of the FBS and PPBs and lipid profile. Vikaravighatabhava is the phenomenon where Vyadhikshamatva gets reduced because of affected complementary system. The concomitant relation between complementary system and Prameha are well established in respect to Vikaravighatabhava through this study.

### References

1. Dalhan , Nibandha Samgraha commentary on Susruta Samhita commentary, Edited by Yadavji Trikamji Acharya, published by – Chowkhamba Sanskrit Pratisthan, Varanasi. 6<sup>th</sup> edition. Sutrasthan, chapter 1, sloka 7, page 3
2. Dalhan , Nibandha Samgraha commentary on Susruta Samhita commentary, Edited by Yadavji Trikamji Acharya, published by – Chowkhamba Sanskrit Pratisthan, Varanasi. 6<sup>th</sup> edition. Chikitsasthan, chapter 27, sloka 1-2, page 499
3. Arundutta, Sarvanga Sundara commentary on Astanga Hriday of Vagbhat, Edited by- Hari Sastri Paradkar Vaidya, published by- Chowkhamba Oriental, Varanasi, 7<sup>th</sup> edition, 1982. Uttartantra, chapter 39, sloka 1-4, page 923
4. Sharangadhar, Sharangadhar Samhita, edited by Dr. Shailaja Srivastava, Chaukhamba Orientalia, Varanasi, 4<sup>th</sup> Ed. 2005, Purvakhanda, 4<sup>th</sup> chapter, sloka 14, page 33
5. Dalhan , Nibandha Samgraha commentary on Susruta Samhita commentary, Edited by Yadavji Trikamji Acharya, published by – Chowkhamba Sanskrit Pratisthan, Varanasi. 6<sup>th</sup> edition. Sutrasthan, chapter 33, sloka 4, page 144. ; Arundutta, Sarvanga Sundara commentary on Astanga Hriday of Vagbhat, Edited by- Hari Sastri Paradkar Vaidya, published by- Chowkhamba Oriental, Varanasi, 7<sup>th</sup> edition, 1982. Nidanstan, chapter 8, sloka 30, page 497
6. Chakrapani Dutta, Ayurved Deepika commentary on Charak Samhita of Agnivesha Edited by – Yadavji Trikamji Acharya, published by- Chowkhamba Oriental, Varanasi, 2009 ed. Sutrasthan, chapter 25, sloka 40. page 132
7. Arundutta, Sarvanga Sundara commentary on Astanga Hriday of Vagbhat, Edited by- Hari Sastri Paradkar Vaidya, published by- Chowkhamba Oriental, Varanasi, 7<sup>th</sup> edition, 1982. Nidanstan, chapter 10, sloka 7, page 502
8. Chakrapani Dutta, Ayurved Deepika commentary on Charak Samhita of Agnivesha Edited by – Yadavji Trikamji Acharya, published by- Chowkhamba Oriental, Varanasi, 2009 ed. Chikitsasthan, chapter 6, sloka 8. page 445
9. “The 10 leading causes of death in world in 2000 & 2012”, World Health Organization, available on the official website – www.who.int
10. Diabetes Fact File, World Health Organization, available on the official website – www.who.int
11. Harrison’s Principle of Internal Medicine, Introduction to immune system, chapter 314, Mc. Graw Hill Publication, 18<sup>th</sup> edition, 2011, E-book
12. Engestron Gunnar, Hebald B., Errikson K., Janson L., “ Complement C3 is a risk factor for the development of diabetes – A population based cohort study” , Journal of American Diabetes Association, Vol 54, February 2005

13. Saleh Mohammad A., "Study complement activity and humoral immune response in type 2 diabetes mellitus," *Diyala Agricultural Science Journal*, Volume 3(1) , 2011, page 34-46.
14. Chakrapani Dutta, *Ayurved Deepika commentary on Charak Samhita of Agnivesha* Edited by – Yadavji Trikamji Acharya, published by- Chowkhamba Orientalal, Varanasi, 2009 ed. Chikitsasthan, chapter 1/1, sloka 8. page 377
15. Agnivesh, *Charaka, Dridhavalala ; Charaka Samhita with Ayurved Deepika commentary of Chakrapani Dutta*; Edited by –Yadavji Trikamji Acharya; published by- Chowkhamba Orientalal, Varanasi ; 2009 ed. ; Nidansthan, chapter 4, sloka 47, page 215 & Chikitsasthan , chapter 6, sloka 13 & 14 ; page - 446 ; Vagbhata ; *Astanga Hridayam with Sarvanga Sundara commentary of Arun Dutta & Ayurved Rasayana commentary by Hemadri* ; edited by - Paradakara Hari sadasiv Sastri ; published by- Chowkhamba Orientalal, Varanasi ; 2012 ed. ; Nidansthan, chapter 10, sloka 07, page 502
16. Agnivesh, *Charaka, Dridhavalala ; Charaka Samhita with Ayurved Deepika commentary of Chakrapani Dutta*; Edited by –Yadavji Trikamji Acharya; published by- Chowkhamba Orientalal, Varanasi ; 2009 ed. ; Vimansthan, chapter 8, sloka 89, page 275
17. Agnivesh, *Charaka, Dridhavalala ; Charaka Samhita with Ayurved Deepika commentary of Chakrapani Dutta*; Edited by –Yadavji Trikamji Acharya; published by- Chowkhamba Orientalal, Varanasi ; 2009 ed. ; Sutrasthan, chapter 21, sloka 5-9, page 129
18. Agnivesh, *Charaka, Dridhavalala ; Charaka Samhita with Ayurved Deepika commentary of Chakrapani Dutta*; Edited by –Yadavji Trikamji Acharya; published by- Chowkhamba Orientalal, Varanasi ; 2009 ed. ; Nidansthan, chapter 4, sloka 4, page 14
19. Agnivesh, *Charaka, Dridhavalala ; Charaka Samhita with Ayurved Deepika commentary of Chakrapani Dutta*; Edited by –Yadavji Trikamji Acharya; published by- Chowkhamba Orientalal, Varanasi ; 2009 ed. ; Chikitsasthan, chapter 24, sloka 31, page 512
20. Agnivesh, *Charaka, Dridhavalala ; Charaka Samhita with Ayurved Deepika commentary of Chakrapani Dutta*; Edited by –Yadavji Trikamji Acharya; published by- Chowkhamba Orientalal, Varanasi ; 2009 ed. ; Nidansthan , chapter 4, sloka 4 ; page – 212.