STUDY ON MANODAIHIK SIDDHANTA WITH SPECIAL REFERENCE TO PREVALENCE AND CORRELATION OF ANXIETY AND DEPRESSION IN PATIENTS WITH CHRONIC RHEUMATOID ARTHRITIS AND ITS MANAGEMENT

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ABSTRACT

Background: Anxiety and depression are often appears in longstanding chronic illness. It has been reported that the patients with chronic Rheumatoid arthritis suffers from mental conditions like anxiety and depression. The proper use of psychopharmacological agents in the management of Rheumatoid arthritis with anxiety depression patient still unclear. Objectives: i. To assess the prevalence of anxiety and depression in a population of patient with chronic Rheumatoid arthritis. ii. To assess the level of anxiety and depression in patient with chronic Rheumatoid arthritis and its management by plant medicines. Methods: A randomized double blind placebo control 8 weeks clinical study was conducted in the department of Basicprinciple. The anxiety and depression level in patient with chronic Rheumatoid arthritis were diagnosed clinically by application of different psychological rating scales. Results: 75 patients were randomly assigned into 4 groups. Gr.-A (n=12) served as a control group treated with rice grain powder (3 gm), Gr. B (n= 18) treated with powder of T.Cordifolia, Gr. –C (n=20) treated with root of W. Somnifera (3gm) and Gr. D.(n= 25), treated in combination with T. Cordifolia and W. Somnifera 1.5 gm each.
A significant score reduction were found in Hamilton Anxiety Scale, Hamilton Depression Scale and Distress Symptom Scale in each test group following administration of the test drugs. **Conclusion:** It may be concluded from the our study that T. Cordifolia and W. Somnifera not only possess anti-inflammatory and adaptogenic activity they also reduced blood glucose significantly.

**KEYWORDS:** Rheumatoid arthritis, Anxiety, Depression.

**INTRODUCTION**
The psychosomatic approach in Ayurveda has been established much before the study of modern psychology. This is not a really new approach but the revival of ancient speculation of the pre-scientific era to the concept that all illness appeared from disorders of the body and mind. This extreme point of view is most accepted in Ayurveda but we no longer separate the mind from the body and we are interested more and more about the mode of life and the driving force within the mind which badly directed can leads to disease.

Psychosomatic illness refers to illness in which the mind plays a causative part. Long term wear and tear from successive stress makes the body more susceptible to breakdown resulting in various organic diseases and acute episode of intense emotional stress can directly precipitate different disorders.

According to Ayurvedic literature Asatmaindriyartha samyoga, pragyaparadh and parinam are the causative factors for the manifestation of disease related to psychosomatic phenomena.\[^1\] A number of psychic factors like krodha(anger), soka(grief), bhoya(fear), harswa(joy), visad(sadness), irswa(envy), manodaina etc are included as the causative factors for the manifestation of different psychiatric disease as well as psychosomatic diseases.\[^2\] The roles of emotional factors like visad have been emphasized by Charaka. Charaka considered visad is to be the important factors among the nanatmaja vata vyadhi.\[^3\] Charaka mentioned that when psychic or somatic disease becomes chronic due to their intensity they may get combined with each other.\[^4\]

Rheumatoid arthritis was well known to ancient Indian physician as Amavata. Madhavakara was the first author who has described Amavata as separate disease entity in his text ‘Rogaviniscaya’ which is later known as ‘Madhava Nidan’.
Rheumatoid arthritis is a multifactorial chronic inflammatory disease affecting primarily the joints with prevalence of between 0.5% - 1%.[5] Arthritis is the most common chronic health problem in our country. Rheumatoid arthritis a more serious chronic condition, usually starts during young adulthood or middle age continue into old age and it can lead to long term joint damage, resulting in chronic pain, loss of function and disability. Pains, physical handicapped, restriction of activities are associated with changes in psychological state and result in anxiety, depression and feeling of helplessness.[6]

According to World Health Organization (WHO) the rate of this disease in the population is 0.6% - 1.3%. Women suffers from Rheumatoid arthritis more often, the ratio of women and men is 3:1. All over the world there are 58 millions patients suffering from Rheumatoid arthritis. Despite the traditional treatment Rheumatoid arthritis results in severe loss of ability to work in 16% of the patients during the first five years of the illness. After 20 years of Rheumatoid arthritis approximately 90% of the patients become invalid.

Anxiety and depression often appears to play a part in the course of chronic illness. It has been reported that people who possess emotional condition like anxiety and depression along with chronic Rheumatoid arthritis are most likely to be candidate for this disease and people with chronic Rheumatoid arthritis who have a healthy psychological balance rarely suffer from this disease.[7]

Ahmet Isik reported in his study that total prevalence of anxiety, depression and anxiety depressive disorder was found to be 70.8% in patient group and 7.3% in control group.[8]

Anxiety and depression may lead to many more longstanding medical problems. A diagnostic evaluation may be necessary to diagnose the emotional disorders like anxiety, depression that may require psycho pharmacological intervention. The proper use of psychopharmacological agents in the management of Rheumatoid arthritis, with anxiety and depression patient still remains unclear. No single treatment that consistently leads to better medical outcome in patients suffering from chronic Rheumatoid arthritis with anxiety and depression has been clearly identified.

T.cordifolia and W.somnifera two plants have been used in many clinical conditions since ancient period. Because of the toxicity and drug dependence of modern synthetic antipsychotic drugs the plants material were prefer in the present study. Thus the therapeutic
measure in relation to patient in Rheumatoid arthritis with anxiety and depression the two plants have been taken into consideration in the present study.

**MATERIAL AND METHODS**

The study was conducted in the department of Basic Principle in Institute of Post Graduate Ayurvedic Education & Research at S.V.S.P in Kolkata. Making use of a randomized double blind placebo control study design, data collected from the consecutive patients receiving treatments from out patient department in I.P.G.A.E & R at S.V.S.P and only those subjects giving valid informed consent were included in the present study. The study was approved by the local institutional ethical committee and procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation.

**Material**

Patients: Rheumatoid arthritis patients with anxiety, depression
Drugs: Guduchi (Tinospora cordifolia)
Ashwagandha (Withania somnifera)

The two drugs are collected from the department of Apothecary in I.P.G.A.E & R at S.V.S.P and properly identified from National Research Institute of Ayurvedic Drug Development, Kolkata.

Chemicals: All the chemicals used in the present study were an analytical grade.

**Methods**

**Selection of patients:** Patients were selected on the basis of the criteria develop by the American Rheumatism Association and finally by the application of various psychological parameters and interview assessed. Collection of biological data, sociodemographical data, and presence of co-morbidity, relevant investigation and treatment received were recorded in case report form.

**Patients with Rheumatoid Arthritis randomly selected from the OPD of I.P.G.A.E&R.:**

Study was performed on 86 consecutive cases diagnosed as rheumatoid arthritis with anxiety, depression. All the patients underwent systemic and rheumatological physical examination.

**Inclusion Criteria**

i. Individuals with irrespective of sex, religion and caste.
ii. Age group of 20-70 years.
iii. Patients satisfy at least 5 diagnostic criteria fixed by the American Rheumatological Association.
iv. Patients suffering from chronic Rheumatoid Arthritis more than 3 years.
v. Patients with Rheumatoid Arthritis to obtain at least 20 score on the Distress symptom scale.

**Exclusion Criteria**

i. Women who are pregnant or breast feeding.
ii. Patients under the treatment of anti-psychotic drug.
iii. Patients treated with other than Ayurvedic medicine.
iv. Patients suffering from chronic psychosomatic diseases other than Rheumatoid Arthritis.

**Total study period:** 18 months

**Medication:** 8 weeks

**Parameters were studied**

The individuals with Rheumatoid Arthritis were assessed for psychiatric disorders according to the criteria of diagnostic & statistical manual of mental disorders (DSM IV). Demographic and social characteristic were reported from information related to age, sex, habitat, education etc.

1. **Assessment Criteria**

a) Psychological parameters
i. Hamilton Anxiety ratings scale (HAM-A)
ii. Hamilton Depression rating scale (HAM-D)
iii. Distress symptom scale.

b) Biochemical Parameter
Blood glucose

c. Subjective Parameter
i. Pain
ii. Morning stiffness
iii. Swelling
iv. Tenderness

**Diagnostic Criteria**

a) Psychological parameters:
i. Hamilton Rating Scale for Anxiety (HAM-A).\textsuperscript{[180]}

ii. Hamilton Rating Scale for Depression (HAM-D).\textsuperscript{[181]}

iii. Distress symptom scale.\textsuperscript{[182]}

iv. Depression Anxiety Stress scale (DASS).\textsuperscript{[183]}

b) Serological

i. RA factor  ii. ASO titre  ii. C-Reactive Protein

Methods used for collection of Psychological factors
Psychiatric datas like anxiety and depression were evaluated by using HAM-A, HAM-D, Distress symptom scale, DASS scale were used to screen for the presence of depressive anxiety disorders.

**Distress Symptom Scale**\textsuperscript{[182]}

It is the most widely utilized diagnostic scale for diagnosis of stress disorders. The distress symptom scale consists of 50 items, it correlates highly with a number of other stress related scale, suggesting that it is a valid measure of symptoms.

**Depression Anxiety & Stress scale (DASS) Scale**\textsuperscript{[183]}

It is widely used psychiatric scale evaluation of depression, anxiety and stress. It is a 42 items self report measure of depression, anxiety and stress.

**Hamilton Rating Scale for Anxiety (HAM-A)**\textsuperscript{[180]}

The Hamilton Anxiety rating scale (HAM-A) is a widely used and well validated tool for measuring the severity of a patients anxiety.

**Hamilton Rating Scale for Depression (HAM-D)**\textsuperscript{[181]}

The Hamilton Depression rating scale (HAM-D) has proven useful for many years as a way of determining a patient’s level of depression before, during and after treatment.
Estimation of Biochemical Parameters

Estimation of Serum Glucose Level\cite{184}

Estimation of Hematological Parameters\cite{188}

Erythrocyte Sedimentation Rate (ESR)\cite{189}

Estimation of Serological Parameter\cite{190,191}

RA factor

Study Design and Medication

Study were performed as randomized double blind placebo control and 75 patients were assigned into 4 groups as follows:-

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Medicine</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>Placebo control</td>
<td>12</td>
</tr>
<tr>
<td>Group B</td>
<td>Powder of T. cordifolia (3gm bid)</td>
<td>18</td>
</tr>
<tr>
<td>Group C</td>
<td>Powder of W. somnifera (3gm bid)</td>
<td>20</td>
</tr>
<tr>
<td>Group D</td>
<td>Powder of T. cordifolia + Powder of W. somnifera (1.5gm+ 1.5 gm = 3 gm bid)</td>
<td>25</td>
</tr>
</tbody>
</table>

Statistical Analysis

The data’s were expressed as mean ± SE., Student paired t-test were used in independent groups for parametric variables. Correlation coefficient were used to compared the categorical variables. P<0.05 was consider as significant. ANOVA test were used for determination of significant in different groups.

Table no. 28: Effect of drugs on various serological parameters.

<table>
<thead>
<tr>
<th>Groups</th>
<th>ESR</th>
<th>Hb%</th>
<th>Blood sugar (F)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BT</td>
<td>AT</td>
<td>BT</td>
</tr>
<tr>
<td>Group A (n=12)</td>
<td>42.01</td>
<td>± 4.64</td>
<td>11.13</td>
</tr>
<tr>
<td></td>
<td>± 3.37</td>
<td>± 2.48</td>
<td>11.00</td>
</tr>
<tr>
<td>Group B (n=18)</td>
<td>41.04</td>
<td>± 2.77</td>
<td>11.07</td>
</tr>
<tr>
<td></td>
<td>± 1.88</td>
<td></td>
<td>11.61**</td>
</tr>
<tr>
<td>Group C (n=20)</td>
<td>41.39</td>
<td>± 2.53</td>
<td>10.98</td>
</tr>
<tr>
<td></td>
<td>± 1.83</td>
<td></td>
<td>11.96***</td>
</tr>
</tbody>
</table>

BT = Before treatment  
AT = After treatment  
P < 0.05 = *  
P < 0.01 = **
Table no. 29: Effect of drugs on different subjective parameters in patients RA.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Pain</th>
<th>Morning stiffness</th>
<th>Tenderness</th>
<th>Swelling</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BT (±)</td>
<td>AT (±)</td>
<td>BT (±)</td>
<td>AT (±)</td>
</tr>
<tr>
<td>GroupA (n = 12)</td>
<td>3.25 ± 0.41</td>
<td>3.58 NS ± 0.45</td>
<td>3.08 ± 0.41</td>
<td>3.16 NS ± 0.50</td>
</tr>
<tr>
<td></td>
<td>3.25 ± 0.47</td>
<td>3.00 NS ± 0.45</td>
<td>2.58 ± 0.45</td>
<td>3.00 NS ± 0.45</td>
</tr>
<tr>
<td>GroupB (n = 18)</td>
<td>3.38 ± 0.39</td>
<td>2.00 *** ± 0.24</td>
<td>3.16 ± 0.34</td>
<td>2.16 * ± 0.29</td>
</tr>
<tr>
<td></td>
<td>3.38 ± 0.37</td>
<td>1.66 ** ± 0.30</td>
<td>2.77 ± 0.45</td>
<td>1.66 ** ± 0.30</td>
</tr>
<tr>
<td>GroupC (n = 20)</td>
<td>3.55 ± 0.38</td>
<td>1.95 *** ± 0.18</td>
<td>2.95 ± 0.34</td>
<td>1.75 *** ± 0.20</td>
</tr>
<tr>
<td></td>
<td>3.55 ± 0.36</td>
<td>1.90 ** ± 0.22</td>
<td>2.90 ± 0.35</td>
<td>1.90 ** ± 0.22</td>
</tr>
<tr>
<td>GroupD (n = 25)</td>
<td>3.44 ± 0.31</td>
<td>1.92 *** ± 0.20</td>
<td>3.12 ± 0.27</td>
<td>2.12 *** ± 0.23</td>
</tr>
<tr>
<td></td>
<td>3.44 ± 0.30</td>
<td>1.52 *** ± 0.17</td>
<td>2.56 ± 0.28</td>
<td>1.52 *** ± 0.17</td>
</tr>
</tbody>
</table>

Anova test

<table>
<thead>
<tr>
<th></th>
<th>BT</th>
<th>AT</th>
<th></th>
<th>BT</th>
<th>AT</th>
<th></th>
<th>BT</th>
<th>AT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significance</td>
<td>P&lt;0.001</td>
<td>P&lt;0.05</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>

BT = Before treatment
AT = After treatment

Table no 30: Effect of Drugs on different Psychological parameters.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Distress symptom scale</th>
<th>Hamilton anxiety scale</th>
<th>Hamilton depression scale</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BT (±)</td>
<td>AT (±)</td>
<td>BT (±)</td>
</tr>
<tr>
<td>GroupA (n = 12)</td>
<td>47.66 ± 4.41</td>
<td>47.75 NS ± 4.59</td>
<td>16.91 ± 2.10</td>
</tr>
<tr>
<td></td>
<td>14.25 ± 1.78</td>
<td>14.91 NS ± 1.72</td>
<td></td>
</tr>
<tr>
<td>GroupB (n = 18)</td>
<td>46.83 ± 2.20</td>
<td>43.55 ** ± 1.72</td>
<td>17.77 ± 1.89</td>
</tr>
<tr>
<td></td>
<td>13.38 ± 1.58</td>
<td>10.72 ** ± 1.02</td>
<td></td>
</tr>
<tr>
<td>GroupC (n = 20)</td>
<td>45.05 ± 2.69</td>
<td>40.80 *** ± 2.28</td>
<td>17.90 ± 2.03</td>
</tr>
<tr>
<td></td>
<td>14.05 ± 1.22</td>
<td>11.00 *** ± 0.69</td>
<td></td>
</tr>
<tr>
<td>GroupD (n = 25)</td>
<td>47.64 ± 2.91</td>
<td>44.32 *** ± 2.42</td>
<td>17.00 ± 1.33</td>
</tr>
<tr>
<td></td>
<td>14.64 ± 1.28</td>
<td>11.48 *** ± 0.78</td>
<td></td>
</tr>
</tbody>
</table>
BT = Before treatment  AT = After treatment

\[ P < 0.05 = * \]

P<0.05, considered as significant

\[ P < 0.01 = ** \]

\[ P < 0.001 = *** \]

\[ P > 0.05 = NS \]

**OBSERVATIONS AND RESULTS**

*Socio-demographical profile*

**Clinical Trial**

Study was conducted on 86 individuals diagnosed as RA with anxiety and depression and 41 age, sex matched individuals involved as healthy control group. Out of 86 individuals 11 patients were drop out before the completion of clinical trial. Finally results of the clinical trial of 75 patients summarized into 4 groups.

GroupA (n=12) serve as control group treated with rice grain powder (3gm), GroupB (n=18) treated with powder of T.cordifolia(3gm), Group C (n=20) treated with W.somnifera(3gm) and GroupD (n=25) combined treated in combination with T.cordifolia and W.somnifera (1.5gm + 1.5gm).

There were significant increases in ESR level, significantly decreases in Haemoglobin(gm %) in individuals with Rheumatoid Arthritis as compared their corresponding values of healthy control.

The level of anxiety, depression and mixed anxiety depressive disorders were significantly increased in different psychological rating scale in comparison to healthy control group.

Concentration of haemoglobin (gm %) of blood at before and after treatment presented in in table no17 and fig no.21. The haemoglobin percentage level significantly elevated in groupD (P<0.001) treated with both T.cordifolia & W.somnifera, in groupB (P<0.01) and groupC (P<0.01). But no significant changes were observed in placebo control groupA (P>0.05).

Concentration of fasting blood sugar at before and after treatment presented in in table no18 and fig no.22. The serum blood sugar level significantly decreased in groupB (P<0.001) and groupC(P<0.001) and followed by groupD (P<0.01).
Efficacy of different drugs on ESR level presented in table no.19 and fig no.23. There were significant decrease in ESR level in groupD (P<0.001) followed by groupB (P<0.01) and groupC (P<0.01). Whereas no significant changes of ESR level were found in placebo control groupA (P>0.05).

Efficacy of different drugs on pain in Rheumatoid Arthritis patients with anxiety and depression is presented in table no.20 fig no. 24. A significant reduction of pain scoring was found in groupB (P<0.001), groupC (P<0.001), groupD (P<0.001). Whereas no significant reduction was found in placebo control groupA (P>0.05) which was statistically insignificant.

Efficacy of different drugs on morning stiffness in Rheumatoid Arthritis patients with anxiety and depression is presented in table no21. fig no.25. A significant changes of scoring of morning stiffness was found in groupD (P<0.001) and groupC (P<0.001), followed by groupB (P<0.05). Where as no significant changes were observed in placebo control groupA (P>0.05).

The effect of different drugs on tenderness in RA patients with anxiety, depression is presented in table no.22 fig no.26. A significant score reduction was found in groupC (P<0.001), groupD (P<0.001), groupB (P<0.01). Whereas no significant reduction was found in placebo control groupA (P>0.05).

The effect of different drugs on swelling in RA patients with anxiety & depression is presented in table no.23 fig no.27 A significant score reduction was found in groupD (P<0.001), followed by groupB (P<0.01), & groupC (P<0.01). Whereas no significant score reduction was found in placebo control groupA (P>0.05).

The effect of different drugs on scoring of distress symptom scale in patients with RA presented in table no.24 and fig no.28. A significant score reduction was found in groupC (P<0.001) treated with W.somnifera followed by groupD (P<0.001) treated with T.cordifolia and W.somnifera and groupB(P<0.01) treated with T.cordifolia. Whereas no significant changes were found in placebo control groupA (P>0.05).

The effect of different drugs on scoring of Hamilton Depression scale in patients with RA presented in table no.25 and fig no29. A significant score reduction was found in groupC (P<0.001) and groupD (P<0.001) followed by groupB(P<0.01). Whereas no significant changes were found in placebo control groupA (P>0.05).
The effect of different drugs on scoring of Hamilton Anxiety scale in patients with RA presented in table no.26 and fig no.30. A significant score reduction was found in groupD (P<0.001) treated with T.cordifolia and W.somnifera followed by groupC (P<0.01) treated with W.somnifera and groupB (P<0.05) treated with T.cordifolia. Whereas no significant changes were found in placebo control groupA (P>0.05).

DISCUSSION

The review of ancient Ayurvedic literature on manodaihik siddhanta indicates that the psychosomatic approach in Ayurveda has been established before the study of modern psychology. Many references are being given in the literary part of the work in order to elucidate the fact that ancient Ayurvedic scholars were well acquainted with the fundamentals of psychosomatic medicine.

The sociodemographical data of individuals with Rheumatoid Arthritis showed that the incidence of Rheumatoid Arthritis is higher in female, with female to male ratio is 3:1. These findings are very much consistent with the findings of our present study. It is well known factor that sex hormone may have a key role in the genesis of Rheumatoid Arthritis. Sex influence like many other autoimmune diseases Rheumatoid Arthritis occurs more commonly in female than in male 3:1 ratio. Given these preponderance of female, various theories have been proposed to explain the possible role of estrogen in disease pathogenesis. Most of the theories centre on the role of estrogen in enhancing the immune response. Some experimental studies have shown that estrogen can stimulate production of tumour necrosis factor TNF α, a major cytokine in the pathogenesis of Rheumatoid Arthritis.\[196\]

In the present study the prevalence of anxiety and depression in patients with Rheumatoid Arthritis were found maximum in 38.67% are found in middle age group. The age distribution of the patients reveals that the prevalence of the disease is more in middle age group. The best available data suggests that incidence of Rheumatoid Arthritis in women increases with age until approximately one third that in women, but increases steadily age and approaches that of women older than 65 years. The prevalence of Rheumatoid Arthritis increases with each decade.\[197\]

Total prevalence of anxiety, depression and stress disorder are found to be 66.15% (n=86). The present study showed that the anxiety and depression were significantly higher in patients group comparing to healthy control group. These findings are very much consistent
with the study of Ahmet Isik, Suleyman Serdar Koca reported in the study that the total prevalence of anxiety, depression and mixed depressive disorders were found to be 70.8% in the patients group.\[200\]

The present study highlighted the co morbidity of anxiety, depression and stress with Rheumatoid Arthritis. The prevalence of anxiety, depression and stress was found to be anxiety (26.66%), depression (56%) and stress (32%).

The chronicity and recurrent attack of disease as well as pain, restricted movement of the effected joints are the possible for possess of anxiety & depression with individuals of Rheumatoid Arthritis. In the present study there were positive correlation between pain & depression (P<0.01), pain & depression (P<0.01) which suggested that the impact of pain in patients with Rheumatoid Arthritis raise a key role for manifestation of anxiety & depression.

The above findings of the present study very much consistent in the study of Barow J.H, Cullen L.A reported that pain, physical disability & restriction of activities are associated with changes in psychological state and results in anxiety, depression.

Depression commonly co-occurs with Rheumatoid Arthritis in the range of 13-14%.\[201\]

It is likely that the depression and anxiety influence Rheumatoid Arthritis were different mechanism. A recent study found both to have a direct effect on pain, although the direct effect effect of anxiety was significantly have than that of depression.\[202\]

Stress results in changes in the connective tissue structures, disturbance of the endocrine system, suppression of the immune system. At the same time it is shown that the stabilization of the patients psychic state results in the positive changes in the immunological status.\[203\]

It was observed in the present study that the serum glucose level was significantly elevated almost in all groups in comparison to healthy control group. The elevation of glucose concentration in anxiety, depression in patients with Rheumatoid Arthritis due to presence of general stress condition which contribute to greatly enhance the secretion of ACTH. Cortisol induced insulin resistance and gluconeogenesis that comes increase concentration of serum glucose.

The serum blood glucose significantly reduced in groupB and groupC (P<0.001) treated with T.cordifolia and W.somnifera repectively.
Dhaliwal.K.S reported that the T.cordifolia has significant role in reduction of blood glucose.\[^{143}\]

Raghunathan.K, Sharma.P.V reported in their experimental study that T.cordifolia has a potent antidiabetic activity.\[^{142}\]

A recent research finding suggested that administration of extract of T .cordifolia roots for 6 weeks resulting in significant reduction in serum and tissue cholesterol, phospholipids and frees fatty acid in alloxan diabetic rats.\[^{204}\]

A significant reduction in pain scoring was found in group B, group C, and group D in our present study. It may be due to anti inflammatory action of W.somnifera and T. cordifolia.

Wesley J J, Christina A.J, Chidambaranathan N, showed that alcoholic extract of T.cordifolia has been found to exert anti-inflammatory action in models of acute & sub-acute inflammation.\[^{138}\]

Another study carried out on anti-inflammatory of Ashwagandha reported that Withaferin A exhibits fairly potent anti-arthritic & anti-inflammatory activities. Anti-inflammatory activity has been attributed to biologically active steroids of which Withaferin A is a major component.\[^{167}\]

A significant psychiatric rating score reduction was found in Hamilton anxiety scale, Hamilton depression scale and widely used Distress symptom scale after the administration of powder of stem of T.cordifolia and powder of root of W.somnifera.

Therefore the findings of the above information indicates that the herbal agents T .cordifolia and W.somnifera have a significant adaptogenic and anti stress activity as shown by its integrating effects on several psychological, bio chemical perturbation.

The above findings suggest that the T.cordifolia, and W.somnifera not only possesses anti inflammatory and anti psychotic potency but also they significantly reduces serum lipid and serum glucose level in different trial group.

**SUMMARY AND CONCLUSION**

The present study concluded that anxiety and depression symptoms are common in patients of Rheumatoid arthritis. It was observed in our present study that prevalence of anxiety and
depression were higher in Rheumatoid arthritis group than healthy control group, regardless of whether they are consider separately or as a combined construct. Patients of Rheumatoid arthritis with anxiety and depression co morbidity tend to have more chronic and recurrent form of illness that require long term treatment. These puts a premium on medication such as guduchi (T.cordifolia) and ashwagandha(W.somnifera) that have broad spectrum efficacy wide therapeutic windows and are well tolerated in terms of side effect, contributing to compliance with long term treatment. Last of all the present study conclude that psychosomatic concept of ancient literature in Ayurveda are very much systematic, methodical and somewhere it is outstanding in respect to modern view.

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