Journal of Stress Physiology & Biochemistry, Vol. 7 No. 1 2011, pp. 66-78 ISSN 1997-0838

ORIGINAL ARTICLE

EVALUATING THE CLINICAL EFFICACY OF A POLYHERBAL FORMULATION AROGH PLUS ON STRESS – A RANDOMISED CLINICAL STUDY

Anoop Austin[1], Elsie C.S.[2] and Thirugnanasambantham P.[2]

[1] *Rumi Herbals R & D centre, 40/41, Spartan Avenue, Mugappair East, Chennai – 600 037 India*

[2] *Rohini Holistic Health Centre, 40/41, Spartan Avenue, Mugappair East, Chennai – 600 037 India*

[1] For correspondence and reprints: E-mail : anoopaustin@gmail.com

Received February 3, 2010

Background : Stress is a common entity, widely spoken about among the working population, for which a safe and effective remedy is needed.

Purpose of the study : To evaluate the clinical effectiveness of Arogh plus a polyherbal formulation, towards stress relieving properties in a randomized clinical trial in volunteers.

Results : Ten volunteers from Marketing field, evaluated to be under stress, completed the full course. All were clinically evaluated based upon symptoms, anthropometric evaluation, hematological, diabetic and serum cortisol and urine profile. All the parameters were evaluated during 0 day, 15th day, 30th day and on 45th day after stopping the drug internally. Three grams of Arogh plus was given twice daily for a period of 30 days was found to decrease symptoms due to stress and the benefits was reinforced by way of significant reduction in serum cortisol with a reduction of 36.99 % within a month.

Conclusion :Arogh plus is an effective formulation in relieving stress and improving the quality of life.

Key words: Arogh Plus / Polyherbal / Stress / Cortisol / Anxiety

ORIGINAL ARTICLE

EVALUATING THE CLINICAL EFFICACY OF A POLYHERBAL FORMULATION AROGH PLUS ON STRESS – A RANDOMISED CLINICAL STUDY

Anoop Austin[1], Elsie C.S.[2] and Thirugnanasambantham P.[2]

[1] *Rumi Herbals R & D centre, 40/41, Spartan Avenue, Mugappair East, Chennai – 600 037 India*

[2] *Rohini Holistic Health Centre, 40/41, Spartan Avenue, Mugappair East, Chennai – 600 037 India*

[1] For correspondence and reprints: E-mail : anoopaustin@gmail.com

Received February 3, 2010

Background : Stress is a common entity, widely spoken about among the working population, for which a safe and effective remedy is needed.

Purpose of the study : To evaluate the clinical effectiveness of Arogh plus a polyherbal formulation, towards stress relieving properties in a randomized clinical trial in volunteers.

Results : Ten volunteers from Marketing field, evaluated to be under stress, completed the full course. All were clinically evaluated based upon symptoms, anthropometric evaluation, hematological, diabetic and serum cortisol and urine profile. All the parameters were evaluated during 0 day, 15th day, 30th day and on 45th day after stopping the drug internally. Three grams of Arogh plus was given twice daily for a period of 30 days was found to decrease symptoms due to stress and the benefits was reinforced by way of significant reduction in serum cortisol with a reduction of 36.99 % within a month.

Conclusion :Arogh plus is an effective formulation in relieving stress and improving the quality of life.

Key words: Arogh Plus / Polyherbal / Stress / Cortisol / Anxiety

Stress was first coined by Hans Selye during 1930's, which referred to the consequence of failure to respond appropriately to emotional or physical threats, whether actual or imagined. In recent past,

this has become a commonplace of popular parlance (Selye, 1956). The symptoms commonly include a state of alarm and adrenaline production, short-term resistance as a coping mechanism, and exhaustion, as well as irritability, muscular tension, inability to concentrate and a variety of physiological reactions such as headache and elevated heart rate (Bernard and Krupat, 1994). Sheldon *et al.* (2007) reported that stress is one of the largest Killer of man today, which is becoming, more accepted as being crucially related to our physical, mental and emotional health, So reducing the stress level can not only protect from diseases but can also enhance our quality of life enormously (Thoits, 2010).

Tranquilizers, antidepressants and anti-anxiety medications are widely prescribed in stress management (Anonymous, 2000), but the incidence of toxicity and dependence has limited the therapeutic usage of those drugs (Moncrieff *et al*., 2010). Herbal formulations have been in use for many years not only in Asian countries but also globally for human well-being. The herbal formulations claimed to enhance physical endurance; mental functions and non-specific resistance of the body have been reported to possess anti-stressor (Archana and Namasivayam, 1999) and "adaptogenic" properties (Saggu *et al.*, 2007), as well as the ability to affect the hypothalamic-pituitary-adrenal axis (Al-Qarawi *et al.,* 2002). The potential utility of safer and cheaper herbal medicines as antistress agents have been reported as they can withstand stress without altering the physiological functions of the body (Naik *et al.,* 2006). Various herbs like *Asparagus racemosus, Bacopa monnieri*, *Centella asiatica*, *Emblica officinalis, Hypericum perforatum, Matricaria recutita, Mentha piperita, Nepeta cataria, Ocimum sanctum, Passiflora incarnate, Piper methysticum, P. longum Tribulus terrestris, Valeriana officinalis* and *Withania somnifera* are claimed to have immunomodulatory, adaptogenic and anabolic effects along with the ability to improve vital energy (Naik *et al.,* 2006; Bansal and Yadav, 2010). Though herbal medicines are known to act synergistically in combination (Toews and Bylund, 2005), only limited work has been carried out on poly herbal formulation for Stress. With this basis this study was initiated.

Arogh plus, is one such herbal Instant formulation manufactured by Rumi Herbals Pvt. Ltd, Chennai, containing *Nelumbo nucifera, Hibiscus rosa-sinensis, Rosa alba, Terminalia chebula, Hemidesmus indicus, Glycyrrhiza glabra*, *Zingiber officinale*, *Quercus infectoria* and *Eclipta alba.* Detailed studies have revealed its therapeutic efficacy on hypercholesteremia (Anoop Austin *et al.,* 2006; Ganesh *et al.,* 2006; Asokan *et al.,* 2010), arthritis (Mohan *et al.,* 2009), Stress and anxiety (Balaraman *et al.,* 2007), Myocardial infraction (Suchalatha and Shyamala Devi, 2004) and Oxidative stress (Suchalatha *et al.,* 2004). With this basis, a randomized clinical trial was carried out on the formulation, to evaluate its clinical efficacy, by way of evaluating their performance, Physical and mental characteristics, and blood and hormonal investigation to have an better insight and understanding its effectiveness in volunteers under stressful situation.

Materials and Methods:

Arogh Plus, an Ayurvedic polyherbal formulation, gifted by M/s. Rumi Herbals Pvt. Ltd., Chennai was subjected for a detailed randomized clinical trial at Rohini Holistic Health Centre, Chennai during the period of July to September 2010. A detailed clinical protocol was prepared and was approved by the Institutional Human Ethics committee. The study was carried out on the

volunteers, who were working in marketing field for more than five years. After receiving their consent, they were explained about the entire study and, after acceptance, they were included for the study. The study was organized for a period of 30 days and those who completed the study were only included for evaluation.

The volunteers evolved to be under stress who were included in this study, administered 3 gm of powder (1 Sachet full) twice daily, morning and evening, dissolved in warm water for a period 30 days. Any specific diet schedule was not prescribed to the volunteers. All volunteers involved in the study were thoroughly screened on 0 day, 15th day and 30th day. After completion of the study period on 45th day all volunteers were again subjected to all parameters again.

Ten human volunteers diagnosed to be under stress were selected, for this present randomized study. All patients selected for this study were interrogated and a detailed history was recorded in the prescribed case history sheet. The individual who have symptoms of stress disorders with or without raised serum cortisol levels, were subjected to clinical trial. Out of 12 volunteers selected, 10 completed the full treatment schedule (i.e., 30 days) and they were only taken for the full evaluation in this study. The clinical pattern (Fait *et al*., 2006) were studied in all 10 cases for incidence of age, sex (male & female), religion, occupation, economic status, educational status, social status and symptoms of stress disorders following the incidence of blood cortisol (Mattingly *et al.,* 1989) and routine examination of Blood, Stool and Urine (Burtis *et al.,* 2006) were carried out, in addition, to the observation, of subjective features. Clinical symptoms *viz.,* Anorexia, Apprehension, Breathlessness, Constipation, Diarrhea, Disinterest of life, Dizziness, Fatigue, Frequency of micturation, Headache, Hopelessness/Helplessness, Inability to work, Insomnia, Lack of concentration, Lack of self confidence, Loss of libido, Loss of weight, Pain-chest/Abdomen, Recurrent thought for death /suicide, Slowing of thinking, Slowing of speed, Skin rashes /ulcer, Sweating and Tremor were analysed during each visit on 0 day, 15th day, 30th day and after 45th day in all the volunteers (Fait *et al*., 2006). The observations made out of the investigations, are statistically expressed as the means ± standard error of the means (S.E.M.) and statistical analysis was carried out using student's *t*-test (O'Mahony and Michael, 1986).

Results:

The present study consists of total 10 volunteers, who have symptoms of stress disorders and completed the full course of treatment schedule (i.e. 30 days). Though we had registered 12 cases for the present study, only 10 volunteers (5 male and 5 female) completed the full course of treatment, and they only were included in the complete study. So the clinical pattern will be discussed with the observations and investigation carried out with those ten cases, only.

The volunteers involved in the present study ranged within the age group of 20 to 60. 1 male (10 %) and 4 females (40 %) were between 21 to 30 years age, 1 male (10 %) between 31-40 and 1 (10 %)female between 41-50 age group and 3 (30 %) males between 51 – 60 age group participated in the study. Out of the 10 volunteers, 5 were males (50 %) and the remaining were females (50 %). Their occupation status revealed that all were working and the 5 females (50 %) involved in the study were housewives, with their economic status revealing 1 male (10 %) in low income and 3 males (30 %) and

5 females (50 %) in middle class group and 1 male (10 %) in high class group.

The volunteers involved in the study were from Urban area and 1 male (10 %) and 1 female (10 %) completed Higher Secondary education, 2 male (20 %) and 3 females (30 %) completed their graduation, 1 male (10 %) and 1 female (10 %) completed their post graduation and 1 male (10 %) completed his doctorate. The volunteers involved in the study were all non vegetarians. The nature of work among the volunteers differed to an extent, where, 2 males (20 %) and 1 female (10 %) had sedentary work style, 2 males (20 %) and 2 females (20 %) had moderate and active work culture and 1 male (10 %) and 2 females (20 %) were striving hard in their work nature. Among the group 1 female (10 %) was unmarried and remaining 5 males (50 %) and 4 females (40 %) were married.

The observations pertaining to clinical symptoms and their observations before and after the treatment were found to be interesting with respect to the degree of reduction in symptoms, which are well elicited in Table 1. From this it is interesting to observe that more than 70 % of relief was observed in symptoms like apprehension, breathlessness, constipation, disinterest of life, frequency of micturition, headache, insomnia, lack of concentration, lack of self confidence, suicidal tendency, slowing of thinking, and tremor. More than 50 % of relief was observed in symptoms like dizziness, fatigue, hopelessness/helplessness, inability to work, slowing of speed and sweating. In other symptoms, the relief found was less than 50 %.

The improvements on objective features like anthropometric evaluation (Table 2), Hematological, Diabetic and Serum Cortisol profile (Table 3) and urine profile (Table 4) revealed many interesting findings. Anthropometric evaluation revealed that Arogh Plus did not alter the observed parameters like the height, weight, BMI, respiration, pulse, blood pressure and Rapid Eye Movement (REM), within the short span of treatment time. The total count was found to be significantly increased, which reverted after the ingestion period, signifying the improvement of immune system (LaFleur-Brooks, 2008). Among the study group two were Type II diabetics, and were under OHA. Their diabetic control was not significant and that was found to reflect in the borderline in glycated haemoglobin level. Serum cortisol was found to be decreasing during the course of treatment and which are reverted after discontinuing the treatment. The cortisol level was found to be more pronounced in normal individuals where the percentage of decrease was observed to be 36.99 % with a month time, whereas in those 2 diabetic persons the serum cortisol was found to be 9.1 ± 1.7 on 0 day, 7.9 ± 1.43 on 15^{th} day, 7.6 ± 1.55 on 30^{th} day and reverted to 8.2 ± 1.55 after the treatment period suggesting only 16.48 % of reduction on the 30^{th} day, which is more significant from the study. Urine analysis revealed an interesting finding in reducing the deposit level, which needs further evaluation. Further there was no undesired effects observed during the course of study with the drug and revealed the safety of the formulation.

Discussion:

Stress is a common problem which might reflect by way of cognitive, emotional, physical or behavioural changes (Gallo and Matthews, 2003). Stress can result in poor judgement, negative outlook, excessive worrying, moodiness, irritability, agitation, inability to relax, feeling lonely, isolated or depressed, aches and pains, altered bowel habits, nausea, dizziness, chest pain, rapid heartbeat, eating

too much or not enough, sleeping too much or not enough, social withdrawal, procrastination or neglect of responsibilities, increased alcohol, nicotine or drug consumption, and nervous habits such as pacing about or nail-biting (Hawkley and Cacioppo, 2003).

Arogh Plus, a polyherbal formulation was evaluated clinically in volunteers working under stressful situation and revealed many interesting finding. Daily intake of the formulation for a period of continuous 30 days was found to decrease the symptoms observed due to stress, which was reduced and their work performance was found to be increased.

Table 1. Response of treatment on subjective criteria

Sl. No.	Symptoms	Number of Patients before treatment	Number of Patients after treatment	Percentage of relief
1	Anorexia	6	4	33.33
2	Apprehension	9	2	77.78
3	Breathlessness	2	0	100
4	Constipation	2	0	100
5	Diarrhea	0	0	0
6	Disinterest of life	2	0	100
7	Dizziness	3	1	66.67
8	Fatigue	5	2	60
9	Frequency of micturation	3	0	100
10	Headache	4	1	75
11	Hopelessness/Helplessness	2	1	50
12	Inability to work	6	2	66.67
13	Insomnia	1	0	100
14	Lack of concentration	6	1	83.34
15.	Lack of self confidence	4	1	75
16.	Loss of libido	0	0	0
17.	Loss of weight	0	0	0
18.	Pain-chest/Abdomen	0	0	0
19.	Recurrent thought for death /suicide	1	0	100
20.	Slowing of thinking	4	1	75
21.	Slowing of speed	3	1	66.67
22.	Skin rashes /ulcer	1	0	100
23.	Sweating	6	2	66.67
24.	Tremor	5	1	80

Clinical features observed from stressed individual, among the 10 volunteers

Table 2. Anthropometric Parameters

Sl. No	Anthropometric Parameters	0 day	15 days	30 days	45th day
1	Height	63.8 ± 1.26	63.78 ± 1.26	63.78 ± 1.26	63.78 ± 1.26
2	Weight	68.5 ± 46.8	68.6 ± 4.83	68.05 ± 4.67	68.2 ± 4.59
3	BMI	25.8 ± 1.33	26.02 ± 1.37	25.82± 1.33	25.68± 1.31
4	Pulse rate	74.6 ± 1.8	74.4 ± 1.68	73.6 ± 1.76	73.6 ± 1.76
5	Respiratory rate	18.5 ± 0.44	18.4 ± 0.4	18.4 ± 0.4	18.3 ± 0.4
6	Temperature, ^{0}F	98.4 ± 0	98.4 ± 0	98.4 ± 0	98.4 ± 0
7	Systolic blood Pressure	128.0 ± 2.59	124 ± 3.07	122 ± 2.11	122 ± 1.67
8	Diastolic blood Pressure	84 ± 1.52	82 ± 2.15	80 ± 1.58	80 ± 1.39
9	REM	4.3 ± 0.47	3.5 ± 0.17	3.2 ± 0.13	3.8 ± 0.20

Results are expressed in mean ± SEM, where n = 10,

BMI – Body Mass Index, REM – Rapid Eye Movement

Table 3. Hematological, diabetic and serum cortisol profile

Sl. No	Parameters	0 day	15 days	30 days	45th day
1	Total Count	8450 ± 361.74	8320 ± 364.17 *	8850 ± 709.81 ***	8480 ± 536.82
2	Differential Count				
a	Polymorph	56.9 ± 1.61	56.2 ± 1.59	59.6 ± 1.88	58.0 ± 1.39
b	Lymphocytes	36.2 ± 1.77	41.2 ± 1.55	37.6 ± 1.94	39 ± 1.32
c	Eosinophil	2.7 ± 0.19	2.6 ± 0.27	2.8 ± 0.44	2.8 ± 0.46
d	Monocytes	0.2 ± 0	0 ± 0	0 ± 0	0.2 ± 0
3	ESR	16.8 ± 3.6	17.4 ± 3.35	16.7 ± 3.35	16.6 ± 3.61
4	Hb %	13.2 ± 0.44	13.38 ± 0.55	13.54 ± 0.54	13.6 ± 0.55
5	MCV	83.8 ± 1.17	82.79 ± 1.14	83.66 ± 1.14	83.82 ± 1.18
6	MCH	28.3 ± 0.51	28.26 ± 0.57	29.94 ± 0.54	29.76 ± 0.55
7	Sugar (F)	99.4 ± 10.18	92.6 ± 7.31	93.5 ± 7.53	103 ± 10.22
8	Glycated Hb%	5.8 ± 0.25	5.74 ± 0.22	5.89 ± 0.2	5.85 ± 0.25
9	Serum Cortisol	9.3 ± 0.54	6.30 ± 0.22 *	5.86 ± 0.2 *	7.83 ± 0.25

Results are expressed in mean ± SEM, where n = 10,

*p<0.05, ***p<0.001, as compared to control

Table 4. Urine analysis

Sl. No	Parameters	0 day	15 days	30 days	45th day
1	Albumin	NIL	NIL	NIL	NIL
2	Sugar	NIL	NIL	NIL	NIL
3	Deposits	3.3 ± 0.18	2.8 ± 0.15	2.0 ± 0.11	1.8 ± 0.11 ***

Results are expressed in mean ± SEM, where n = 10,
***p<0.001, as compared to control
NIL - absent

Haematological studied revealed an significant change in the Total count, during the treatment period, which is considered to increase immunity (LaFleur-Brooks, 2008), which needs further studies. But findings have suggested that reverting stress will also improve the immunity and the sense of well being (Avitsur *et al.,* 2006). During exertion, the sympathetic nervous system stimulates splenic contractions, which increase total counts, supporting the claims of reduced stress (Rose and Allen, 1985).

Cortisol is often used as an indicator of stress due to stimulation of the hypothalamic-pituitary-adrenal axis (Roshan e*t al.,* 2010), which is a common physiological response to various stressors. The effect of stress on central nervous system and hypothalamic-pituitary-adrenal axis includes an increase in cortisol, and a disruption in circadian rhythm of cortisol secretion (Roshan e*t al.,* 2010). A reduction in cortisol during the study period can be interpreted as a reduction of stress (Stull and Rodiek, 2002) and in turn will increase catecholamine neuro transmitters, such as serotonin and dopamine (Field *et al.,* 2005), which will also help in stress relieving, but needs a detailed evaluation.. Further decreased levels of cortisol, on long-term can prevent neuronal damages (Spiegel *et al.*, 1999). The difference of lowering the cortisol level in diabetics is due to the metabolic derangement, which has affected the decrease in cortisol level and it clearly illustrates the poor response in the diabetic group, which is highly warranted.

The effectiveness of the formulation on Stress can be attributed to its synergestic activity (Toews and Bylund, 2005). Various studies carried out on the ingredients were also found to be strengthening the claims. Compounds 3-O-beta-d-glucopyranoside and Qc 3-O-beta-d-glucuronopyranoside isolated from *N. nucifera* was responsible for relieving stress (Jung *et al.,* 2008) and *H. rosa-sinensis* was able to relieve oxidative stress in ischemic reperfusion injury (Nade *et al.,* 2010) and hypotensive (Nade *et al.,* 2009). *N. nucifera* (Chopra *et al.*, 1969) and *Z. officinale* (Bone and Gupta, 1997) are found to be cardotonics and hypertensive's. The vasodilation, positive inotropic, and cardioprotective activity of *H. indicus* and *H. rosa-sinensis* were reported by Vinoth *et al.,* (2010). *T. chebula* has been reported to act directly on the heart muscle (Srivastava *et al.,* 1991), where negative chronotropic, inotropic and hypotensive responses observed might protect the myocardium by decreasing its overload (Vinoth *et al.,* 2010). In support to this observation, previous study carried out on the formulation by Balaraman *et al.* (2007) also proved the anxiolytic activity of the formulation in albino rats, *by virtue* of its

diminished serotonergic transmission and decreased duration of catalepsy indicating potentiation of dopaminergic transmission and modified 5-HT and DA mediated behaviour.

The antioxidant, anti inflammatory and free radical scavenging properties of *G. glabra* (Alam and Gomes, 1998), *T. chebula* (Aeshbaech *et al.,* 1994), *H. indicus* (Chandra *et al.,* 1987), *Z. officinale* (Sreeramamurthy *et al.,* 1993), *E. alba* (Kim and Hong, 1996) might synergistically enhance the efficacy of Arogh Plus to scavenge the free radicals, minimize lipid peroxidation, thereby preventing membrane damage and leakage of enzymes. Body functions, including cellular respiration depends on the oxygen supply, which can be attributed by its antioxidant and free radical properties is justified.

The antioxidant effects of *H. indicus* (Rao, *et al.,* 2005) may be associated with tannins (Hong *et al.,* 1995), one of the main constituents. Likewise, saponins have also been shown to have beneficial effects on cardiovascular diseases (Matsuura, 2001). Flavonoids produce vasodilation by regulating endothelial nitric oxide (NO) production (Schmitt and Dirsch, 2009) and interaction with ion channels (Akhlaghi and Bandy, 2009). Moreover, flavonoids are known to protect the I/R-induced myocardial injury by their multifaceted properties, such as antioxidant, antiinflammatory, vasodilatory, and antiplatelet aggregation (Akhlaghi and Bandy, 2009). Therefore, it is conceivable that the cardioprotective effect can be related to the combined effects of saponins, tannins, and flavonoids. *H. rosa-sinensis* has been shown to enhance the endogenous antioxidant activity and protect the heart from isoproterenol-induced injury (Karunakaran *et al.,* 2006). The interpretations made with the ingredient were also in line with the observations made by Suchalatha *et al.* (2004), where the drug was able to possess inhibition of lipid peroxidation, maintaining the levels of superoxide dismutase and catalase, enhancing the activity of glutathione peroxidase and glutathione-s-transferase, which can scavenge superoxide radicals and prevent free radical formation and lipid peroxidation.

G. glabra present in the formulation is a proven adaptogen (Winston and Maimes, 2007), which is capable of increasing succinate dehydrogenase [SDH] in brain and decreasing brain neurotransmitters like norepinephrine (NE), dopamine (DA), serotonin (5-HT) and acetylcholine (ACh) (Deore and Khadabadi, 2009) and decrease in beta-endorphin level (Gregory and. Kelly, 2001).

The study clearly elucidates that Arogh Plus, as a suggestive drug in treating stress by *virtue* of its cortisol lowering activity, antioxidant and free radical properties, thereby influencing the neurotransmitters. The limitation of this study is that it has carried out in a small selected group and further detailed investigations, with respect to various neurotransmitters, in a large group and cross over studies will through more light on the effectiveness of the formulation.

Conclusion

Arogh Plus, is found to reduce the stress by *virtue* of its cortisol lowering activity in a short duration of 30 days, and can be taken to relieve stress and improve their quality of life.

Acknowledgments:

The authors are thankful to M/s. Rumi Herbals Pvt. Ltd., Chennai for supplying the study material and funding to carry out the study.

References

Aeshbaech, R., Loliger, J., Scott, B.C., Murcia, A., Butters, J., Halliwell, B. and Arouma, O.I. (1994) Antioxidant activities of thymol, carvacrol, 6-gingerol, zingerone and hydroxytyrosol. *Food Chem. Tox.*, **32** : 31-36.

Akhlaghi M. and Bandy, B. (2009) Mechanisms of flavonoid protection against myocardial ischemia-reperfusion injury. *J. Mol. Cell. Card.,* **46** : 309–317.

Alam, M.I. and Gomes, A. (1998) Viper venom induced inflammation and inhibition of free radical formation by pure compound (2-hydroxy-4 methoxy benzoic acid) isolated and purified from *H. indicus* root extracts. Toxicon., **36** : 207-215.

Al-Qarawi, A.A., Abdel-Rahman, H.A. Ali, B.H. and El Mougy. S.A. (2002) Liquorice (*Glycyrrhiza glabra*) and the adrenal-kidney-pituitary axis in rats, *Food Chem. Tox.*, **40** : 1525 - 1527.

Anonymous, (2000) United States Department of Health and Human Services. Healthy People 2010, Washington, DC.

Anoop Austin, Senthilvel, G., Thirugnanasamb-antham, P. and Mayisvren, E. (2006) Clinical efficacy of a Polyherbal Instant Formulation (Arogh) in the management of Hyperlipid-aemia. *Cardiol.,* **2** : 36-38.

Archana, R. and Namasivayam. A., (1999) Antistressor effect of *Withania somnifera. J. Ethnopharmacol.,* **64** : 91 - 93.

Asokan, B.R, Jaikumar, S, Ramaswamy, S, Thirugnanasambantham, P. and Nirmala, P. (2010) Anti-hyperlipidemic activity of a polyherbal formulation in experimental models. *Pharmacologyonline*, **1**: 433-442.

Avitsur, R., Padgett, D.A. and Sheridan, J.F. (2006). Social interactions, stress and immunity. *Neurol. Clin.*, **24** : 483 - 491.

Balaraman, R., Mohan, M, Aurangabadkar, V.M., Jadhav, G.B., Anoop Austin and Thirugnanasambatham P. (2007) Effect of a polyherbal formulation on anxiety and behavior mediated via monoamine neurotransmitters, *OPEM*, **7** (4) : 409 – 417.

Bansal, N. and Yadav, S. (2010) Stress the Stress. *Int. J. Pharm. Biosci.*, **1** : 686 – 693.

Bernard, L. C. and Krupat, E. (1994) *Health Psychology: Biopsychosocial factors in Health and Illness*. Harcourt Brace College Publishers, New York.

Bone, K. and Gupta (1997) Traditional uses, chemical constituents, antiplatelet, anti inflammatory, cardiovascular and antioxidant properties of ginger. *Bri. J. Phytotherap.,* **4** : 110-120.

Burtis, C.A., Ashwood, E.R. and Bruns, D.E. (2006) Tietz, *Textbook of Clinical Chemistry and Molecular Diagnostics,* Fourth Edition. St. Louis, Elsevier Saunders, 2448 pp

Chandra, T., Sadique, J. and Somasundaram, S. (1987) Anti inflammatory activity of *E. alba. Fitoterapi,*. **58** : 28.

Chopra, R.N., Chopra, I.C. and Varma, B.S. (1969) *Supplement to Glossary of Indian Medical Plants*. CSIR. New Delhi. p.73.

Deore S.L. and Khadabadi S.S. (2009) Screening of antistress properties of *Chlorophytum borivilianum* tuber. *Pharmacologyonline* **1** : 320-328.

Desai, S.K., Desai, S.M., Navdeep, S., Arya, P. and Pooja T. (2011) Antistress activity of *Boerhaavia diffusa* root extract and a polyherbal formulation containing *Boerhaavia diffusa* using cold restraint stress model. *Int. J. Pharm. and Pharmaceut. Sci.,* **3** : 130132.

Faith, R.E., Murgo, A.J., Good, R.A. and Plotnikoff, N.P. (2006) *Cytokines : Stress and Immunity.* Second Edition, Taylor & Francis Group, 2 Park Square, Milton Park Abingdon, Oxon, United Kingdom.

Field, T., Hernandez-Reif M, Diego, M., Schanberg, S. and Kuhn, C. (2005) Cortisol decreases and serotonin and dopamine increase following massage therapy. *Int. J. Neuros*ci., **115** : 1397-1413.

Gallo, L.C. and Matthews, K. A. (2003) Understanding the association between socioeconomic status and physical health: Do negative emotions play a role? *Psycholog. Bull.,* **129** : 10 - 51.

Ganesh, R., Narayanan, N., Thirugnanasambantham, P., Viswanathan, S. and Parvathavarthini, S. (2006) Effect of Arogh on Hyperlipidemia. *Int. J. Trop. Med.,* **1** : 18 – 22.

Gregory, S. and. Kelly, N.D. (2001) *Rhodiola rosea* A possible plant adaptogen. *Alt. Med. Rev.,* **6** : 291 - 296.

Hawkley, L. C., and Cacioppo, J. T. (2003) Loneliness and Pathways to Disease. *Br. Behav. Immun.,* **17**, : 98 - 105.

Hong, C.Y., Wang, C.P., Huang, S.S. and Hsu, F.L. (1995) The inhibitory effect of tannins on lipid peroxidation of rat heart mitochondria, Journal of Pharmacy and Pharmacology, **47** : 138–142.

Jung, H.A., Jung, Y.J., Yoon, N.Y., Jeong, da, M., Bae, H.J., Kim, D.W., Na, D.H. and Choi, J.S. (2008) Inhibitory effects of *Nelumbo nucifera* leaves on rat lens aldose reductase, advanced glycation end products formation, and oxidative stress. *Food Chem. Tox.,* **46** : 3818-3826.

Karunakaran, G., and Mohamed, S., and Peter, T., Vinoth, P., Krishnamoorthy Karthikeyan, K., Niranjali, D., and Jayaprakash, S. (2006) Cardioprotective effect of the *Hibiscus rosa sinensis* flowers in an oxidative stress model of myocardial ischemic reperfusion injury in rat. *BMC Comp. Alt. Med.,* **6** : 32.

Kim, N.J. and Hong, N.D. (1996) Studies on the processing of crude drugs on the constituents and biological activities of glycyrhiza. *Korean J. Pharmacog*., **27** : 196-206.

LaFleur-Brooks, M. (2008) *Exploring Medical Language: A Student-Directed Approach* 7th Edition. St. Louis, Missouri, USA: Mosby Elsevier. pp. 398

Matsuura, H., (2001) Saponins in garlic as modifiers of the risk of cardiovascular disease. *J. Nut.*, **131** : 1000–1005.

Mattingly, D., Martin, H. and Tyler, C. (1989) Fluorimetric method for simultaneous estimation of cortisol,corticosterone, and testosterone in plasma. *J. Clin. Pathol.*, **42** : 661–666.

Mohan, M., Gulecha, V.S., Aurangabadkar, V.M., Balaraman, R., Anoop Austin and Thirugnanasampathan, P. (2009) Analgesic and anti-inflammatory activity of a polyherbal formulation (Arogh). *OPEM*. **9** : 232-237.

Moncrieff, J., Wessely, S. and Hardy, R. (2010) Active placebos versus antidepressants for depression. *Coch. System. Review.*, **28** : 1 – 28.

Singh, N., Nath, R., Lata, A., Singh, S.P. Kohli, R.P. and Bhargava, K.P. (1982) *Withania somnifera* (Ashwagandha) A rejuvinator herbal drug which enhances survival during stress (An Adaptogen). *Int. J. Crude Drug Res.*, **20** : 29.

Nade, V.S., Dwivedi, S., Kawale, L.A., Upasani, C.D. and Yadav, A.V. (2009) Effect of *Hibiscus rosa-sinensis* on reserpine-induced neurobehavioral and biochemical alterations in rats. *Indian J. Exp. Biol.*, **47** : 559-563.

Nade V.S., Kawale, Laxman, A., Dwivedi, Subhash, Yadav and Adhikrao, V., 2010. Neuroprotective effect of Hibiscus rosa-sinensis in an oxidative stress model of cerebral post-ischemic reperfusion injury in rats. *Pharmaceut. Biol.*, **48** : 822-827.

Naik, S. R., Azmathulla, S. and Hule, A.K. (2006) Evaluation of adaptogenic activity profile of herbal formulation. *Indian J. Exp. Biol.*, *44* : 574-579.

O'Mahony and Michael (1986) *Sensory Evaluation of Food: Statistical Methods and Procedures.* CRC Press. pp. 487.

Rao, G.M.M., Venkateswararao, C.H., Rawat, A.K.S., Pushpangadan, P. and Shirwaikar, A. (2005) Antioxidant and antihepatotoxic activities of *Hemidesmus indicus* R. Br, *Acta Pharmaceutica Turcica*, **47** : 107–113.

Rose, R.J., and Allen. J.R.. (1985) Hematologic response to exercise and training, *Vet. Clin. North Am. Equ. Pract*., **1** : 461 - 475.

Roshan. S., Abdullah K. and Sadath, A. (2010) To study the effect of *Allium sativum* on swimming endurance, anoxia tolerance and cold stress. *J. Glob. Pharm Tech.,* **2** : 27-32.

Saggu, S., Divekar, H.M., Gupta, V., Sawhney, R.C., Banerjee, P.K. and Kumar, R. (2007) Adaptogenic and safety evaluation of seabuckthorn (*Hippophae rhamnoides*) leaf extract: A dose dependent study. *Food Chem. Tox.*, **45** : 609–617.

Schmitt, C. A. and Dirsch, V. M. (2009) Modulation of endothelial nitric oxide by plant-derived products. *Nitric Oxide*, **21** : 77–91.

Selye, H. (1956) *The Stress of Life*. McGraw-Hill, New York.

Sheldon, C., Denise, J.D., and Gregory M. E. (2007) Psychological Stress and Disease. *J. Am. Med. Ass.,* **298** : 1685–1687.

Spiegel, K,, Leproult, R. and Van-Cauter, E. (1999) Impact of sleep debt on metabolic and endocrine function, *Lancet,* **354** : 1435 – 1439.

Sreeramamurthy, T., Ganga Rao, B., Satyanarayana, T. and Krishna Rao, R.V., (1993) Hepatoprotective activity of *Eclipta alba. J. Res. Edu. Indian Med.*, **2** : 41-43.

Srivastava, R.D., Dwivedi, S., Sreenivasan, K.K. and Chandrasekar, C.N. (1991) Cardiovascular effects of *Terminalia* species of plants. *Indian Drugs.* **29** : 144-149.

Stull, C.L., and Rodiek. A.V. (2002) Effects of cross-tying horses during 24 h of road Transport. *Equ. Vet. J.*, **34** : 550-555.

Suchalatha, S. and Shyamala Devi, C.S. (2004) Effect of Arogh - a polyherbal formulation on the marker enzymes in isoproterenol

induced myocardial injury. *Indian J. Clin. Biochem*, **19** : 184-189.

Suchalatha, S., Thirugnanasambandam, P., Maheswaran, E. and Shyamala Devi, C.S. (2004) Role of Arogh, a polyherbal formulation to mitigate oxidative stress in experimental myocardial infarction. *Indian J. Exp. Biol.*, **42** : 224-226.

Thoits, P.A. (2010) Stress and Health - Major findings and policy implications. *J. Health Soc. Behav.,* **51** : 41 - 53.

Toews, M.L. and Bylund, D.B. (2005) Pharmacologic principles for combination therapy. *Proc. Am. Thor. Soc.*, **2** : 282 - 291

Vinoth K.M.K., Balaraman**,** R.**,** Pancza, D. and Ravingerova, T. (2010) *Hemidesmus indicus* and *Hibiscus rosa-sinensis* affect Ischemia reperfusion injury in isolated rat hearts. *Evid. Based Comp. Alt. Med.*, **1** : 1-8.

Winston, D. and Maimes, S. (2007) *Adaptogens: Herbs for Strength, Stamina, and Stress Relief.* Rochester Vt. Healing Arts Press.