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RESEARCH ARTICLE

Role of *Hippophae rhamnoides* L. in the Management of Depression by Regulating Hyperhomocysteinemia

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ABSTRACT

Depression is one of the major health burden in almost all the societies particularly in urban community. As per the World Health Organization, depression will be the second largest disease burden due to the urban way of lifestyle. The modern era is full of stress and strains the people are living in the most competitive society than the previous year. Although many antidepressant drugs have been develop to manage anxiety, stress and depression due to adverse side reaction, most of the drug could show satisfactory results. Considering the above fact, we have selected a drug *Hippophae rhamnoides* which contain many phyto molecules showing preventing role of anxiety and depression by regulating some of the biochemical parameters.

Keywords: Depression, folic acid, *Hippophae rhamnoides*, homocysteine

INTRODUCTION

In recent years, the prevalence of neuropsychiatric disorders is increasing due to stress and strain of urban way of living. In the present day, society is a full way of stress and strain due to the complexities of modern societies.[1,2] Many psychosocial factors are responsible for the development of neuropsychiatric disorders particularly depression.[3] Several pharmacologic and non-pharmacologic parameters have been develop to manage anxiety, stress, and depression, but due to complex etiology none of the drugs could prevent or cure the depression among the lightly victims.[4] Although the conventional synthetic drug is more potent to manage neuropsychiatric and behavioral problems, continuous oral administration may produce severe neuroendocrine and metabolic disorders.[5] Among non-pharmacologic producers, meditation, relaxation, and counseling are more effects in the initial stage.[6] However, it is difficult to predict complete cure in the lightly victims. Recently, global attention has been directed towards the utilization of traditional medicine for the prevention and management of neuropsychiatric disorders. But due to lack of standardization and quality control of herbal products could not get acceptance in the global market. Though, conventional therapy has shown significant effect but long term application may generally produce many neuro-endocrine and behavioral side effects. Considering the above, psychiatrists and neurologists are exploring to identify new chemical entity from botanical resources.[7,8] Among many plant-based drugs, sea buckthorn is one of the plants showing immense therapeutic value in the management of depression by regulating certain biochemical parameters associated with neuropsychiatric disorders.

Sea buckthorn (*Hippophae rhamnoides*) is a grown in dry temperate and cold dessert of Himalaya particularly in Ladakh, Himachal Pradesh, Uttarakhand, Sikkim, and Bhutan. Sea buckthorn belongs to the family of Elaeagnaceae is a shrug with generally grown higher attitude, the local people are using the fruit of this plant for pickles, In the recent years, the nutritional and medicinal properties of these plant have been thoroughly investigated.[9] The fruit pulp of this plant contains high quantity of Vitamin C, Folic acid, Vitamin B12, and Vitamin K, the biological properties particularly the application of fruit pulp a certain in the prevention and management of cardiovascular and neurodegenerative disorders.

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The evaluation of nutritional value for increasing general body immunity was also confirmed. Considering the immense therapeutic value, we have decided to study the effect of the fruit pulp of the (*H. rhamnoides*) on various biochemical and behavioral parameters associated with depression.

MATERIALS AND METHODS

The present study has been designed to investigate the beneficial effect of *H. rhamnoides* in the prevention and management of neuropsychiatric disorders particularly depression. To achieve the above goals, we have selected 182 cases belonging age group of 22–50 of both genders. Out of 182 cases, 98 were females and the remaining 84 cases were males. In the present series, we have selected only urban population of Varanasi city. A comprehensive history was recorded by including general health status as well as presence of any chronic illness including family history of neuro-psychiatric disorders. The socio-cultural and economic status was also determined. The economic and educational status of the selected individuals was also recorded. The BDI and Hamilton Anxiety Score were utilized to diagnosed anxiety and depression as per DSM IV. The homocysteine and folic acid were measured using ELISA kit. Sea buckthorn pulp extract was given orally in the form of capsule supplied by Primok Naturelle Care Pvt. Ltd., New Delhi. The results were analyzed and compared with normal subjects.

RESULTS

As per the objective of the work under, 182 cases were subjected for evaluation of therapeutic efficacy of an organic extract of Sea buckthorn (*H. rhamnoides* L.) in two divided doses. As mention in Table. 1, the cases were divided into two major groups on the basis of score obtained by application of BDI score; based on the score, cases were divided into mild and moderate depression. Out of 98 cases, 48 were mild depression and the remaining 50 cases were moderate depression. Table 2 indicates the level of depression scores in the normal population as well as mild-to-moderate cases of depression. Similarly, the anxiety score as measured by Hamilton anxiety also found elevated in females than the males. It indicates that females are more prone to anxiety and depression than the males the average anxiety score varied from 17.86 to 21.14 in male and 22.01 to 24.39 in female. The females in normal series female cases showed a higher level of depression than males, similar pattern was observed in mild and moderate depression also in mild cases the depression score varied from 11.59 to 14.01 in mild and 27.43 to

Table 1: Average score of beck depression inventory in normal and mild-to-moderate depression cases

Treated groups	Sex	Number of cases	BDI			95% CI of the limit of mean (initial value)
			Initial	After 1 month	After 3 months	
Normal (*n*–84)	Male	38	6.5±1.85	5.2±1.92	4.8±1.70	5.91–7.08
	Female	46	7.8±1.5	6.7±1.6	5.4±1.32	7.37–8.23
Mild (*n*–48)	Male	20	12.8±2.8	10.2±1.76	9.6±1.07	11.59–14.01
	Female	28	14.6±1.03	12.4±1.28	10.8±1.09	14.23–14.6
Moderate (*n*–50)	Male	22	28.5±2.52	25.8±2.75	22.6±1.08	27.43–29.57
	Female	28	36.4±3.9	32.3±3.02	26.6±2.98	34.96–37.84

CI: Confidence interval, BDI: Beck depression inventory

Table 2: Hamilton Anxiety Scale anxiety score for the assessment of anxiety neurosis in normal and depressed subjects

Treated groups	Sex	Number of cases	Anxiety score (HAM-A)			95% CI of the limit of mean (initial value)
			Initial	After 1 month	After 3 months	
Normal (n–84)	Male	38	8.9±2.70	7.8±2.32	6.2±1.32	8.05–9.75
	Female	46	13.4±2.88	12.2±2.37	10.6±2.17	12.57–14.23
Mild (n–48)	Male	20	19.5±3.75	17.8±2.60	14.5±3.4	17.86–21.14
	Female	28	23.2±3.22	20.4±3.86	17.9±2.78	22.01–24.39
Moderate (n–50)	Male	22	26.9±3.24	24.6±2.87	21.8±3.20	25.55–28.25
	Female	28	28.1±2.20	25.3±2.72	23.2±4.88	27.29–28.91

CI: Confidence interval, HAM-A: Hamilton anxiety scale

Table 3: Level of folic acid in normal as well as depression cases

Treated groups	Sex	Number of cases	Folic acid			95% CI of the limit of mean (initial value)
			Initial (ng/ml)	After 1 month (ng/ml)	After 3 months (ng/ml)	
Normal (*n*–84)	Male	38	9.3±0.08	8.1±0.88	7.8±0.78	9.28–9.32
	Female	46	13.6±2.75	11.8±1.08	10.2±1.42	12.81–14.39
Mild (*n*–48)	Male	20	18.8±3.20	16.9±2.45	14.6±2.17	17.4–20.2
	Female	28	22.2±1.77	20.7±2.09	18.8±2.26	21.55–22.85
Moderate (*n*–50)	Male	22	21.1±3.20	18.2±3.07	15.9±2.19	19.77–22.43
	Female	28	28.7±2.87	25.7±3.27	24.1±3.20	27.64–29.76

CI: Confidence interval

Table 4: Level of homocysteine in normal as well as depression cases

Treated groups	Sex	Number of cases	HCY			95% CI of the limit of mean (initial value)
			Initial (μmol/L)	After 1 month (μmol/L)	After 3 months (μmol/L)	
Normal (*n*=84)	Male	38	6.4±1.50	5.8±1.36	5.2±1.12	5.93–6.87
	Female	46	7.8±0.98	6.4±1.38	5.9±1.29	7.53–8.07
Mild (*n*=48)	Male	20	11.6±1.74	9.7±1.02	7.6±0.99	10.86–12.34
	Female	28	14.2±2.51	12.8±1.98	10.9±1.03	13.28–15.12
Moderate (*n*=50)	Male	22	28.5±3.20	24.9±2.77	21.3±3.42	27.17–29.83
	Female	28	34.3±2.75	31.6±3.20	27.8±3.70	33.29–35.31

HCY: Homocysteine, CI: Confidence interval

29.57 in moderate (male) and 14.23–14.06 in mild and 34.96–37.84 in moderate (female).

Folic acid was measured in 38 male cases and 46 female cases; the average folic acid was found 9.3 ng/mL in males and 13.6 ng/mL in female's mild depression cases. When folic acid in normal cases was compared with mild depression cases, a significant difference was noticed. In moderate depression cases, the folic acid was found 21.1ng/mL in males and 28.7 ng/mL in females. When the organic extract *H. rhamnoides* was given in the dose of 500 mg twice a day, there was a significant reduction. After oral administration of *H. rhamnoides,* in diagnosed cases of depression low level of folic acid were found in the blood in comparison to the normal population. While in depressed patients, the level was found significantly elevated in the treated group, the difference was found specifically significant. From the table, it indicated that Sea buckthorn, when given orally, has the capacity to increase the level of folic acid, and thus it influences the metabolism of homocysteine, it is apparent that folic acid plays an important role in the maintenance of folic acid. It influences the homocysteine metabolism which is apparent from the comparison when homocysteine is corrected following oral administration of *H. rhamnoides*. It can be concluded that the pulp of *H. rhamnoides* which contains folic acid plays a key role in regulating homocysteine metabolism (Tables 3 and 4). The fruit pulp of *H. rhamnoides* is found beneficial in the regulation of homocysteine metabolism particularly in depresses patients.

DISCUSSION

Hyperhomocysteinemia is associated with many clinical conditions particularly in atherosclerosis leading to coronary heart disease.[10] Similarly, a genetic factor particularly MTHFR gene polymorphism is also responsible for the behavioral disorder from the table it is evident that folic acid deficiency may lead to depression and later on increase the precipitating factors such as hyperhomocystenemia, hypertension, and atherosclerosis. In another series of study, it is pointed out that depression is significantly associated with malnutrition and low level of folic acid results in an elevated level of homocysteine. Recently, several studies conducted worldwide indicated the growing evidence of depression due to currently stress and strain of modern society. Am-pull evidence is now available to demonstrate that stressful life situations may influence hypothalamus, hypophyseal, neuroendocrine axis leading to an increase the level of plasma cortisol

and produces an imbalance between sympathetic and parasympathetic system. Depression is not only a behavioral disorder but it also influence many vital functions including alters the neuroendocrine axis. Therefore, attention should be focus toward the maintenance of physiological homeostasis. A depressed person is a burden not only in the family but also in the whole society. There is always a possibility that if an environmental situation is not modified patients may enter into this stage of severe depression.[11]

In our finding, depress persons presented most common physical symptoms such as fatigue, gastrointestinal disturbance and loss of hepatitis, insomnia and headache, lack of interest in day to day activities, and lack of concentrations leading to poor mental performance. The psychological problems also generally exhibited with poor cognitive functions including loss of memory. The major approach for the prevention and management of depression is to improve the immune system by enhancing general body immunity. In a series of study, it is well established that in depression general body immunity is decline.[12] As per recent hypothesis, depression is correlated with the elevated level of pro-inflammatory cytokines particularly IL-1β, IL-6, and tumor necrosis factor-α (TNF-α), high-sensitivity C-reactive protein, and TNF-¥ all showed the altered level in depression. In the initial phase of depressive symptoms, there is a mark decline in various physical, psychological, and behavioral types. Therefore, the management study should be planned to correct the baseline deficiency in both groups. Considering above we have selected *H. rhamnoides* as a therapeutic major to correct the deficiencies in depressed patients. In our own series of study, we have observed that hyperhomocysteinemia is associated with depression. This condition triggers the pro-inflammatory markers as well as reduces the absorption and general body metabolism.[13] Hyperhomocysteinemia is a condition having to prominent etiological factor, folic acid deficiencies, and MTHFR gene polymorphism; ultimately, it is responsible for atherosclerosis, cardiac heart disease, and neurodegenerative disorders. *H. rhamnoides* containing a lot of alpha-tocopherol and vitamins and folic acid it also contains a lot of micro-nutrients including a massive quantity of Vitamin C.[14] Deficiency of folic acid may lead to hyperhomocysteinemia in both genders. In our series of the study, we have noticed that the oral administration pulp of *H. rhamnoides* may improve the health status by supplementing the various nutritious elements. Agrawal *et al*. 2009 extensively study the immunomodulating study of Sea buckthorn extract in aged populations these authors notice that oral administration of Sea buckthorn regulates the immune system. Result also indicated that the oral administration pulp of extract *H. rhamnoides* increase the level of folic acid and decreases the level of homocysteine. Thus, it provides a preventive measure to protect cardiovascular events.

CONCLUSION

The present study showed the depress patients exhibited with anxiety, stress, sleep insomnia, and poor immunity, the biochemical investigation also indicated nutritional deficiency particularly folic acid and B12. At present, available drug has many side effects effecting neuroendocrine metabolic and neurological side effects. Sea buckthorn (*H. rhamnoies*) when given orally in depress patients improves the level of folic acid and thus reduce the elevated level of homocysteine. From the present study, it is concluded that organic extract of *H. rhamnoides* when given from continuously for 3 months, increase the level of folic acid and reduces the level of homocysteine. It also regulate the neurobehavioral functions specially in relation to anxiety and stress among depressed patients. It is concluded that (*H. rhamnoies*) may serve as an important adjuvant to manage the depression along with conventional therapy.

REFERENCES

1. Tamar H. The brain and stress: In: Day SB editor Life Stress. Vol-3, New York: van Nostrand Reinhold Company; 1982. p. 21-9.
2. Agrawal A, Dixit SP, Dubey GP. Clinical evaluation of anti-depressant property of basant (*Hypericum perforatum*). Pharmacopsychoecol Assoc 1994;7:253-6.
3. Beardsley G, Goldstein MG. Psychological factors affecting physical condition. Psychosomatics 1993;34:12-9.
4. Dubey GP, Agrawal A, Rajamanickam GV. Age consistent hyperhomocysteinemia and risk of neurodegeneration-benefits of *Hippophae rhamnoides*. J Neurochem 2009;109:1272-84.
5. Kumari R, Agrawal A, Singh GP, Dubey GP.

Hyperhomocysteinemia and DNA hypomethylation, reduced the monoamines synthesis in depression: A case control study. J Syst Integr Neurosci 2015;1:36-40.
6. Enderami A, Zarghami M. The effects and potential mechanisms of folic acid on cognitive function: A comprehensive review. Neurol Sci 2018;39:1667-75.
7. Beno P, Sramka M, Valach M. Aktualne Problemy Zdravotnictva a Socialnej Prace: Zbornik Vedeckych Prac k 10.VYROCIU ZALOZENIA USTAVU sv. Cyrila a Metoda Vysokej Skoly Zdravotnictva a Socialnej Prace sv. Alzbety v Partizanskom. Bratislava: Vysoka Skola Zdravotnictva a Socialnej Prace sv. Alzbety; 2019. p. 221-33.
8. Folstein M, Liu T, Peter I, Buell J, Arsenault L, Scott T, *et al*. The homocysteine hypothesis of depression. Am J Psychiatry 2007;164:861-7.
9. Chengfeng S, Wei L, Xinxing W, Lei W, Rui Z, Lingjia Q. Hyperhomocystenemia is a result, rather than a cause of depression under chronic stress. PLoS One 2014;9:e106625.
10. Tiemeier H, van Tuiji HR, Hofman A, Meijer J, Kiliaan AJ, Breteler MM, *et al*. Vitami B12, folate and homocysteine in depression: The Rotterdam study. Am J Psychiatry 2002;159:2099-101.
11. Austin MP, Mitchell P, Goodwin GM. Cognitive deficits in depression. Possible implications for functional neuropathology. Br J Psychiatry 2001;178:200-6.
12. Strenberg DE, Jarvik ME. Memory functions in depression. Arch Gen Psychiatry 1976;33:219-24.
13. Rao TS, Asha MR, Ramesh BN, Rao KS. Understanding nutrition, depression and mental illnesses Indian J Psychiatry 2015;50:77-82.
14. Kessler RC. The efferts of stressful life events on depression. Annu Rev Psychol 1997;48:191-214.