International Standard Serial Number (ISSN): 2319-8141

International Journal of Universal Pharmacy and Bio Sciences 11(2): March-April 2022 INTERNATIONAL JOURNAL OF UNIVERSAL PHARMACY AND BIO SCIENCES

IMPACT FACTOR 4.018* ICV 6.16*****

Pharmaceutical Sciences

Research Article.....!!!

EVALUATION OF THE EFFECT OF MAJOON HALAILA (UNANI FORMULATION) IN HEALTH PROMOTION OF ELDERLY PEOPLE (MASHAIKH) - A RANDOMIZED PLACEBO CONTROLLED STUDY Dr Filza Eqbal

Assistant professor, Dept of Tahaffuzi wa Samaji Tib, Inamdar Unani Medical College and Hospital Kalaburagi 585105.

ABSTRACT

KEYWORDS:

Majoon halaila; elderly; health promotion. FOR CORRESPONDENCE: Dr Filza Eqbal * ADDRESS: Assistant professor,

Dept of Tahaffuzi wa Samaji Tib, Inamdar Unani Medical College and Hospital Kalaburagi 585105.

Objectives: To improve the expectancy and quality of life of elderly persons by providing safe and effective Unani formulation, Majoon halaila. Methods: 40 eligible subjects were randomly assigned into two groups; 30 in test and 10 in control group. Test group was given 10gm Majoon halaila orally at bedtime for 2 months. Control group was treated with 10 gm placebo orally at bedtime for 2 months. Effect of the drug was assessed by Appetite score, Weight, Grip strength score, Physical activity score, 6-CIT score on every 15th day and complete haemogram, lipid profile, AIP, LVEF pre and post treatment. Results: Strongly Significant increase (p<0.001) was observed in Appetite score, Weight, Grip strength score, Physical activity score, Serum HDL, LVEF and suggestive significant increase in Haemoglobin (p<0.018), strongly significant decrease (p<0.001) was observed in Serum cholesterol, Serum triglycerides, Serum LDL, AIP, ESR, and in 6-CIT Score in test group with respect to control group. Effect on TLC and DLC was statistically insignificant. Safety parameters were within normal range. Discussion: On the basis of observations and results it may be concluded that the Majoon Halaila is safe and effective in health promotion in Mashaikh (elderly).

INTRODUCTION:

Old age is an incurable disease.¹ Ageing can be defined as a progressive constriction of the homeostatic reserve of every organ system.² It is a natural process. The rate and extent of this decline of each organ system of the body is influenced by genetic factors, environment, diet and personal habits.² The definition of 'old age' has been accepted by most western countries as being ≥ 65 years of age.³ In Unani classical literature also, old age (Mashaikh) is considered as being ≥ 60 years of age.⁴

Old age is seen to begin at the point when active contribution is no longer possible.³ The elderly population (aged 60 years or above) in India accounted for 7.4% of the total population in 2001, 8.6% (104 million; 53 million females and 51 million males) in 2011 and has been projected to increase to 19% by the year 2050. 5,6

In India, the elderly people suffer from dual medical problems, i.e. both communicable as well as noncommunicable diseases. It is estimated that one out of two elderly in India suffers from at least one chronic disease which requires life-long medication. This is further compounded by impairment of special sensory functions like vision and hearing. A deterioration in immunity as well as change in the psychology due to age leads to an increased burden of communicable diseases in the elderly.^{7,8}

It is uncertain as to why we age. Despite being a universal phenomenon, the exact mechanism or sequence of events are not yet definitively known. Frequently described biochemical markers of ageing include increase in chromosome structural abnormalities, increase in DNA cross-linking, decrease in DNA methylation, loss of DNA telomeric sequences, decline in gene expression, deterioration of mitochondrial structure, increase in post-translational changes in protein structure such as cross linking, glycation, deamidation and oxidation and intra cellular accumulation of metabolic products.⁹

Over the years, scientific researchers have put forth several theories of aging that show a common modality. These modern aging theories generally fall into two camps: structural damage theories and programmed obsolescence theories.^{10,11}

Structural damage theories are concerned with the molecular damage that accumulates inside cells over time. Programmed obsolescence theories engage the concept that aging and death are the inevitable consequence of the workings of an internal biological clock that is programmed at conception. ^{11,12,13}

In *sin*—*al*— *shaikhookhat* (old age), the quantity of *ratoobat ghariziyah* required for the preservation of *hararate ghariziyah* and to continue the bodily normal metabolism is super added with and dominated by *ratoobat gharibah ballah* (abnormal metabolic products). In this period, deterioration in the powers and faculties of the body is marked. *Ratoobat ghariziyah* and *hararat ghariziyah* are markedly reduced. This changes the *mizaj* of the elderly individuals to relatively *Barid Yabis*.^{14,15} Unani physicians described three causative factors for ageing

- Coldness and dryness of temperament that keeps on increasing with age whereas hararat and rutoobat is essential for life.
- Weakness of hararat e ghareeziah i.e. weakness of innate heat of body
- Weakness of powers due to which different organs of body gets weakened and diseases occur.

Considering these factors, the regimens and medicines that increase the innate heat and strengthen the faculties of the body must be used in order to maintain equilibrium in humours and to delay ageing or prolong life.¹⁶

Majoon Halaila is polypharmaceutical preparation of Unani System of Medicine given to delay the ageing process and to prevent early ageing such as greying of hair, decreased body strength, decreased memory power, weakness of heart etc. *Majoon Halaila* is reported to be cardiac tonic ^{17,18} stomachic ¹⁸ and cephalic tonic ^{17,18} laxative ^{17,18}.

The ingredients of *Majoon Halaila* as given in Qarabadeen Azam are; Halaila siyah (*Terminalia chebula*,) Balaila (*Terminalia belerica*), Kundur (*Boswellia serrata*), Tabasheer safaid (*Bambusa arundinacea*), Sandal safaid (*Santalum album*), Tukhm e kasni (*Cichorium intybus*), Filfil siyah (*Piper nigrum*), Zanjabeel (*Zingiber officinale*), Gul e surkh (*Rosa damascene*), Waj (*Acorus calamus*) and Qand safed(sugar).¹⁹

MATERIALS AND METHODS

A randomized placebo controlled trial was conducted at National Institute of Unani medicine hospital (NIUM) between Mar 2018 and Jan 2019 to evaluate the efficacy of *Majoon Halaila* in health promotion of elderly people. Institutional Ethics Committee for Biomedical Research of NIUM approved the protocol on 18th May 2017 vide no. NIUM/IEC/2016-17/018/TST/03. This study is registered with clinical trial registration of India vide CTRI/2018/02/012082.

An informed consent sheet was provided to the persons fulfilling the inclusion criteria with details regarding the nature of the study, the drug to be used, method of treatment etc. If they agreed, they were asked to sign the informed consent form. Patients of ≥ 60 years of age, of either sex, with H/o weight loss, Frequency of infection, Slow walking/gait speed and with stable general condition were included in the study.

Patients below the age of 60 years with uncontrolled Diabetes mellitus, Hypertension, COPD, Ischemic Heart Disease or other chronic diseases like cancer & AIDS, unstable cardiac or renal disease were not included in the study.

Selected subjects were allocated into test group and control group by using computer generated randomization table. During the selection procedure, complete history including general physical and systemic examination was carried out and recorded on a prescribed proforma which was designed

International Standard Serial Number (ISSN): 2319-8141

according to the objectives of the study. The patients were enquired about their name, age, sex, marital status, address, occupation, education, diet, religion and socio-economic status. For socio-economic status, patients were enquired about their monthly income, education and occupation and were graded into different socio-economic strata by using Kuppuswamy's Socioeconomic Status Scale modified in Jan 2018. All the subjects were interrogated about their chief complaints and duration of suffering in detail especially about age related problems like weight loss, loss of appetite, recurrent infections, gait abnormality, age related dementia, fatigue and general weakness. Dietary habits, type of diet, smoking habits, Alcohol, pan chewing etc were enquired in personal history. After history, general and physical examination was done with special emphasis on pulse, blood pressure, temperature, respiratory rate, respiratory distress with simple activities, built, clubbing of finger, cyanosis, pallor, oedema, lymphadenopathy to look for involvement of any other serious illness.

A careful systemic examination of cardiovascular system, respiratory system, gastro intestinal system, renal system and nervous system was also done to look for any findings of other serious illness. Blood samples were taken for required investigations.

SAMPLE SIZE ESTIMATION

Sample size was calculated by the formula $N = (r+1) (Z_{\alpha/2} + Z_{1-\beta})^2 \sigma^2 / rd^2$ Where $r = n_1/n_2$ is the ratio of sample size required for two groups, it was kept as 3 for the sample size distribution in two groups as 3 : 1, Z α is the normal deviate at α level of significance (Z $_{\alpha}$ is 1.96 for 5 % level of significance) Z_{1- β} is the normal deviate at 1- β % power with β % of type 2 error (0.84 at 80 % statistical power) σ and d are the pooled standard deviation and difference of means of two groups .

Follow up

Two months study was divided into four visits of follow up, which were made at an interval of 15 days. Concomitant treatment was not allowed during treatment in both groups.

Efficacy assessment

Effect of the drug in the test and control groups was assessed by assessment of Appetite score, Weight, Grip strength score, Physical activity score and 6-CIT score on every 15th day and complete haemogram, lipid profile, AIP, LVEF pre and post treatment.

In this study, Council of Nutrition appetite questionnaire (CNAQ) was used to assess the appetite stimulating effect of our test formulation. Body weight was assessed to the nearest 0.1 kg without shoes and in light clothing. Grip strength was assessed at every follow up by hand held dynamometer. For the assessment of physical activity, Katz index of Independence in Activities of Daily Living was used. Memory status of the elderly subjects was assessed by administration of 6-Cognitive impairment test score at every follow up.

International Standard Serial Number (ISSN): 2319-8141

AIP (Atherogenic Index of Plasma): Atherogenic index of plasma (AIP) is a logarithmically transformed ratio of molar concentrations of triglycerides to HDL-cholesterol. It is suggested that AIP values of -0.3 to 0.1 are associated with low CV risk, 0.1 to 0.24 with medium and AIP above 0.24 is associated with high CV risk.

LVEF (Left ventricular ejection fraction): It is the fraction of blood ejected from left ventricle of the heart with each heartbeat. It is calculated by dividing the stroke volume by the end-diastolic volume, and is an inherent volumetric measure of the pumping efficiency of the heart.

Safety assessment

Safety assessment of treatment was done on the Clinical assessment at every visit of follow up and Bio chemical assessment viz; LFT, RFT and Fasting blood sugar before and after intervention.

Statistical analysis

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean \pm SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance.

Significant figures

- + Suggestive significance (P value: 0.05<P<0.10)
- * Moderately significant (P value: $0.01 < P \le 0.05$)
- ** Strongly significant (P value: P≤0.01)

Statistical software: The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS AND DISCUSSION

In present study, maximum number of subjects 60.0% (24) was in the age group of 60-65 years as compared to 37.5% (15) in 65-70 years and 2.5% (1) in 70-75 years.

| Demographic | | No. of | Percentage |
|----------------|-------------|----------|------------|
| data | | Patients | (%) |
| | | (n=40) | |
| | 60-65 | 24 | 60 |
| Age group | 65-70 | 15 | 37.5 |
| | 70-75 | 1 | 2.5 |
| Gender | Male | 26 | 65 |
| Gender | Female | 14 | 35 |
| | Hindu | 26 | 65 |
| Religion | Islam | 14 | 35 |
| Marital status | Married | 40 | 100 |
| Wantar status | Unmarried | 0 | 0 |
| | Mixed | 34 | 85 |
| Diet | Vegetarian | 6 | 15 |
| | Lower | 1 | 2.5 |
| | Lower | 11 | 27.5 |
| Socioeconomic | middle | 11 | 27.5 |
| status | Upper lower | 17 | 42.5 |
| | Upper | | |
| | middle | | |
| | Skilled | 5 | 12.5 |
| Occuration | Semiskilled | 2 | 5 |
| Occupation | Unskilled | 5 | 12.5 |
| | Unemployed | 28 | 70 |
| | <18.5 | 3 | 7.5 |
| DNI | 18.5 - 25 | 20 | 50 |
| BMI | 25 - 30 | 15 | 37.5 |
| | >30 | 2 | 5 |
| | Heavy | 4 | 10 |
| Physical | Moderate | 5 | 12.5 |
| activity | Sedentary | 31 | 77.5 |

Table 1: Demographic characteristics of participants included in the study

EFFICACY ASSESSMENT

Improvement in appetite score in test group might be due to *mushtahi, muqawwi meda, muqawwi jigar* and *hazim* properties of all constituents of *Majoone halaila* ie. *Halaila*^{20,21} *Balaila*^{20,22}, *Kundur*^{20,23}, *Tabasheer*²⁴, *Sandal*²⁵, *Tukhm e Kasni*²⁰, *Filfil Siyah*²⁶, *Zanjabeel*²⁷, *Gul e Surkh*²⁶, and *Waj*^{20,25}documented in Unani literature.

Researchers have documented the hepatoprotective activity of *Halaila*²⁸, *Balaila*²⁹, *Kundur*³⁰, *Sandal*³¹, *Tukhm e Kasni*³², *Filfil Siyah*³³, *Zanjabeel*³⁴, *Waj*³⁵; gastroprotective effect of *Halaila*³⁶, *Balaila*³⁷, *Kundur*³⁸, *Sandal*³⁹. *Zanjabeel*⁴⁰ digestive activity of *Filfil siyah*^{41.42} and *Zanjabeel*⁴³. These studies support appetite stimulant and digestive effect of some ingredients of *Majoone halaila*.

| Variables | Appetite score | | Weight (kg) | | Grip Strength score | |
|---------------------------|------------------|------------------|-------------|---------------|---------------------|------------------|
| | Test Group | Control Group | Test Group | Control Group | Test Group. | Control Group |
| 0day | 19.80±3.13 | 20.80±2.30 | 62.87±11.53 | 60.20±7.33 | 15.45±3.22 | 14.82±2.73 |
| 15 th day | 22.17±3.00 | 21.40±1.83 | 63.40±11.58 | 59.80±7.39 | 18.29±3.19 | 15.62 ± 3.28 |
| 30 th day | 24.27 ± 2.78 | 21.20 ± 1.98 | 64.13±11.53 | 59.70±7.36 | 21.97 ± 4.08 | 15.61±3.46 |
| 45 th day | 25.90 ± 2.78 | 21.00 ± 2.40 | 64.43±11.69 | 59.60±7.50 | 25.35±4.57 | 14.99 ± 2.74 |
| 60 th day | 26.47 ± 2.78 | 21.30±2.05 | 64.97±11.81 | 59.50±7.26 | 29.73±5.59 | 15.24 ± 2.28 |
| Difference | | | | | | |
| 0day-15 th day | 2.367 | 0.600 | 0.533 | -0.400 | 2.835 | 0.800 |
| 0day-30 th day | 4.467 | 0.400 | 1.267 | -0.500 | 6.518 | 0.790 |
| 0day-45 th day | 6.100 | 0.200 | 1.567 | -0.600 | 9.900 | 0.170 |
| 0day-60 th day | 6.667 | 0.500 | 2.100 | -0.700 | 14.282 | 0.420 |
| P value | | | | | | |
| 0day-15 th day | < 0.001** | 0.193 | 0.003** | 0.168 | < 0.001** | 0.180 |
| 0day-30 th day | < 0.001** | 0.103 | < 0.001** | 0.096 | < 0.001** | 0.317 |
| 0day-45 th day | < 0.001** | 0.167 | <0.001** | 0.140 | <0.001** | 0.119 |
| 0day-60 th day | < 0.001** | 0.051+ | < 0.001** | 0.226 | < 0.001** | 0.066+ |

Table 2: Efficacy parameters at every follow up

| Variables | Physical Activity Score | | 6-CIT Score | |
|---------------------------|-------------------------|-----------------|-----------------|------------------|
| | Test Group | Control Group | Test Group | Control Group |
| 0day | 5.57±0.77 | 6.00±0.00 | 12.10±4.57 | 12.90±4.18 |
| 15 th day | 5.70±0.70 | 6.00 ± 0.00 | 9.57 ± 5.48 | 11.10 ± 4.07 |
| 30 th day | 5.87±0.35 | 6.00 ± 0.00 | 8.00 ± 5.23 | 10.90±4.12 |
| 45 th day | 5.97±0.18 | 6.00 ± 0.00 | 6.80±4.91 | 10.10±3.78 |
| 60 th day | 5.97±0.18 | 6.00 ± 0.00 | 6.27 ± 4.64 | 10.30±3.83 |
| Difference | | | | |
| 0day-15 th day | 0.133 | - | -2.533 | -1.800 |
| 0day-30 th day | 0.300 | - | -4.100 | -2.000 |
| 0day-45 th day | 0.400 | - | -5.300 | -2.800 |
| 0day-60 th day | 0.400 | - | -5.833 | -2.600 |
| P value | | | | |
| 0day-15 th day | 0.043* | - | < 0.001** | 0.019* |
| 0day-30 th day | 0.005** | - | < 0.001** | 0.032* |
| 0day-45 th day | 0.003** | - | < 0.001** | 0.001** |
| 0day-60 th day | 0.003** | - | < 0.001** | 0.006** |

Table 3: Efficacy parameters pre and post treatment

In test group appetite score increases significantly at every follow up.

| Variables | Test Group | Control Group | P value |
|---------------------|--------------|---------------|-----------|
| Hb | | | |
| Before Treatment | 13.66±1.58 | 13.42±1.23 | 0.661 |
| After Treatment | 14.35±1.20 | 13.57±1.04 | 0.073+ |
| Difference | 0.690 | 0.15 | |
| P value | 0.018* | 0.674 | |
| ESR | | | |
| Before Treatment | 35.13±20.90 | 29.40±20.62 | 0.456 |
| After Treatment | 20.33±13.55 | 20.00±13.85 | 0.947 |
| Difference | -14.800 | -9.400 | |
| P value | < 0.001** | 0.054+ | |
| Serum Cholesterol | | | |
| Before Treatment | 167.35±31.48 | 169.10±15.00 | 0.867 |
| After Treatment | 135.17±18.91 | 172.80±31.82 | < 0.001** |
| Difference | -32.187 | 3.700 | |
| P value | < 0.001** | 0.662 | |
| Serum Triglycerides | | | |
| Before Treatment | 164.57±98.46 | 130.70±33.81 | 0.296 |
| After Treatment | 118.97±71.83 | 135.20±38.07 | 0.501 |
| Difference | -45.603 | 4.500 | |
| P value | < 0.001** | 0.379 | |
| LDL | | | |
| Before Treatment | 96.47±27.01 | 110.40±14.45 | 0.129 |
| After Treatment | 83.04±21.78 | 112.90±23.70 | 0.001** |
| Difference | -13.427 | 2.500 | |
| P value | <0.001** | 0.715 | |
| HDL | | | |
| Before Treatment | 36.77±5.12 | 33.70±6.29 | 0.129 |
| After Treatment | 41.10±6.54 | 32.50±5.30 | 0.001** |
| Difference | 4.330 | -1.200 | |
| P value | 0.001** | 0.255 | |
| AIP | | | |
| Before Treatment | 0.60±0.24 | 0.58±0.14 | 0.846 |
| After Treatment | 0.42±0.20 | 0.61±0.15 | 0.013* |
| Difference | -0.173 | 0.026 | - |
| P value | < 0.001** | 0.290 | |
| LVEF | | | |
| Before Treatment | 61.00±3.84 | 62.20±3.46 | 0.387 |
| After Treatment | 66.87±4.00 | 63.80±2.78 | 0.031* |
| Difference | 5.867 | 1.600 | - |
| P value | <0.001** | 0.019* | |

International Standard Serial Number (ISSN): 2319-8141

Barbara et al. (2017) found poor appetite in older adults leads to sub-optimal food intake and resulted in poor nutritional status which leads to impaired functional status and general health. According to their study improvement in appetite improves nutritional status in elderly. Our results are in conformity with this study. Thus it can be concluded that improvement in appetite improves the general nutritional status in elderly and enhance health care outcomes in elderly.^{44,45,46.}

In this study, Test group showed increase in body weight. The mean increase in body weight in test group at 60th day was 2.1 kg whereas control group showed decrease in body weight.

The test drug improves the appetite and digestive functions hence the nutritional status which in turn increases the weight in elderly. There is a J shaped curve association with mortality and body weight with increased mortality with low and high BMIs. At a BMI < 22 there is a steady increase in mortality and the combined effect of being underweight and increasing age has a deleterious effect on mortality.

Grip strength Score

Mean increase in Grip strength Score in test group at 60^{th} day was 14.282 kg. The result showed that Grip strength Score significantly increases at every follow up in test group with respect to base line (p< 0.001^{**}).

The improvement in grip strength may be attributed to the fact that the test drug improves the nutritional status hence the general body strength in elderly. The improvement in nutritional status would be because of *mushtahi*, *hazim*, *muqawwi-e-maida*, *muqawwi-e-jigar* activities of most of the ingredients of *Majoon-e-halaila*. Our results are in line with several scientific studies. Normane et al (2011) explained that increase in muscle function is associated with increased nutritional status. In the elderly increased nutritional intake will result in body compensation in the form of protein increase. Increase in weight and muscle mass can lead to increase in muscle strength. ^{48,49}.

Physical Activity Score

Results showed that the Physical Activity Score increased significantly at every follow up in test group. Increase in muscle strength correlates with performance of functions (directly proportional). In present study *Majoone Halaila* was found more effective in increasing grip strength so giving strongest reflection in physical activity too.

Haemoglobin

Haemoglobin level tends to decrease with increasing age. In our study, increase in haemoglobin level is moderately significant (p=0.018). It might be due to muallid e dam⁸¹ properties of some of the ingredient of *Majoon Halaila*, improvement in the digestive functions resulting in increase in appetite and food intake, which in turn results in improvement of nutritional status of elderly. Study by Silva CL

International Standard Serial Number (ISSN): 2319-8141

(2002) confirmed that low haemoglobin level was associated with lower serum albumin, BMI and more physicians' visits to elderly. ⁵⁰ Therefore by improving the nutritional status in elderly we can improve their haemoglobin level.

ESR In present study Mean decrease in ESR in test group was 14.800. Decrease in ESR indicates decrease in infection and inflammation. Decrease in ESR might be due to improvement in immune status as *Majoon e halaila* prevent decline in immune status as it slightly increases TLC thus balances destruction and production of WBC because normally TLC decreases with increasing age that is reflected in control group.

TLC and DLC

In test group mean increase in TLC from base line was 52.667. TLC tends to decrease with increasing age. *Majoon halaila* slightly increases TLC; it balances destruction and production of WBC. It may be due to increase in T lymphocytes proliferation in thymus. Control group treated with placebo showed reduction in TLC it might be due to age related changes in cell mediated immunity and oxidative stress. WBCs are the body's best defensive weapon in the fight against germs and disease. So when WBC count drops, it put the person in a vulnerable position without adequate protection and infectious agents becomes much more serious threats. Thus we can conclude that *Majoon Halaila* prevent further decline in immune status of the subject compared to control group.⁵¹

LIPID PROFILE and AIP

Our study showed *Majoon halaila* significantly reduced total serum cholesterol (p<0.001), serum triglyceride (p<0.001), LDL (p<0.001), AIP (Atherogenic Index of plasma) (p<0.001) and increases HDL (p<0.001). Decrease in total serum cholesterol in test group is due to combined effect of proven hypolipidemic activity of many ingredients of *Majoon halaila*. B Ahirwar, AK Singhai, AK Dixit (2003) reported significant hypolipidemic activity of Halaila (Terminalia chebula).⁵²

RCR Latha and P Daisy (2010) reported Balaila (*Terminalia belerica*) prevented dyslipidemia.⁵³ Kundur (B. Serrata)^{54.} silicon⁵⁵ Santalum album has potential antihyperlipidemic activities.^{56.} chlorogenic acid (found in kasni). ⁵⁷ filfil siyah (piper nigrum). ^{58,59,60} gul e surkh (R. Damascena). ^{61,62.} Srinivasan K (1991) and Sharma I (1996) found oral administration of Zanjabeel (ginger extract) could stimulate the conversion of cholesterol to bile acids thus eliminate the cholesterol from the body. ^{63,64} The study showed *Majoon e halaila* significantly increases HDL and reduces AIP. Our study is in line with studies that proved sandal ⁶⁵ kundur ⁶⁶ filfil siyah ^{67,68,69} and waj ^{70.} increases HDL in animal models. Increase in HDL indicates reduction in lipid peroxidation which is an indicator of atherosclerosis. Scientific studies proved some of the ingredients of Majoon halaila viz; halaila ^{71.},

International Standard Serial Number (ISSN): 2319-8141

25 | P a g e

balaila ^{72.}, kundur ^{73.}, tabasheer ^{74.} and ginger ^{75.} reduced the lipid peroxidation in animal models. It means *Majoon Halaila* prevents lipid peroxidation, thus prevents atherosclerosis. ^{76,77} Thus we can conclude that *Majoon Halaila* has cardio-protective effect.

Left Ventricular Ejection Fraction

Mean increase in Left Ventricular Ejection Fraction (%) at 60^{th} day in test group with respect to base line was 5.867. using Student's t test (paired) the mean increase was found to be strongly significant (p<0.001).

It may be due to effect of many ingredients of *Majoon e halaila* on contractile force of heart muscles. Kobayashi et al (1987) tested gingerol and found that it produced increase in the degree and rate of longitudinal contraction. Gingerol also increased the contractile force of the left atria.⁷⁸

Chebulanic acid's cardiotonic activity was greater on a hypodynamic heart than a normal one. These studies support our results. Research to evaluate the effect of other ingredients on LVEF must be carried out. Thus it can be concluded that *Majoone Halaila* has cardio-tonic activity.^{79,80,81,82,83}

6-CIT Score

Mean decrease in 6-CIT Score in test group at 15^{th} day, 30^{th} day, 45^{th} day and 60^{th} day with respect to 0 day test was strongly significant (p< 0.001^{**})

These results showed that the 6-CIT Score improved at every follow up in test group. Control group also showed significant improvement at 45th day and 60th day. This could be due to short interval between follow ups and on the other hand the subjects remembered questions asked on previous follow up suggests that they had no loss or weakness of memory so subjects with more cognitive loss should be selected for the trial.

Different researches showed neuroprotective and antidepressant activity of many ingredients of *Majoone Halaila*. Rajmohamed MA (2017) found Halaila possesses neuroprotective effect in Alzheimer's disease in animal models and free radical scavenging activity in-vitro cell free antioxidant assays.^{84.}

Neilson FH (2014) reported that silica prevented chronic aluminium accumulation and neurodegeneration in brain by forming aluminosilicate. ⁸⁵ Sandalwood extract. ⁸⁶ piperine. ^{87,88} ginger rhizome. ⁸⁹ acorus calamus. ⁹⁰

All these studies confirmed the neuro-protective effect of Majoon Halaila.

Age-associated functional losses are due to the accumulation of Reactive oxygen and nitrogen species (RONS).-induced damages. These damages result in cardiovascular diseases, chronic obstructive pulmonary disease, chronic kidney disease, neurodegenerative diseases, cancer, sarcopenia and frailty. Negative effects of RONS are neutralized by antioxidant defenses.⁹¹

International Standard Serial Number (ISSN): 2319-8141

Majoone halaila contains various ingredients which are stomachic, gastroprotective, hepatoprotective, neuroprotective, memory enhancer, cardioprotective, cardiotonic with proven anti oxidant effect viz *Halaila* (Terminalia chebula) ⁹², *Kundur* (Boswellia serrata) ^{93.}*Tabasheer* (Bambusa arundinacea) ^{94.}, *Sandal* (Santalum album) ^{95,96,97,98,99,100,101} *Tukhme Kasni* (Cichorium intybus) ^{102.}*Filfil Siyah* (piper nigrum) ¹⁰³, *Zanjabeel* (Zingiber officinale) ^{104,105,106}, *Waj* (Acorus calamus) ^{107.}Rosa damascena's. ¹⁰⁸

| Safety Parameters | | | |
|----------------------------|---------|--------------|----|
| Table 4: Safety parameters | pre and | post treatme | nt |

| Variables | Test Group | Control Group | P value |
|--------------------|--------------|------------------|---------|
| SGOT (IU/L) | | | |
| Before Treatment | 22.73±10.78 | 19.14±3.44 | 0.311 |
| After Treatment | 25.63±9.51 | 35.6±43.79 | 0.240 |
| difference | 2.907 | 16.460 | - |
| P value | 0.074+ | 0.258 | - |
| SGPT (IU/L) | | | |
| Before Treatment | 23.60±10.31 | 19.06±5.57 | 0.194 |
| After Treatment | 26.23±8.66 | 36.90±53.99 | 0.292 |
| • difference | 2.637 | 17.840 | - |
| P value | 0.063+ | 0.308 | - |
| SAP | | | |
| Before Treatment | 214.02±53.63 | 188.60±38.05 | 0.175 |
| After Treatment | 197.13±52.22 | 213.00±46.26 | 0.398 |
| • Difference | -16.890 | -24.400 | - |
| P value | 0.085+ | 0.183 | - |
| Total Bilirubin | | | |
| Before Treatment | 0.61±0.21 | 0.59±0.25 | 0.765 |
| After Treatment | 0.66±0.14 | 0.70±0.24 | 0.569 |
| • Difference | 0.049 | 0.109 | - |
| P value | 0.169 | 0.058+ | - |
| Blood Urea (mg/dl) | | | |
| Before Treatment | 29.25±6.92 | 30.90±7.52 | 0.527 |

| After Treatment | 30.47±6.36 | 31.20±6.20 | 0.752 |
|-----------------------------|-------------|------------|-------|
| Difference | 1.213 | 0.300 | - |
| P value | 0.285 | 0.910 | - |
| Serum Creatinine (mg/dl) | | | |
| Before Treatment | 0.79±0.13 | 0.86±0.16 | 0.181 |
| After Treatment | 0.82±0.13 | 0.83±0.14 | 0.837 |
| Difference | 0.029 | -0.028 | - |
| P value | 0.358 | 0.700 | - |
| FBS (mg/dl) | | | |
| Before Treatment | 95.07±9.97 | 96.7±8.74 | 0.647 |
| After Treatment | 91.07±10.34 | 92.2±8.5 | 0.756 |
| • difference | -4.000 | -4.500 | - |
| P value | 0.047* | 0.193 | - |

In order to determine the adverse effects of the *Majoone Halaila*, safety parameters like RFT (Blood Urea, Serum Creatinine), LFT (SGOT, SGPT, Serum Alkaline phosphatase, Serum bilirubin), Blood sugar fasting were carried out at the baseline and at the end of the study. It was found that all the safety parameters were within the normal range after the completion of the trial. This suggests that the use of *Majoon Halaila* for health promotion in elderly is safe.

The protocol discussion reveals that the overall effect of *Majoon Halaila* in health promotion of elderly people was found to be significant in improving parameters like Appetite score, Weight, Grip strength score, Physical activity score, Haemoglobin, ESR, lipid profiles, Atherogenic Index of Plasma (AIP), Left Ventricular Ejection Fraction (LVEF) and 6-CIT Score. However no significant improvement was observed in parameters like TLC and DLC.

In classical Unani literature *Majoon e halaila* described as stomachic ¹⁸ hepatoprotective, gastroprotective, appetite stimulant, digestive, cephalotonic ¹⁸ cardiotonic ¹⁸ laxative ¹⁸, anti ageing. ^{109,110} It contains 10 ingredients. Their actions reported as *kundur, filfil siyah*, *Zanjabeel* and *waj* stimulate innate heat ^{23,26} which is essential for *Quwa* to perform *afa'al* (functions). *Halaila, balaila, sandal, gule surkh* and *waj* by virtue of their mulattif property ^{20,111} liquifies the ghaleez madda by their moderate heat. *Tukhme kasni, filfil siyah, zanjabeel*, and *gule surkh* by their *mufatteh sudud*^{111.} action break the *akhlate luzuja* in small pieces which can be evacuated from the body. *Tukhme kasni* and *filfil siyah* due to their *mudire bol* ^{111.} property and *halaila, balaila, zanjabeel* and *gule surkh* by their laxative

International Standard Serial Number (ISSN): 2319-8141

action ^{112.} evacuate phlegm and atrabilious humour through bowel and bladder. *Halaila, balaila, sandal, filfil siyah, zanjabeel* and *waj* by their *mushtahi* property ^{111.}increases appetite. *Halaila, kundur, tabasheer, sandal, tukhme kasni, filfil siyah, zanjabeel, gule surkh,* and *waj* due to their *muqawwie me'da* ^{25,26} *muqawwie jigar*²⁵ and digestive action ¹¹¹ strengthen and improve the *Quwwate Tabiya,* thereby provide the substitute of *tahleel. Halaila, kundur, tabasheer, sandal, tukhme kasni* and *gule surkh* by their *mufarrah wa muqawwie qalb* ¹¹¹action provide strength to the *quwwate haiwania. Halaila, kundur, sandal, filfil siyah, zanjabeel* and *waj* by their *muqawwie dimagh* ^{112.} property and *muqawwie hafiza* ^{25,26,111} property strengthen *quwwate nafsania*. From the above discussion we can conclude that *Majoon halaila* stimulate innate heat, evacuate *fazil* and superflous matter, strengthen *quwwate tabiya, haiwania* and *nafsania* thereby regulate/improve the functions of the body thus increase life expectancy and improve quality of life.

Thus we can conclude that *Majoon halaila* is safe and effective antiaging formulation and has encouraging potential in the health promotion of *Mashaikh*.

LIMITATIONS

Limitations of the study include small sample size, short duration of study, inclusion of maximum subjects having normal physical activity score, cognition scale containing easy questions and shorter follow up. Thus it is recommended that the clinical trial should be done on larger sample size and for longer study duration with appropriate follow up days.

CONCLUSION

The study revealed that the test drug appeared to be efficacious in the geriatric problems and exhibited significant effects in improvement of appetite score, weight, grip strength score, physical activity score and 6-CIT score. Hence it can be said that this intervention can have a major impact on the patient and family's well being and on the cost of long term care. No adverse effects or toxicity has been reported during or after the trial. Thus, it can be stated that the test drug is safe and effective in elderly to promote their health and can be used prophylactically to counter the effects of ageing.

ACKNOWLEDGEMENT

The author is thankful to the authorities of National Institute of Unani Medicine, Bangalore for providing financial assistance and ample facilities for clinical trial, and also thankful to the patients who participated in the study. Author also thanks Dr. K.P Suresh (Biostatician) for the statistical analysis of data.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

- Park K. Textbook of Preventive and Social Medicine. 24th edition. Jabalpur M.P: M/s Banarasidas Bhanot(P); 2017.631-632.
- Algappan R.Manual of Practical Medicine.5th ed. Jaypee brothers medical publishers; 2014.918-923.
- 3) WHO definition of an older or elderly person (cited) 2014 Feb 10; available from http://www.who.int/healthinfo/survey/ageingdefinolder/en/index/html.
- 4) Sina I. Alqanoon fil tib (Urdu translation by Kanturi GH). Vol 1. New Delhi: Idara Kitabul Shifa;2010.26-28,162,194-196,1246-1247.
- Jeylakshmi S, Chakrabart S, Gupta N. Situation Analysis of the Elderly in India. Central Statistics Office. New Delhi. Ministry of Statistics & Programme Implementation Government of India 2011:1-8,20.
- 6) Rath SP, Das B, Puthan P, Sharma AK, Nair L. Demography Of India: The Dynamics And Differences - A Reflective Study Of Census 2011. International Journal of Research in Commerce, Economics & Management 2011;1(6):42-55.
- Ingle GK, Nath A. Geriatric health in India: Concerns and solutions: The Indian Journal of medical research 2008;33(4):214-218.
- Chanana HB, Talwar PP. Aging in India: Its Socioeconomic and Health Implication. Asia-Pacific Population Journal YNM;2(3):23-38.
- Shah SN. API Textbook of medicine. Vol 2. 8th ed. Mumbai: The association of physicians of India; 2008.1578-1581.
- 10) William LM. Modern Theories of Aging. Members only Newsletter April 2002;1-4.
- 11) Jin K. Modern Biological Theories of Aging. Aging and disease 2010;1(2):72-74.
- 12) Costa et al. A synopsis on aging—Theories, mechanisms and future prospects. Ageing Research Reviews 2016;29:90–112.
- 13) Charles Mobbs. Molecular and Biologic Factors in Aging. In: Cassel CK, editor. Geriatric medicine- an evidence based approach. 4th edition. New York, USA: Springer; 2003.17-24.
- 14) Ahmed SI. Introduction to Al Umur al Tabi'yah.2nd edition. New Delhi: CCRUM; 2009.165,172-173,181-182.
- 15) Nafis BD. Kulliyat e nafisi (Urdu translation by Kabeeruddin H). New Delhi: Idara Kitabul Shifa;1994.50,367-372.
- 16) Zillur Rehman HS. Ainul hayat. Aligarh: Ibn Sina Academy;2007.10-22,144,152,155-162,172,173,181,182

- 17) All India Unani Tibbi Conference. Qarabadeen Majeedi. 9th edition. New Delhi: Ajanta Offset Limited; 1986.400.
- Said HM. Hamdard Pharmacopoeia of Eastern Medicine. Delhi: Sri Satguru Publications, Indian Book Centre; 1997.292.
- 19) Khan M. A. Qarabadeen Azam. New Delhi: CCRUM, Ministry of H & FW; 2009.489
- 20) Ibn sina. Alqanoon fil tib (Urdu translation by G H Kantoori). Vol II. New Delhi: Idara kitabul Shifa; 2010.296,324-328,353,360,361,426,433
- 21) Baghdadi IH. Al-Mukhtarat fit Tib. Part II. New Delhi: CCRUM; Ministry of H & FW; 2005.83,118,121-123,126,162,168,229,239.
- 22) Khan MA. Maheet azam.Jild I. New Delhi: CCRUM, Ministry of H & FW; 2012.p741-742
- 23) Razi ABZ. Kitab Al Hawi Fit Tib. Vol 21st Part 1st New Delhi: CCRUM, Ministry of H & FW;2007.p 90,97-98,139-141,187-189
- Khan MA. Maheet azam. Jild III. New Delhi:CCRUM, Ministry of H & FW; 2014.p643-645,487-488.
- 25) Antaki DZ. Tazkirah ulul albab. Part I New Delhi: CCRUM; Ministry of H & FW; 2007.114,115,153,337,338,421,422,430,431,472,473,635,636,641,642.
- Mohiuddin G. Fasihuddin C. Rehnuma e aqaqeer. Vol 2. New Delhi: Aejaz Publishing House; 2004.116-124,233-243,294-299.
- 27) Haleem MA. Mufradat azeezi, New Delhi: CCRUM. Ministry of H & FW; 2009.
 p14,17,18,20,21,29-31,43,48,52,55,58,75,79,90,91,98,102, 104,107,117,118
- 28) Choi et al. Hepatoprotective Effect of Terminalia chebula against t-BHP-Induced Acute Liver Injury in C57/BL6 Mice. Hindawi Publishing Corporation Evidence-Based Complementary and Alternative Medicine Volume 2015, Article ID 517350, 11 pages
- Shukla S, Jadon A, Bhadauria M. Protective effect of Terminalia belerica Roxb, and gallic acid against carbon tetra chloride induced damage in albino rats. Journal of Ethnopharmacology. 2006;109:214-218.
- Jyothi Y, Jagadish V, Asad KM. Effect of Hexane Extract of Boswellia Serrata Oleo-Gum Resin on Chemically Induced Liver Damage. Pak J Pharm Sci, 2006;19(2):125-129.
- 31) Vengal RP, Ashok CK, Ashwini G, Ambareesh KR, Sangeetha S. Evaluation of Hepatoprotective Activity of Santallum Album (Stem) Against Paracetamol Induced Hepatotoxicity in Albino Wistar Rats. International Journal of Innovative Pharmaceutical Research. 2014;5(1):370-373.

- 32) Gilani AH, Janbaz KH. Evaluation of the liver protective potential of *Cichorium intybus* seed extract on Acetaminophen and CCl4-induced damage. Phytomedicine, 1994;1:193-197.
- 33) Nirwane AM, Bapat A R. Effect of methanolic extract of Piper nigrum fruits in Ethanol-CCl4 induced hepatotoxicity in Wistar rats. Der Pharmacia Lettre 2012;4(3):795-802.
- 34) Atta AH, TA, Mouneir SM, Kamel GN, Alwabel A, Zaher S. Hepatoprotective Effect of Methanol Extracts of Zingiber officinale and Cichorium intybus. Indian J Pharm Sci. 2010 Sep-Oct;72(5):564–570.
- 35) Palani S, Raja S, Kumar RP, Venkadesan D, Devi K, Sivaraj A, et al. Therapeutic efficacy of antihepatotoxic and antioxidant activities of Acorus calamus on acetaminophen- induced toxicity in Rat. Int J Integ Biol 2009;7:39-44.
- 36) Tamhane M D, Thorat S P, Rege N N, Dahanukar S A. Effect of oral administration of Terminalia chebula on gastric emptying: an experimental study. J Postgrad Med 1997;43:12
- Choudhary GP. Anti-ulcer activity of the ethanolic extract of Terminalia belerica Roxb. Oct-Dec 2012;1(4):1293-1297.
- 38) Singh S et al. The gastric ulcer protective effect of boswellic acids, a leukotriene inhibitor from Boswellia serrata, in rats. Phytomedicine. 2008; 408-415
- 39) Ahmed et al. Anti-ulcer Activity of Sandalwood (Santalum album L.) Stem Hydroalcoholic Extract in Three Gastric-Ulceration Models of Wistar Rats. Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas 2013;12(1):81-91.
- Yamahara J, Miki K, Chisaka T et al. Cholagogic effect of ginger and its active constituents. J Ethnopharmacol 1985;13(2):217-225.
- Platel K, Srinivasan K. Influence of dietary spices or their active principles on digestive enzymes of small intestinal mucosa in rats. See comment in PubMed Commons below Int J Food Sci Nutr 1996;47:55-59.
- 42) Platel K and Srinivasan K. Studies on the influence of dietary spices on food transit time in experimental rats. Nutr Res 2001;21:1309-14.
- 43) Platel K, Srinivasan K. Influence of dietary spices or their active principles on digestive enzymes of small intestinal mucosa in rats. International Journal of Food Sciences and Nutrition 1996;47(1):55-59.
- 44) Barbara SMVD, Wijnhoven HAH, Lee JS, Houston DK, Hue T, Harris TB, Kritchevsky SB, Newman AB, Visser M. Poor appetite and dietary intake in community dwelling older adults. Journal of American geriatric society 2017;65(10):2190-2197.

- 45) Pilgrim AL, Robinson SM, Sayer AA, Roberts HC. An overview of appetite decline in older people. Nurs Older People 2015;27(5):29-35.
- 46) Giezenaar C, Chapman I, Luscombe-Marsh N, Feinle-Bisset C, Horowitz M, Soenen S. Ageing Is Associated with Decreases in Appetite and Energy Intake--A MetaAnalysis in Healthy Adults. Nutrients 2016;8(1):28.
- 47) Tanvir Ahmed and Nadim Haboubi. Assessment and management of nutrition in older people and its importance to health. Clin Interv Aging. 2010;5:207-216.
- 48) Norman K, Stobäus N, Gonzalez M C, Schulzke J-D and Pirlich M .Hand grip strength: Outcome predictor and marker of nutritional status Clin. Nutr. 2011;30:135–42.
- 49) Anne E. Wind, Tim Takken, Paul J. M. Helders, Raoul H. H. Engelbert. Is grip strength a predictor for total muscle strength in healthy children, adolescents, and young adults. European Journal of Pediatrics March 2010;169(3):281–287.
- 50) Silva CL, Lima Costa MF, Firmo JO, Peixoto SV. Haemoglobin level in older adults and the association with nutritional status and use of health services: Bambui project. Cad Saude Publica 2002;28(11):2085-94.
- 51) Lefebvre JS, Haynes L. Ageing of the CD4 T Cell compartment. Open Longev Sci. 2012;6:83-91.
- 52) B Ahirwar, AK Singhai, AK Dixit. Effect of terminalia chebula fruits on lipid profiles of rats. Journal of natural remedies. Jan 2003;3(1):359
- 53) RCR Latha and P Daisy. Influence of terminalia belericaRoxb fruit extract on biochemical parameters in streptozotocin induced diabetic rats. International journal of pharmacology 2010;6(2):89-96.
- 54) Zutsi U, Rao PG, Kaur S. Mechanism of Cholesterol Lowering Effect of Salai guggal ex-Boswellia serrata Roxb. Indian J Pharmacol 1986;18:182-3.
- 55) Garcimartín A, Santos-López JA, Benedí J, Bastida S, Sánchez-Muniz FJ. Effects of silicon inclusion in restructured meat-enriched diet on lipoprotein profile and composition in aged wistar rats. Atherosclerosis, 2014; 235(2): e202-e203.
- 56) Kulkarni CR, Joglekar MM, Patil SB, Arvindekar AU. Antihyperglycemic and antihyperlipidemic effect of Santalum album in streptozotocin induced diabetic rats. Pharmaceutical Biology, 2012;50:360-365.
- 57) Cho AS et al. Chlorogenic acid exhibits anti-obesity property and improves lipid metabolism in high-fat diet-induced-obese mice. Food and chemical toxicology 2010;48:937-943

- 58) R. Aruna, Sathiyarajeswaran P, Gopakumar K, Ramaswamy RS. Cardioprotective effects of kitchen culinaries mentioned in Siddha literature. Journal of Pharmacognosy and Phytochemistry 2014;3(3):71-79.
- 59) Wakade SA, Shah SA, Kulkarni PM, Juvekar RA. Protective effect of Piper longum L. on oxidative stress induced injury and cellular abnormality in adriamycin induced cardiotoxicity in rats. Indian J Exp Biol 2008;46:528-533.
- 60) Vijayakumar RS, Surya D, Senthilkumar R, Nalini N. Hypolipidemic effect of black pepper (Piper nigrum Linn.) in rats fed high fat diet. J Clin Biochem Nutr 2002;32:31-42.
- 61) Gholamhoseinian A, Shahouzehi B, Joukar S, Iranpoor M. Effect of *Quercus infectoria* and *Rosa damascena* on lipid profile and atherosclerotic plaque formation in rabbit model of hyperlipidemia. Pak J Biol Sci 2012;15(1):27-33.
- 62) Gholamhoseinian A, Shahouzehi B, Sharififar F.Inhibitory effect of some plant extracts on pancreatic lipase. Int J Pharmacol, 2010;6(1):18-24.
- 63) Sharma I, Gusain D, Dixit VP. Hypolipidemic and antiatherosclerotic effects of zingiber officinale in cholesterol fed rabbits. Phytother Res 1996;10(6):517-518.
- 64) Srinivasan K, Sambaiah K. The effect of spices on cholesterol 7 alpha hydroxylase activity and on serum and hepatic cholesterol levels in the rat. Int J Vitam Nutr Res 1991;61(4):364-369.
- 65) Kulkarni CR, Joglekar MM, Patil SB, Arvindekar AU. Antihyperglycemic and antihyperlipidemic effect of Santalum album in streptozotocin induced diabetic rats. Pharmaceutical Biology, 2012;50:360-365.
- 66) Zutsi U, Rao PG, Kaur S. Mechanism of Cholesterol Lowering Effect of Salai guggal ex-Boswellia serrata Roxb. Indian J Pharmacol 1986;18:182-3.
- 67) R. Aruna, Sathiyarajeswaran P, Gopakumar K, Ramaswamy RS. Cardioprotective effects of kitchen culinaries mentioned in Siddha literature. Journal of Pharmacognosy and Phytochemistry 2014;3(3):71-79.
- 68) Wakade SA, Shah SA, Kulkarni PM, Juvekar RA. Protective effect of Piper longum L. on oxidative stress induced injury and cellular abnormality in adriamycin induced cardiotoxicity in rats. Indian J Exp Biol 2008;46:528-533.
- 69) Vijayakumar RS, Surya D, Senthilkumar R, Nalini N. Hypolipidemic effect of black pepper (Piper nigrum Linn.) in rats fed high fat diet. J Clin Biochem Nutr 2002;32:31-42.
- 70) Mamgain P, Singh RH. Control clinical trial of the lekhaniya drug vaca (Acorus calamus) in case of ischemic heart diseases. J Res Ayur Siddha 1994;15:35-51.

- 71) Mahesh R, Begum VMB. Antioxidant Effect Of Terminalia Chebula Aqueous Extract On Age-Related Oxidative Stress In Heart. Iranian Journal Of Pharmacology & Therapeutics 2007;6:197-201.
- 72) Tanaka M, Kishimoto Y, Saita E, Suzuki-Sugihara N, Kamiya T et al. Terminalia belerica extract inhibits low density lipoprotein oxidation and macrophage inflammatory response in vitro. Antioxidants,2016:5:20.
- 73) Yi Ding etal. Neuroprotection by Acetyl-11-Keto-β-Boswellic Acid, in Ischemic Brain Injury Involves the Nrf2/ HO-1 defense Pathway.Scientific Reports, 2014;4(7002):1-9.
- 74) Garcimartín A, Santos-López JA, Benedí J, Bastida S, Sánchez-Muniz FJ. Effects of silicon inclusion in restructured meat-enriched diet on lipoprotein profile and composition in aged wistar rats. Atherosclerosis, 2014; 235(2): e202-e203.
- 75) Sharma I, Gusain D, Dixit VP. Hypolipidemic and antiatherosclerotic effects of zingiber officinale in cholesterol fed rabbits. Phytother Res 1996;10(6):517-518.
- 76) Philip Barter .The role of HDL cholesterol in preventing atherosclerotic disease. European Heart Journal Sup F 2005;7:F4-F8.
- 77) Tribble DL, Chu BM, Gong EL, Venrooij VF, Nichols AV. HDL antioxidant effects as assessed using a non exchangeable probe to monitor particle specific peroxidative stress in LDL-HDL mixtures. J Lipid Res. 1995;36(12):2580-89.
- 78) Kobayashi M, N Shoji, Ohizumi Y. Gingerol, a novel cardiotonic agent, activates the Ca2+ pumping ATPase in skeletal and cardiac sarcoplasmic reticulum. Biochim Biophys Acta 1987;903(1):96-102.
- 79) Awasthi, L. Nath B. Chemical Examination Of Terminalia Chebula Roxb. Part I. A New Cardiac Glycoside. Journal Of Indian Chemical Society, 1968;45:913
- VRC. Ramana Kumari, S.V. Reddy, B.M., Azeem MA., Prabhakar, MC, Appa Rao, A.B.N. Cardiotonic Activity Of The Fruit Of Terminalia Chebula. Fitoterapia, 1990;61:517-525.
- 81) Azim MA. Reddy, B.M. Appa Rao, AVN Prabhakar. MC Prasad, MSK. Effect Of Termialia Chebula Extracts On Frog Heart Muscle (Sodium Ion, Potassium Ion, Magnesium Ion) ATPase.Fetoterpia, 1992;63;300-303.
- Srivastava RD, Dwivedi S, Shreenivasan KK, Chandrashekhar. Cardiovascular Effects Of Terminalia Species Of Plants. Indian Drugs 1992;29:144-149
- 83) Reddy B.M., Ramesh M, Appa Rao, A.B.N., Prabhakar MC, Isolation An Studies On Cardiotonic Activity Of Active Principles From The Fruits Terminalia Chebula.Proceeding of 46th Annual Indian Congress Chandigarh, 28-30th Dec 1994

- 84) Rajmohamed MA, Natarajan S, Palanisamy P, Abdulkader AM, Govindaraju A. Antioxidant and Cholinesterase Inhibitory Activities of Ethyl Acetate Extract of Terminalia chebula: Cellfree In-vitro and In-silico Studies. Pharmacognosy Magazine 2017;13(Suppl 3):S437-S445.
- 85) FH Neilson. Update on the possible nutritional importance of silicon. Journal of trace elements in medicine and biology 2014;30(30):1-3.
- 86) Kumar R, Anjum N, Tripathi VC. Phytochemistry and pharmacology of Santalum album L; A review. World journal of pharmaceutical research 2015;4(10):1842-1876.
- 87) <u>Mao QQ, Huang Z, Zhong XM, Xian YF, Ip SP</u>. Piperine reverses the effects of corticosterone on behavior and hippocampal BDNF expression in mice. <u>Neurochem Int.</u> 2014 Jul;74:36-41.
- 88) Hritcu L, Noumedem JA, Cioanca O, Hancianu M, Kuete V, et al. Methanolic extract of Piper nigrum fruits improves memory impairment by decreasing brain oxidative stress in amyloid beta(1-42) rat model of Alzheimer's disease. Cell MolNeurobiol 2014;34:437-449.
- 89) Emig HM, The pharmacological action of ginger. J Amer Pharm Ass 1931;20:114-116.
- 90) Tripathi AK, Singh RH. Clinical study on an indigenous drug vaca (Acorus calamus) in the treatment of depressive illness. J Res Ayur Siddha 1995;16:24-34.
- 91) Liguori I, Russo G, Curcio F, Bulli G1, Aran L, Della-Morte D, Gargiulo G, Testa G, Cacciatore F, Bonaduce D, Abete P. Oxidative stress, aging, and diseases, Clin Interv Aging. 2018 Apr 26;13:757-772.
- 92) Mahesh R, Begum VMB. Antioxidant Effect Of Terminalia Chebula Aqueous Extract On Age-Related Oxidative Stress In Heart. Iranian Journal Of Pharmacology & Therapeutics 2007;6:197-201.
- 93) Yi Ding etal. Neuroprotection by Acetyl-11-Keto-β-Boswellic Acid, in Ischemic Brain Injury Involves the Nrf2/ HO-1 defense Pathway.Scientific Reports, 2014;4(7002):1-9.
- 94) Garcimartín A, Santos-López JA, Bastida S, Benedí J, Sánchez-Muniz FJ. Silicon enriched restructured pork affects the lipoprotein profile, VLDL oxidation, and LDL receptor gene expression in aged rats fed an atherogenic diet. The Journal of nutrition, 2015;145(9):2039-2045.
- 95) Scartezzini P, Speroni E, Review on some plants of Indian traditional medicine with antioxidant activity. J. Ethnopharmacol., 2000;71:23-43.
- 96) Jagetia GC, Baliga MS, Evaluation of Nitric Oxide scavenging activity of certain Indian medicinal plants in-vitro: a preliminary study. J Med Food, 2004;7:343-348.
- 97) Patrick LO, Timothy J. Antioxidants in medicines and spices as cardioprotective agents in tibetan highlanders. Pharmaceutical Biology, 2002;40:346-357.

- 98) Khan, MS, Singh M, Khan, MA, Ahmed S. Protective effect of Santalum album on doxorubicin induced cardiotoxicity in rats. 2014;3(2):2760-2771.
- 99) Pedapati SHS, Khan MI, Prabhakar P, Giridhar P. Cyanidin-3 glucoside, nutritionally important constituents and in vitro antioxidant activities of Santalum album L. berries. Food Research International 2013;50(1):275-281
- 100) Misra BB, Dey S. Phytochemical analyses and evaluation of antioxidant efficacy of in vitro callus extract of East Indian Sandalwood Tree (Santalum album L.). Journal of Pharmacognosy and Phytochemistry, 2012;1:8-18.
- 101) Misra BB, Dey S, Evaluation of in vivo anti-hyperglycemic and antioxidant potentials of α -santalol and sandalwood oil. Phytomedicine, 2013; 20(5):409-416.
- 102) Mehmood N, Zubair M, Rizwan K, Rasool N, Shahid M, Ahmad V. Antioxidant, Antimicrobial and Phytochemical Analysis of Cichorium intybus Seeds Extract and Various Organic Fractions .Iranian Journal of Pharmaceutical Research 2012;11(4):1145-1151.
- 103) Hritcu L, Noumedem JA, Cioanca O, Hancianu M, Kuete V, et al. Methanolic extract of Piper nigrum fruits improves memory impairment by decreasing brain oxidative stress in amyloid beta(1-42) rat model of Alzheimer's disease. Cell MolNeurobiol 2014;34:437-449.
- 104) Shobana S, KA Naidu. Antioxidant activity of selected Indian spices. Prostaglandins Leukot Essent Fatty Acids 2000;62(2):107-110
- 105) Ahmed RS, V Seth, ST Pasha, BD Banerjee. Influence of dietary ginger zingiber officinale roscoe on oxidative stress induced by malathion in rats. Food Chem Toxicol 2000; 38(5):443-450
- 106) Sekiwa YK. Kubota. A Kobayashi. Isolation of novel glucosides related to gingerdiol from ginger and their antioxidative activities. J Agr Food Chem 2000;48(2):373-377.
- 107) Subathraa K, Poonguzhali TV. In vitro studies on antioxidant and free radical scavenging activities of aqueous extract of Acorus calamus L. Int J Curr Sci 2012;1:69-73.
- 108) Jafari M, Zarban A, Pham S, Wang T. *Rosa damascena* Decreased Mortality in Adult *Drosophila*. J Med Food. 2008;11:9–13.
- 109) Kabeeruddin H. Alqarabadeen. New Delhi: CCRUM, Ministry of H & FW; 2006.1219.
- 110) Kabeeruddin M. Bayaz e kabeer. Vol 1. Hyderabad: Hikmat Book Depot(P); 1935.144, 145.
- 111) Ghani N. Khazainul Advia. New Delhi: Idara Kitabul Shifa; YNM.348-349,395-396,421-422,869-870,932,997,998,1069,1070,1133-1135,1231-1233,1352-1354.

International Standard Serial Number (ISSN): 2319-8141

112) Nadkarni AK, Indian Materia Medica. 3rd edition. Vol 1. Bombay: Popular Book Depot; 1976.
35-37,172-174,312-314, 969⁻972,1072-1073, 1098-1102, 1202-1210,1308-1314