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Original Article

Safety Profile and Effect on Libido of a Combined *Bryophyllum pinnatum, Moringa oleifera* and Vitamin C Phytotherapeutic Agent

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ABSTRACT

Introduction: Both *Moringa oleifera* and *Bryophyllum pinnatum* are well known phytotherapeutics with a range of potential applications that capitalize on their anti-oxidant properties, ranging from improving risk factors for cardiovascular disease to increasing sexual desire. The literature, however, mainly focuses on these effects *in-vitro* or in non-human subjects. **Aims:** We aimed to investigate the side effects of a combination agent with known proportions of these two phytotherapeutics, as well as to determine any effect on the human sexual drive. **Method:** Sixty nine (n=69) participants were enrolled in a prospective cohort study and followed up for a minimum of six months. Data regarding adverse effects and libido was determined from a 22-item Quality of Life questionnaire as well as a checklist of common side-effects completed at each monthly follow-up. **Results:** Eight participants were lost to follow-up; in the remaining participants there were no reported major adverse effects. No abnormal bleeding, urinary tract infections, asthma exacerbations, or changes in memory were reported. Minor issues reported by participants taking the agent included fluctuations in appetite (22.9%) and sleep pattern (16.4%), gastrointestinal upset (14.7%), respiratory symptoms, such as shortness of breath or wheezing (8.1%), and muscle aches (8.1%). Women did not report a change in libido whereas 31.8% of men reported a statistically significant increase in libido by their second to third follow up ($p<0.05$). **Conclusion:** This study acts as a small preliminary report and suggests that combination *M. oleifera*, *B. pinnatum* and vitamin C has a favorable safety profile and may increase libido in human males.

Key words: Antioxidant, Male sexual function, *Moringa*, Side-effects, Supplement.

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INTRODUCTION

Moringa oleifera and *Bryophyllum pinnatum* are plants with a wide range of potential medicinal uses and which have both been found to possess significant antioxidant activity. *Moringa oleifera*, the most well-known of the 13 *Moringa* varieties,[1] is native to the Indian subcontinent, but has since been cultivated worldwide in tropical and sub-tropical regions.[2] Therapeutic uses of this plant, which is composed of all-edible parts, dates back to antiquity, but interest in its vast prospective uses has experienced a recent surge, especially in western countries.[2] The entire *Moringa* plant, also known by the regional names drumstick tree or saijan,[1] is rich in protein, carbohydrates, minerals such as iron and calcium, vitamins, and essential amino acids.[3] A multitude of antioxidants have been isolated from the plant, and it is the rich concentration of these antioxidants, especially those derived from the flavonoids in the leaves that are thought to be responsible for its beneficial effects.[2] The potent antioxidant activity and radical scavenging properties of *Moringa* have been the investigated by various research teams who have demonstrated antioxidant activity as high as 65.1% and 66.8% in the β-carotene – linoleic acid system,[4] and a free radical scavenging effect comparable to reference antioxidants, thus lending the ability to prevent and protect against major bio molecular oxidative damage.[5] One *ex vivo* study showed that in hyper-cholesterol rabbits, *Moringa* extracts significantly lowered cholesterol levels ($p<0.05$) in an effect that was comparable to traditional statin medication.[6] This study, along with others that suggest *Moringa* has anti-inflammatory, anti-hypertensive, and hypoglycemic effects[2,6] illustrate the potential for the plant's use in the prevention of cardiovascular disease. Additionally, other studies have indicated that *Moringa oleifera* may act as an antibiotic, anti-mutagenic, anti-spasmodic and male sexual enhancer.[2,7-8]

Bryophyllum pinnatum, also known as leaf of life, life plant, and the miracle plant is a perennial herb native to Madagascar[9] but now widely cultivated in tropical areas throughout the world.[10] Analysis of the plant demonstrates a variety of phytochemicals, including alkaloids, phenols, carotenoids, bufadienolides glycosides and flavonoids.[10] Pharmacological applications for the plant has included its use as an antimicrobial, antihypertensive,[11] immune-modulatory agent, wound healing agent, muscle relaxant (with promising utility during human labour) and sedative.[10] Similar to *Moringa*, the plant produces antioxidants with free radical scavenging properties,[12] with one study showing a 50% oxidative inhibition rate.[10]

Based on the evidence for great medicinal value from these plants, a supplement was formulated: the "Life" supplement, which combines *Moringa oleifera*, *Bryophyllum pinnatum* and vitamin C (which also exhibits protection against oxidative stress).[11] The literature hints at the potential for these plants to ameliorate a variety of human pathologies, as outlined previously, but clinical studies on efficacy and safety are lacking.[2] A prospective longitudinal study was initiated with the aim of determining the potential of the 'Life' phytotherapeutic agent in managing the risk factors for cardiovascular disease. The objectives of this article are to specifically investigate the side effects of this agent in the intervention population as well as to ascertain any effect on the human sexual drive.

MATERIALS AND METHODS

Persons were considered for enrolment if they met the following inclusion criteria: adult, with two or more risk factors for heart disease, including elevated total cholesterol levels (≥ 5.2mmol/L) and/or elevated LDL cholesterol levels (4.13mmol/L or higher), high blood pressure (≥ 140/90mmHg), a sedentary lifestyle (<2 days a week of physical activity apart from Activities of Daily Living), a body mass index (BMI) greater than 30kg/m^2 and/or a history of diabetes (diagnosed over a year prior to the study and a 126mg/dL or higher fasting plasma glucose) or pre-dia-

betes (100mg/dL to 125mg/dL fasting plasma glucose on three or more occasions.). Critically ill persons; persons with kidney disease, renal insufficiency, one or no risk factors for heart disease; and an inability or unwillingness to provide informed consent were excluded from the study. After reading and signing a mandatory informed consent sheet, participants were admitted into the study and had a baseline blood work and body weight taken. After the results of the blood work were received they commenced once daily, before bedtime, intake of one "Life" supplement capsule containing 25 mg of *Moringa oleifera*, 25mg of *Bryophyllum pinnatum* and 700mg of vitamin C. Over the course of six months, participants reported back for monthly follow-ups consisting of a fasting blood test (cholesterol profile, blood glucose, HbA1C and haemoglobin) blood pressure check, and completion of a quality of life (QOL) questionnaire. The questionnaire contained 22 items appraising various aspects of physical and mental well-being, such as appetite, sleep, libido, male sexual function, energy levels, mental state, and also asked about adverse effects experienced. Body weight was assessed at intake and every three months using the same digital scale. Blood samples were taken by a laboratory technologist and analysis for all samples was performed by a single calibrated Reflotron machine. An individual researcher obtained informed consent, performed all follow-ups, collected, and recorded data in a Microsoft Excel spread sheet. This same software was used for simple percentage calculations and test of association between categorical variables were performed using Pearson's chi-square test with p value of <0.05 being considered statistically significant.

RESULTS

The study enrolled 69 (n=69) participants aged 23 to 83 years old over the course of six months. Approximately equal numbers of the sexes participated, with thirty two being females and thirty seven being males. Five female and three male participants were lost to follow-up. In addition to a pre-defined checklist of experienced/adverse symptoms, a note was made of any other effects mentioned during the follow-up visits. There were no major adverse effects reported during the study period and no episodes of abnormal bleeding, urinary tract infections, asthma exacerbations, or changes in memory. Some minor issues were however reported, and these are presented in Tables 1 and 2. Appetite variations, presenting either as an increase or decrease in same, was the most commonly reported issue in the total sample (22.9%), followed by changes in sleeping patterns (16.4%) and gastrointestinal upset (14.7%). Less than 10% of the participants reported various other minor complaints such as muscle aches, shortness of breath or wheezing, drier or moister skin, cold or flu and anxiety. Reported issues were further broken down according to participants' gender and revealed that approximately equal percentages of males and females reported appetite fluctuations and changes in sleeping patterns. More women reported respiratory symptoms and anxiety but these issues were statistically non-significant between the sexes. Gastrointestinal symptoms included constipation, flatulence and diarrhoea and were significantly more reported by women ($p < 0.05$). None of the female participants described a change in libido, but by the second or third follow-up, 31.8% of men had reported a statistically significant increase in libido (p<0.05).

DISCUSSION

The "Life" supplement contains phytotherapeutics with potent antioxidant capacity and demonstrated no significant adverse effects when taken by a cohort of patients with two or more risk factors for cardiovascular disease. The supplement also seems to increase male sexual drive with statistical significance. No literature on the supplement as a single agent exists due to its novel combination of ingredients, however the favourable safety profile of its composite ingredients has been mentioned in various studies. Reported symptoms of toxicity from the *Moringa* plant have been found to include respiratory distress, a change in hair appearance and increased salivation.[13] However, the leaves of the plant have shown no acute or sub-acute toxic effects in several animal and human studies.[2,13-14] One study specifically evaluating the toxicity of the plant in rats found no overt adverse effects but recommended that the daily dose not exceed 70 grams per day[3] - a dose several thousand times that present in the supplement currently under consideration. Similarly, several studies have found no significant adverse effects when *Bryophyllum pinnatum* was used in both animals and humans.[9,15-16] A Swiss research involving the use of Bryophyllum as a sleeping aid in cancer patients showed that the plant was well tolerated, with fatigue, dry throat, difficult digestion and agitation only reported in 6 of the 28 patients.[17] The statistically significant improvement in sleep seen in those patients was not reproduced in our investigation; however the Swiss study used much larger doses of Bryophyllum (350mg to 700mg per day).

Sexual function is a complicated interplay of both physical and psychological factors, with stressors of either nature leading to an appreciable decrease in function. The high prevalence of male sexual dysfunction, estimated to affect between 20 to 30% of men, is a source of distress and can lead to reduced quality of life.[8] Animal studies have shown that *Moringa oleifera* improves sexual performance and drive with postulated mechanisms that partly depend on its antioxidant properties.[8,13,18] The plant is thought to decrease oxidative stress affecting the Leydig cells of the testes, thus allowing more testosterone – which increases libido - to be produced. The plant is also thought to increase endogenous dopamine, which increases sexual motivation. It is posited that this is achieved both via suppression of the Monoamine Oxidase system as well as by supplying high levels of phenylalanine, which serves as a precursor for dopamine synthesis.[8] This study's finding that male sexual drive is increased to a statistically significant degree suggests that these mechanisms also operate in humans and warrant further large scale investigation. The finding of a gender discrepancy in gastrointestinal symptoms, though a minor issue, should also be the subject of larger scale research.

Table 1: Reported physical health issues

Physical Health Parameters	Males (%)	Females (%)	TOTAL (%)
Skin hydration	2 (5.8)	3 (11.1)	5 (8.2)
Hair loss	0	1 (3.7)	1 (1.6)
Urinary tract infections	0	0	0
Abnormal bleeding	0	0	0
Arthritis flare	1 (2.9)	0	1 (1.6)
Muscle aches	3 (8.8)	2 (7.4)	5 (8.2)
Asthma exacerbations	0	0	0
Cold or Flu	2 (5.8)	2 (7.4)	4 (6.5)
Respiratory symptoms	1 (2.9)	4 (14.8)	5 (8.2)
Gastrointestinal symptoms	1 (2.9)	8 (29.6)	9 (14.7)
Appetite	7 (20.5)	7 (25.9)	14 (22.9)

Table 2: Reported mental health and psycho-social issues

Mental Health and Psycho-Social Parameters	Males (%)	Females (%)	TOTAL (%)
Mood	1 (2.9)	0	1 (1.6)
Anxiety	1 (2.9)	3 (11.1)	4 (6.5)
Depression	0	1 (3.7)	1 (1.6)
Memory changes	0	0	0
Sleeping pattern	5 (14.7)	5 (18.5)	10 (16.4)

Several limitations of the study design need to be acknowledged. The study did not retain a control group, thereby reducing the internal validity. A controlled clinical trial would be necessary to confirm the encouraging results of this preliminary investigation. The study population was limited to persons with two or more risk factors for cardiovascular disease, limiting the generalizability of the results to the general populace. However, the findings of increased libido in a group of men with a higher probability of sexual dysfunction due to cardiovascular disease risk, as well as safety in this risk group suggests that libido increase and safety profile in the general population will be satisfactory. The retention rate of the study was 88.4%; although baseline measurements revealed no significant differences in those lost to follow-up and those who completed the study, it would not be possible to extrapolate any adverse effects or changes to libido in the group with missing data.

CONCLUSION

The results of this investigation suggest that a combination agent of *Bryophyllum pinnatum*, *Moringa oleifera*. and Vitamin C presents no significant side effects. The commonly reported issues were appetite fluctuations, gastrointestinal upset and change in sleep patterns, and reported in less than 23% of patients. Further, the agent shows promise as a possible therapeutic option for decreased male sexual drive, showing a significant increase in the libidos of the male, but not the female participants. It is hypothesised that the antioxidants in the agent, especially from *Moringa oleifera* is responsible for this libido-boosting effect. These encouraging preliminary results should be further investigated with larger double-blind interventions.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS USED

LDL: Low Density Lipoprotein; **BMI:** Body Mass Index; **HbA1C:** Hemoglobin A1C; **QOL:** Quality of Life.

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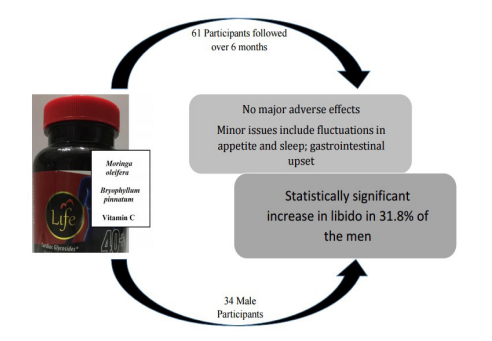
PICTORIAL ABSTRACT



SUMMARY

- The combination agent of Moringa oleifera, Bryophyllum pinnatum and vitamin C is a source of natural potent antioxidants.
- Sixty one participants administered this combination agent and followed for 6 months reported no major adverse effects.
- The combination agent was found to increase male libido to a statistically significant degree.
- These encouraging preliminary results should be further investigated with larger double-blind interventions.

ABOUT AUTHORS

Dr. Alfred Sparman: Is an interventional cardiologist and pioneer of angioplasty in Barbados. After earning his medical degree from the New York Medical College and completing his internship, residency in internal medicine and cardiology fellowship, his interest in research continued. He is the author of two publications; "The Initiation of Coronary Angioplasty and Stenting in a Single Outpatient Centre in Barbados (2008) and "Manchineel Poisoning Bradyarrhythmia. A Possible Association" (2009), which have both been published in the West Indian Medical Journal. Dr. Sparman is currently the CEO of the The Sparman Clinic and 4H Hospital, a state-of-the-art cardiovascular and general medicine hospital which offers their services to the citizens of Barbados and the wider Caribbean.

Kimberlee Thompson MSc: Has held the position of dietitian at The Sparman Clinic from 2010 to present. Upon graduating in 2014 with a Master's degree with distinction, she extended her portfolio to include clinical physiology. Apart from managing the dietary needs of patients and providing counseling, she manages the clinic's Cardiac Rehabilitation and Exercise Programme. Her previous research has focused on nutrition and its role in the management of varying conditions. However, with the recent trends in epidemiological data, her research interests have extended to Noncommunicable Chronic Diseases (NCDs) and exercise as medicine..