Research Article

Efficacy of GLOW™ on Alleviating Symptoms of Inattention, Hyperactivity/Impulsivity, Depression and Sexual Dysfunction; A Preliminary Study

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ABSTRACT

In view of the issues of current pharmacological interventions to mitigate symptoms of major depression and attention deicits and hyperactivity disorders (ADHD), there has been a growing interest in investigating the efficacy and safety of complementary and alternative medicine, such as natural health products.

GLOW™ is a dietary supplement with 9 natural ingredients (Niacin, Zinc, Gingko Biloba, L-arginine, Saw Palmetto Berry, Epimodium Herb Extract (Horny goat weed), Tribulus Terrestris, Tongkat Ali, and Avena Sativa) that was designed to alleviate the symptoms associated with major depression, adult ADHD, and the possible side-effects of their pharmacological treatments, including, poor concentration, forgetfulness, lack of motivation, depression, and sexual dysfunction.

Four survey instruments (Abbreviated ADHD symptom checklist 4, Beck depression inventory, female sexual function index, and international index of erectile function questionnaire) were used to collect data. Data for 63 participants at baseline and follow-ups (Day 15 and Day 30) were analyzed using linear mixed-effects models to determine the efficacy of GLOW™.

Patients could effectively alleviate 1) ADHD related symptoms, such as inattention and hyperactivity/impulsivity, 2) depression, and 3) female sexual dysfunction, such as sexual function in desire, arousal, lubrication, orgasm, and satisfaction, and overall satisfaction, as soon as 15 days of GLOW™ consumption. In this study, the sexual desire for male participants was improved significantly only after using GLOW™ for 30 days. The overall satisfaction of sexual function for male improved after using GLOW™ for 15 days.

This open-label clinical trial demonstrated that GLOW™ is effective and safe to alleviate symptoms of inattention, hyperactivity/impulsivity, depression, and sexual dysfunction.

MeSH Headings/ Keywords: Complementary and alternative medicine; ADHD and depression; Sexual dysfunction

Introduction

Mental disorders are the leading cause of disability as measured by Years Lived with Disability; however, 40.5% of this burden is attributable to major depression [1]. Recent estimates of the prevalence of major depression indicate that 16.6% of adults in the US have been depressed at some point in their lifetime [2]. Symptoms of major depression include low mood, changes in appetite, sleep, or energy, and feelings of guilt or worthlessness [3]. Current medical treatments for major depression primarily involve synthetic antidepressants (e.g., monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants, and selective serotonin reuptake inhibitors (SSRIs)) and psychological interventions (e.g., cognitive behavioral therapy, interpersonal therapy) [3,4]. However, psychological interventions may not be available for patients in need [4], and antidepressants may not effectively treat all depressed patients, with non-response rates of up to 50% [5]. Additionally, adverse effects, such as weight gain, insomnia, headache, anxiety and sexual dysfunction, occur frequently with antidepressant medication [6-8].

Other psychiatric and physical disorders, such as Attention-deficit/hyperactivity disorder (ADHD), can co-occur with major depression [9-12]. ADHD is a highly heritable neurodevelopmental disorder of which patients display persistent core symptoms of inattention, hyperactivity, impulsivity at an abnormal level that would impair their social, academic, or occupational functioning [13,14]. The population prevalence estimate of adult ADHD was approximately 4.4% in the US [15]. Stimulants and non-stimulant medication are the most widely used pharmaceutical treatments for adult ADHD [16]. However, up to 30% of the patients have no satisfactorily response to stimulants, or may not tolerate drugs' common adverse effects such as, appetite loss, insomnia, anorexia, nausea, weight loss, headache, increased blood pressure, abdominal pain, irritability, and mood lability [17-19]. The second-line treatment options for adults with ADHD are nonstimulant medications, primarily including atomoxetine, bupropion, and tricyclic antidepressants [19]. Nonstimulant medications are generally less effective in treating ADHD than stimulants [19]. The most common side effects of atomoxetine are dry mouth, nausea, decreased appetite, insomnia, slightly increased diastolic blood pressure and heart rate, decreased libido, erectile dysfunction, sweating, and dysuria [18,20,21].

In view of the issues of current pharmacological interventions to mitigate symptoms of major depression and ADHD, there has been a growing interest in investigating the efficacy and safety of complementary and alternative medicine, such as natural health products (ex: herbal medicines, vitamins, and minerals) [22-24].

GLOW™ is a dietary supplement with 9 natural ingredients (Table 1) that was designed to alleviate the following symptoms associated with major depression, adult ADHD, and the possible side-effects of their pharmacology treatments,

Table 1: Ingredients of GLOW™ with recommended daily allowances (RDA) for adults given in the same unit.

GLOW ingredients	2 capsules	Male RDA	Female RDA
Niacin	50mg	16mg	14mg
Zinc	30mg	11mg	8mg
Gingko Biloba	100mg	†	†
L-arginine	150mg	†	†
Saw Palmetto Berry	100mg	†	†
Epimodin Herb Extract (Horny goat weed)	60mg	†	†
Tribulus Terrestris	100mg	†	†
Tongkat Ali	300mg	†	†
Avena Sativa	100mg	†	†

including, poor concentration, forgetfulness, lack of motivation, depression, and female/male sexual dysfunction (decreased sexual desire and/or difficulty with orgasm). The combination of the 9 GLOW™ ingredients was determined based on results of rigorous literature research. Previous research has shown that Gingko biloba, a unique species of tree native to East Asia with memory-enhancing effects, may have therapeutic benefits in ADHD [25-27]. Gingko biloba also has been shown to be effective in treating antidepressant-induced sexual dysfunction and generally had a positive effect on all four phases of the response cycle (i.e. desire, excitement, erection and lubrication), orgasm and resolution [28]. Furthermore, Gingko biloba is shown to have mild anti-depression effects [29].

Of the mineral supplements, zinc may have been the most studied and have received much support as an adjunct treatment for ADHD [23]. Reduced impulsiveness, hyperactivity, and socialization difficulties were seen on children supplemented with zinc sulfate (150mg) in a 12-week double-blind study [30]. Low levels of zinc have been associated with inattention, jitters, and delayed cognitive development, which mimic the symptoms of ADHD [30]. Zinc is also considered as a potential nutrient for mood modulation [31].

Niacin (Vitamin B$_3$) is related to oxidation-reduction reactions and metabolism of carbohydrates and tryptophan. Studies have shown that supplementation of niacin may be beneficial in conditions such as chronic fatigue syndrome, depression, and anxiety [32,33]. L-arginine is an amino acid mediating the relaxation of vascular and non-vascular smooth muscle. Administration of L-arginine may be effective in improving erectile function [34,35]. Finally, Saw Palmetto Berry, [36] Epimodium Herb Extract (Horny goat weed) [37,38], Tribulus Terrestris [39,40], Tongkat Ali [41] and Avena Sativa [42,43], are herbal plants with aphrodisiac activity that have been shown to improve sexual function in animal and human studies.

Although the effects of each individual ingredient of GLOW™ are encouraging, no studies have been conducted to investigate the efficacy of their combined effects. Therefore, the objective of this study is to synthesize and evaluate the scientific evidence regarding the potential efficacy and side-effects of GLOW™ for alleviating symptoms of inattention, hyperactivity/impulsivity, depression, and sexual dysfunction.

Methods

Study setting and sampling

This open-label clinical trial was approved by the ethics committee of the Solutions Institutional Review Board (Protocol number: 1205210). The study was in compliance with the Office for Human Research Protections (OHRP) Regulations for the Protection of Human Subjects (45 CFR 46).

671 patients with at least one of the symptoms, anxiety disorders, depression, bipolar type 1 and 2, and ADHD who were referred to a private office specializing in diagnostic evaluation and medication management for adults with psychiatric disorders, between November 12, 2012 and May 25, 2013, in Coral Gables, Florida, were identified for this study. A convenience sampling strategy was employed. The researcher conducted interviews with the patients. During the interview, the researcher inquired the patient's health status and use of health services, and explained the nature of the trial and the other treatment options. Participating in the study was completely voluntary. Participants were informed that GLOW™ would be provided at no cost. No other compensations were provided. After the interview, written informed consent was obtained from all participants who were willing to participate in the study. 68 participants were recruited for the study.

The medications taken by patients at the time of the study included: Adderall (amphetamine salt combo) and Adderall XR (amphetamine salt combo XR), Dexedrine (dextroamphetamine), Dextroamphetamine ER (Dexedrine spansules), Ritalin (mephylphenidate) and Ritalin SR (methylphenidate SR), Viibryd, Lexapro (escitalopram), Celexa (citalopram), Prozac (fluoxetine), Effexor XR (venlafaxine ER), Nardil (phenelzine), Cymbalta (duloxetine), Wellbutrin XL (bupropion XL), Doxepin (sinequan), Deplin, Xanax XR (alprazolam ER), Xanax (alprazolam), Ativan (lorazepam), Ambien CR (zolpidem ER), Ambien (zolpidem), Trazodone (desyrel), Lunesta (eszopiclone), Restoril (temazepam), Antabuse (disulfiram), Abilify (aripiprazole), Lamictal (lamotrigine), Lamictal XR (lamotrigine ER), Lithium, and Depakote (divalproex).

Inclusion criteria were a) age between 18 and 75 years, b) adults with feelings of sadness, attention problems, decreased sexual desire and performance, c) medically and psychiatrically stable (determined by the researcher's judgement) for two months with no signs or symptoms of acute suicidal thinking, homicidal

thoughts, and acute psychotic processes, and with normal vital signs, and d) alert and oriented. Exclusion criteria were any evidence of abusing drugs or alcohol within the last two months prior to the study or cognitive impairment. Subjects with the following conditions were also excluded: active or history of liver disease, active peptic ulcer, arterial bleeding, celiac disease, concomitant anticoagulants/dilators/immunosuppressant/use of aspirin or other antiplatelet medication, diabetes, electrolyte imbalances, history of heart disease, high alcohol consumption, hypersensitive to any of the 9 ingredients of GLOW™, pregnancy, cancer, unstable angina, impaired renal function, and kidney disease.

A power analysis was conducted based on the repeated measures procedure (F tests - ANOVA: Repeated measures, within factors) with 3 measurements (3 time points) using G*power version 3.1.9.2 to determine the minimum sample size required for this study [44]. At least 28 subjects were required to achieve a power of 80% with a large effect size (f = 0.25) for this study.

Interventions

A natural supplement (the GLOW™) was administered to all participants, two tablets daily, in combination with medication that the participants have been taking for 60 days. Patients were consecutively entered into the study. After informed consent, patients were given a 30day supply (60 capsules) and instructed to take 2 daily capsules of GLOW™ in the morning, and to stop immediately if experiencing any adverse effects and call the office or go to emergency room if needed. During the study, occurrence of side-effects and adverse events, was recorded.

Measures

At baseline (Day 1), participants' gender and age were recorded. Symptoms of depression, attention, concentration, and male and female sexual dysfunction were measured at baseline (Day 1) and follow-ups (Day 15 and Day 30), using the following 4 instruments: Abbreviated ADHD symptom checklist 4 (Abbreviated ADHD-SC4), Beck depression inventory (BDI-II), female sexual function index (FSFI), and international index of erectile function questionnaire (IIEF). Note that all participants were evaluated with the abbreviated ADHD-SC4 and BDI-II. Only female participants were evaluated with FSFI and only male participants were evaluated with IIEF. At the end of the study (Day 30), participants were asked to provide feedback for GLOW™.

Abbreviated ADHD symptom checklist 4 (the Abbreviated ADHD-SC4)

The Abbreviated ADHD-SC4 is a behavior rating scale whose items are based on the 18 behavioral symptoms of ADHD as defined by the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) [45,46]. The abbreviated ADHD-SC4 consists of 18 4-point Likert scale items, with 0 = Never, 1 = Sometimes, 2 = Often, and 3 = Very often, representing the inattentive subscale (9 items) and the hyperactive-impulsive subscale (9 items) of ADHD-SC4 [46]. The scores of each sub-scale can be computed by summing the responses of the corresponding items. The scores of each sub-scale range from 0 to 27, with higher scores

indicating more predominantly inattentive (predominantly hyperactive-impulsive). The combined total scores range from 0 to 54, with higher scores indicating more behavioral symptoms of ADHD. The abbreviated ADHD-SC4 has been shown to have good reliability and validity [46].

Beck depression inventory - 2nd edition (BDI-II)

BDI-II is a 21 item self-report instrument intended to assess the existence and severity of symptoms of depression [47]. BDI-II is an extensively used tool that provides overall measures of somatic and cognitive symptoms of depression and has been used in cardiac populations. The questionnaire is a 21 item multiple choice self-report inventory and is designed for individuals aged 13 and over. Each item of BDI-II consists of four statements, scored 0-3, indicating increasing symptom severity [47]. Total raw scores can range from 0 to 63, with higher total scores indicating more severe depressive symptoms [47]. Additionally, the total scores of BDI-II can be converted into descriptive classifications based on the following cut scores: 0-13: minimal depression; 14-19: mild depression; 20-28: moderate depression; and 29-63: severe depression.[47] BDI-II has been shown to have good reliability and validity [47,48].

Female sexual function index (FSFI)

FSFI is a 19-item questionnaire, has been developed as a brief, multidimensional self-report instrument for assessing the key dimensions of sexual function in women [49]. The FSFI consists of the following 6 subscales: desire, arousal, lubrication, orgasm, satisfaction, and pain. Higher scores on each of the FSFI domains indicated fewer problems with sexual functioning (i.e., Higher scores indicate less dysfunction). Additionally, FSFI total scores can be computed by summing the scores of the 6 sub-scales. Higher FSFI total scores indicate less women sexual dysfunction. Furthermore, a total score ≤ 26.55 is classified as female sexual dysfunction [50]. FSFI has been shown to have good reliability and validity [49].

International index of erectile function questionnaire (IIEF)

The 15-question IIEF can be used to clinically assess erectile dysfunction and treatment outcomes in clinical trials [51]. A score of 0-5 is awarded to each of the 15 questions that examine the following 5 domains of male sexual function, including, erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. For each sub-scale, scores ranges are: erectile function (0-30), orgasmic function (0-10), sexual desire (0-10), intercourse satisfaction (0-15), and overall satisfaction (0-10), where higher scores indicating less dysfunction [51]. IIEF has been shown to have good reliability and validity [51].

Statistical analyses

There were 16 measures of interest, including the 3 scores of ADHD (inattentive score, hyperactive-impulsive score, and combined score), the total score of BDI-II, the 7 scores of FSFI (the scores of the 6 subscales, desire, arousal, lubrication, orgasm, satisfaction, and pain, and the total score of FSFI), and the 5 scores of IIEF (the scores of the 5 domains, erectile

function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction). Each measure was measured at three time points (baseline (Day1) and follow-ups (Day 15 and Day 30) in this study. Linear mixed-effects models were conducted to determine if there was a relationship between each of the measures and study time (Day 1, Day 15, and Day 30), i.e., if the efficacy of GLOW™ on relieving symptoms of depression, attention, concentration, and male and female sexual dysfunction was statistically significant.

For the three scores of ADHD and the total score of BDI-II, gender and age were included in the models as control variables. In addition, the interaction effects of gender and study time were investigated in order to determine if the effects of study time varied according to gender (i.e., if the efficacy of GLOW™ on relieving symptoms of depression/attention varied for males and females). For the 7 scores of FSFI and the 5 scores of IIEF, age was included in the models as a control variable. No random effects were constructed. The unstructured covariance matrix was used to model the dependence between observations for each case. The F test was used to test if the effect of a predictor was statistically significant. A p-value less than 0.05 indicated significance. Estimated marginal means were computed for each categorical predictor (i.e., study time and gender). For any factors with more than two levels (for example, study time), if the effect was significant, pairwise comparison was performed to see at which two levels the statistically significance occurred. To control for the family wise error rate, the multiple comparison procedure, Tukey-Kramer test was implemented. Quantile-quantile (QQ) plots of the scaled residuals (obtained after multiplying the raw residuals by Cholesky decomposition) were used to assess the multivariate normality assumption of the linear mixed-effects models. The normality assumption was satisfied for each model. All data analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC).

Results

68 participants were recruited for the study. One participant was excluded from data analysis as there were no records for ADHD and BDI. 4 participants were excluded for only completing surveys at one study time point at most. Thus, the final sample size for this project was 63 (57% female and 43% male). The range of age of the participants was 20-77 years (M = 45.37, SD = 14.14).

Figures 1-4 visualize the measures of interest by showing the bar charts of means and 95% confidence intervals (CI) for the three ADHD scores (Figure 1, N = 56 (Day 1), 53 (Day 15), and 48 (Day 30)), the score for BDI-II (Figure 2, N = 45 (Day 1), 43 (Day 15), and 41 (Day 30)), the scores for the 6 FSFI sub-scales (Figure 3, N = 27 (Day 1), 26 (Day 15), and 48 (Day 21)), and the scores for the 5 IIEF sub-scales (Figure 4, N = 17 (Day 1), 16 (Day 15), and 14 (Day 30)), by study time. There was a decreasing trend of the three ADHD scores (Figure 1) and BDI-II score (Figure 2) over the study period, indicating participants showing less behavioral symptoms of ADHD and less depressive symptoms over time, after being treated with the natural supplement. There was an increasing trend of each of the FSFI subscale scores over the study period (Figure 3), indicating female participants showing less sexual dysfunction over the
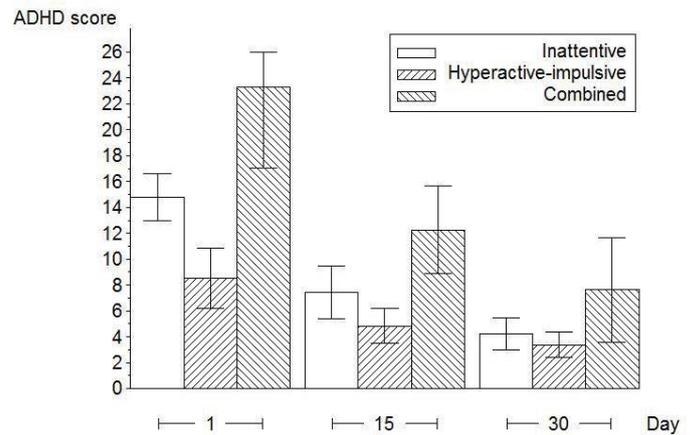

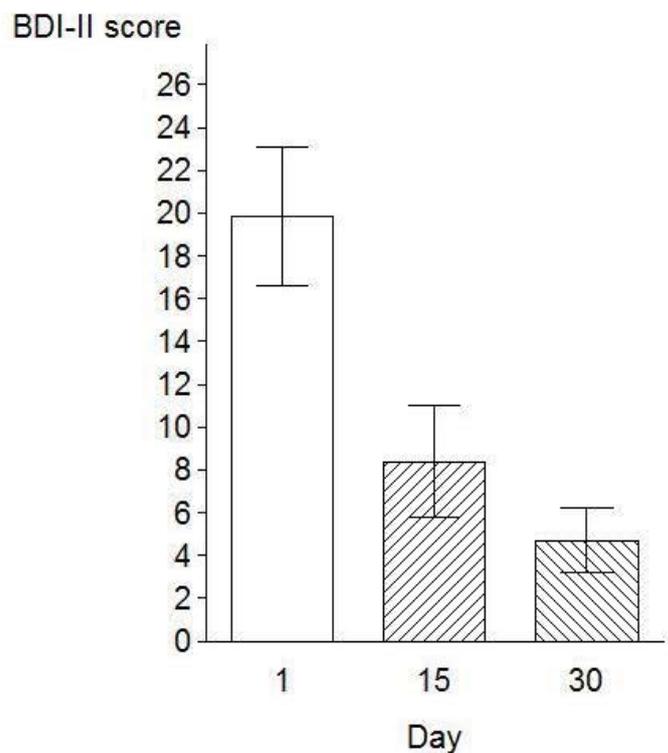**Figure 1**: Bar chart of mean and 95% CI for the three ADHD scores, by study time.

Figure 2: Bar chart of mean and 95% CI for BDI-II scores, by study time.

study period, after the treatment of the natural supplement. There was no apparent pattern of change of the IIEF scores over the study period (Figure 4).

When converting BDI-II scores into classification of depression levels, it seemed that depression severity decreased over time, with 24% severe depression at Day 1 and 0% severe depression at Day 30 (Figure 5). Female participants with a total FSFI score ≤ 26.55 were classified as experiencing female sexual dysfunction. The results indicated that proportion of female participants with sexual dysfunction decreased over time, with 15% no sexual dysfunction at Day 1 and 57% no sexual dysfunction at Day 30 (Figure 6).

The results of the mixed effects models are presented in Tables 2-5. For ADHD-inattentive, a statistically significant interaction effect of gender and study time (p < 0.0001, Table 2) indicated that the
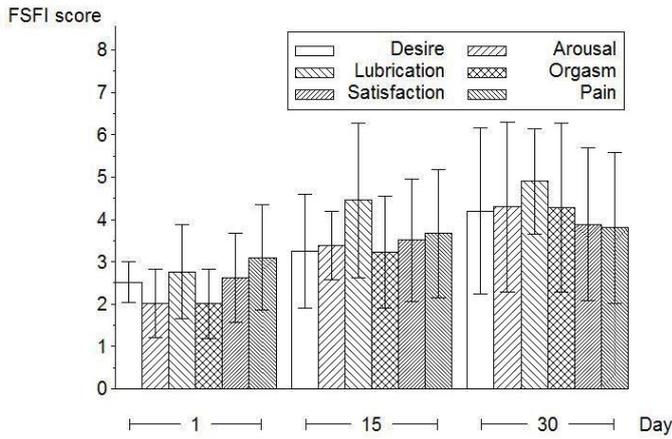
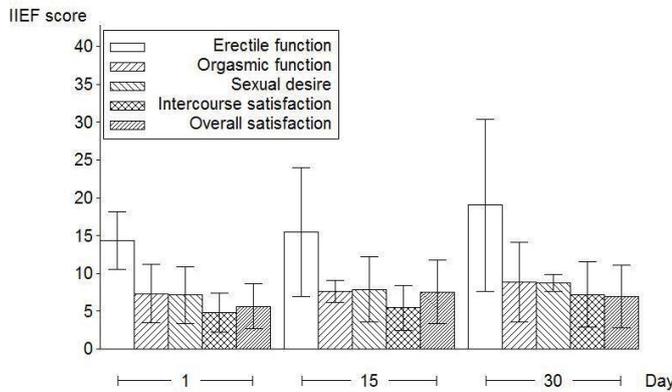**Figure 3:** Bar chart of mean and 95% CI for the 6 FSFI sub-scores, by study time.

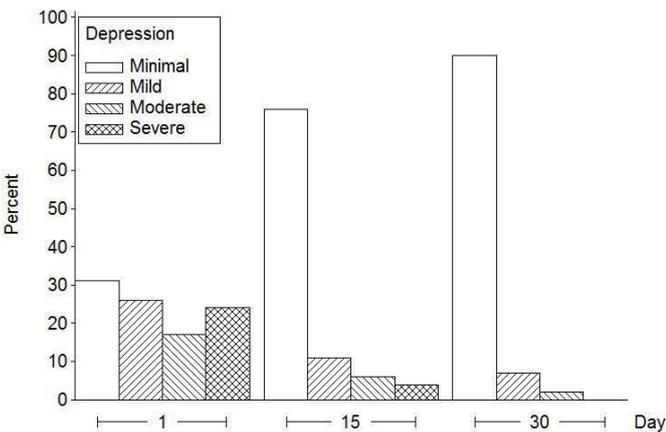**Figure 4:** Bar chart of mean and 95% CI for the 5 IIEF sub-scores, by study time.

Figure 5: Bar charts of % of depression severity.

Figure 6: Bar charts of % of female sexual dysfunction.

Figure 7: Estimated mean score of ADHD-inattentive at each study time point for female and male.

For ADHD-hyperactive-impulsive, there was a statistically significant effect of study time (p < 0.0001), but no statistically significant gender (p = 0.8046), age (p = 0.2616), and gender by time (p = 0.8580) effects (Table 2). The results of pairwise comparisons (Table 5) and estimated means of ADHD-hyperactive-impulsive (Table 3) indicated that regardless of gender and age, participants were less predominantly hyperactive-impulsive over the study period. Similar conclusion was made based on the analysis results for ADHD-combined.

The efficacy GLOW™ on relieving depression was investigated using BDI-II. There was a statistically significant effect of study time (p < 0.0001), but no statistically significant gender (p = 0.2161), age (p = 0.4451), and gender by time (p = 0.0717) effects (Table 2). The results of pairwise comparisons (Table 5) and estimated means of BDI-II (Table 3) indicated that regardless of gender and age, participants were less depressed over the study period, i.e., the estimated mean scores of BDI-II were statistically significantly lower at Day 15 and Day 30 than at Day 1, and statistically significantly lower at Day 30 than at Day 15, Table 5).

efficacy of GLOW™ over time varied for male and female (See Table 3 and Figure 7 for the estimated mean score of ADHD-inattentive at each study time point for female and male). The results of pairwise comparisons (Table 5) and estimated means of ADHD-inattentive (Table 3) indicated that 1) both females and males were statistically significantly less predominantly inattentive over the study period (Table 5, ADHD-inattentive (Female) and ADHD-inattentive (Male)), and 2) females were statistically significantly more predominantly inattentive than males at Day 1 (p = 0.0002) and Day 15 (p = 0.0248), but not at Day 30 (p = 0.1951) (Table 5, ADHD-inattentive (Female vs. Male)).

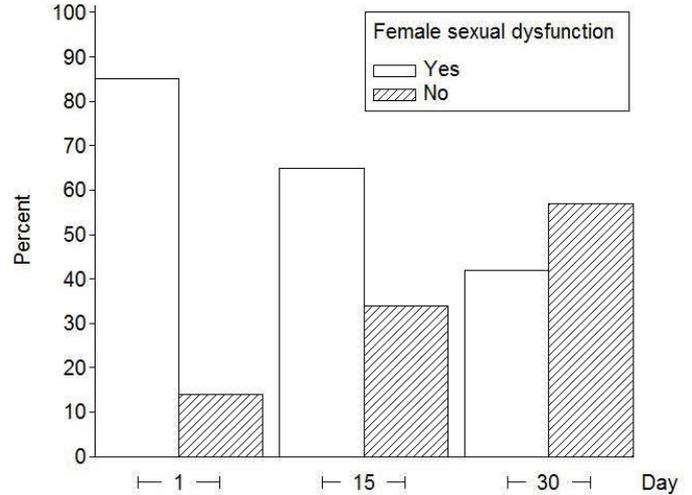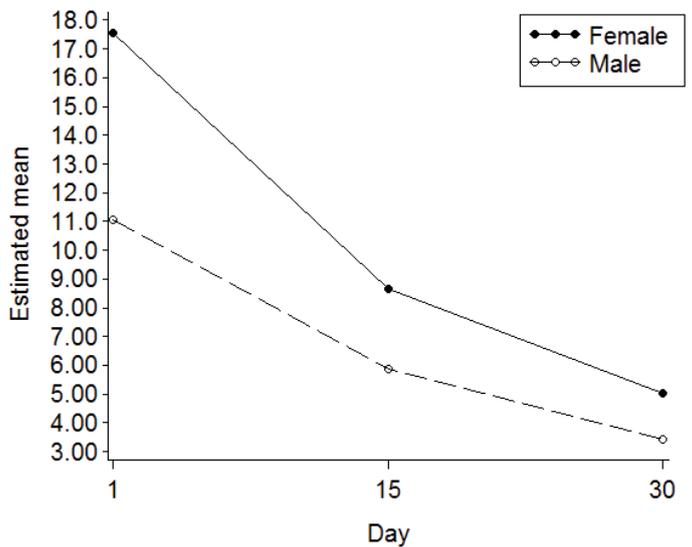**Table 2:** Results (p-values) of mixed effects models.

	Study time	Gender	Age	Study time X Gender
ADHD-inattentive	< 0.0001*	0.0014*	0.9522	0.0268*
ADHD-hyperactive-impulsive	< 0.0001*	0.8046	0.2616	0.8580
ADHD-combined	< 0.0001*	0.054	0.3501	0.2518
BDI	< 0.0001*	0.2161	0.4451	0.0717
FSFI-desire	< 0.0001*		0.0195	
FSFI-arousal	< 0.0001*		0.0327*	
FSFI-lubrication	< 0.0001*		0.0128*	
FSFI-orgasm	0.0003*		0.4339	
FSFI-satisfaction	0.0013*		0.2911	
FSFI-pain	0.1527		0.0382*	
FSFI-total score	< 0.0001*		0.0168*	
IIEF-erectile function	0.0853		0.7805	
IIEF-orgasmic function	0.2277		0.3344	
IIEF-sexual function	0.0111*		0.6685	
IIEF-intercourse satisfaction	0.2022		0.6485	
IIEF-overall satisfaction	0.0212*		0.8116	

Note: * indicates significance at the 0.05 level.

Table 3: Estimated means of scores of ADHD-inattentive, ADHD-hyperactive-impulsive, ADHD-combined, BDI-II.

Study time	Gender	ADHD inattentive	ADHD hyperactive-impulsive	ADHD combined	BDI-II
Day 1	Female	17.56 (1.04)	8.54 (1.17)	26.11 (1.83)	21.39 (2.07)
Day 15	Female	8.65 (0.79)	5.06 (0.91)	13.72 (1.52)	10.04 (1.66)
Day 30	Female	5.02 (0.82)	3.57 (0.72)	8.51 (1.35)	4.85 (1.29)
Day 1	Male	11.08 (1.21)	8.43 (1.36)	19.48 (2.12)	17.53 (2.55)
Day 15	Male	5.87 (0.91)	4.96 (1.04)	10.82 (1.75)	5.77 (2.04)
Day 30	Male	3.41 (0.91)	2.87 (0.80)	6.27 (1.51)	4.42 (1.53)
Day 1		14.32 (0.80)	8.49 (0.90)	22.79 (1.40)	19.46 (1.64)
Day 15		7.26 (0.60)	5.01 (0.69)	12.27 (1.16)	7.91 (1.31)
Day 30		4.22 (0.62)	3.22 (0.54)	7.39 (1.01)	4.64 (0.99)
	Female	10.41 (0.70)	5.72 (0.80)	16.11 (1.30)	12.09 (1.43)
	Male	6.79 (0.81)	5.42 (0.93)	12.19 (1.50)	9.24 (1.75)

Note: Numbers in parentheses are standard error.

Table 4: Estimated means of scores of FSFI-desire, FSFI-arousal, FSFI-lubrication, FSFI-orgasm, FSFI-satisfaction, FSFI-pain, FSFI-total score, IIEF-erectile function, IIEF-orgasmic function, IIEF-sexual function, IIEF-intercourse satisfaction, IIEF-overall satisfaction.

	Day 1	Day 15	Day 30
FSFI-desire	2.52 (0.22)	3.22 (0.24)	4.21 (0.22)
FSFI-arousal	2.03 (0.30)	3.31 (0.37)	4.29 (0.31)
FSFI-lubrication	2.78 (0.44)	4.40 (0.36)	5.04 (0.32)
FSFI-orgasm	2.01 (0.35)	3.17 (0.39)	4.27 (0.45)
FSFI-satisfaction	2.63 (0.34)	3.41 (0.39)	4.01 (0.38)
FSFI-pain	3.12 (0.48)	3.60 (0.47)	3.92 (0.52)
FSFI-total score	15.09 (1.75)	21.05 (1.82)	25.71 (1.63)
IIEF-erectile function	14.31 (1.86)	16.02 (2.49)	18.27 (2.50)
IIEF-orgasmic function	7.25 (0.60)	7.63 (0.90)	8.96 (0.77)
IIEF-sexual desire	7.10 (0.52)	7.83 (0.44)	8.78 (0.33)
IIEF-intercourse satisfaction	4.88 (1.38)	5.79 (1.62)	7.46 (1.69)
IIEF-overall satisfaction	5.66 (0.65)	7.55 (0.57)	6.83 (0.87)

Note: Numbers in parentheses are standard error.

Table 5: Results (p-values) of pairwise comparisons.

	Day 1 vs. Day 15	Day 1 vs. Day 30	Day 15 vs. Day 30
ADHD-inattentive (Female vs. Male)	0.0002*	0.0248*	0.1951
ADHD-inattentive (Female)	< 0.0001*	< 0.0001*	< 0.0001*
ADHD-inattentive (Male)	< 0.0001*	< 0.0001*	0.0011*
ADHD-hyperactive-impulsive	< 0.0001*	< 0.0001*	0.0019*
ADHD-combined	< 0.0001*	< 0.0001*	< 0.0001*
BDI-II	< 0.0001*	< 0.0001*	0.0003*
FSFI-desire	0.0048*	< 0.0001*	0.0014*
FSFI-arousal	0.0007*	< 0.0001*	0.0164*
FSFI-lubrication	< 0.0001*	< 0.0001*	0.0753
FSFI-orgasm	0.0012*	0.0003*	0.0152*
FSFI-satisfaction	0.0149*	0.0009*	0.0671
FSFI-pain	0.4995	0.145	0.782
FSFI-total score	< 0.0001*	< 0.0001*	0.0002*
IIEF-erectile function	0.7397	0.1534	0.2683
IIEF-orgasmic function	0.9325	0.2182	0.4533
IIEF-sexual function	0.3457	0.0215*	0.0273*
IIEF-intercourse satisfaction	0.7453	0.1791	0.4437
IIEF-overall satisfaction	0.0168*	0.3473	0.6596

Note: For ADHD-inattentive (Female vs. Male), the mean scores between male and female were compared at Day 1, Day 15, and Day 30. * indicates significance at the 0.05 level.

The 7 scores of FSFI (the scores of the 6 subscales, desire, arousal, lubrication, orgasm, satisfaction, and pain, and the total score of FSFI) were used to determine the efficacy GLOW™ on improving female sexual dysfunction. The analysis results suggested that female participants had better sexual function in desire, arousal, lubrication, orgasm, and satisfaction over the study period, as the effects of study time were statistically significant (Table 2) and the results of pairwise comparisons indicated that the sub-scores were significantly higher at Day 15 and Day 30 than at Day 1, and significantly higher at Day 30 than at Day 15, except for lubrication (Table 4 and 5). Similar conclusion was made for FSFI-total score. However, the analysis results suggested that female participants had no better sexual function in pain over the study period as there was no statistically significant study time effect ($p = 0.1527$, Table 2).

The 5 scores of IIEF (the scores of the 5 domains, erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction) were used to determine the efficacy GLOW™ on improving male sexual dysfunction. The analysis results suggested that male participants had better sexual desire over the study period ($p = 0.0111$, Table 2). In particular, the sexual desire of the male participants had improved significantly from Day 1 to Day 30 ($p = 0.0215$) and from Day 15 to Day 30 ($p = 0.0273$), but not from Day 1 to Day 15 ($p = 0.3457$) (Table 5). Male participants also had a short boost on overall satisfaction about sexual function as the estimated mean score of IIEF-overall satisfaction (Table 4) was statistically significantly higher at Day 15 than at Day 1 ($p = 0.0168$), but there was no statistically significant difference in the scores of IIEF-overall satisfaction between Day 1 and Day 30 ($p = 0.3473$) and between Day 15 and Day 30 ($p =$

0.6596) (Table 5). However, the analysis results suggested that male participants had no better erectile function ($p = 0.0853$), orgasmic function ($p = 0.2277$), and intercourse satisfaction ($p = 0.2022$) over the study period as there was no statistically significant study time effect (Table 2).

Comments and side-effects during study

20 participants had provided feedback during the study. Participants had spontaneously reported "more energy" ($N = 5$), "more sexual desire" or more "erections" ($N = 10$), "motivated" ($N = 9$), "more focused" ($N = 7$), and "no depression" ($N = 3$). None of the participants had complications or exacerbation of symptoms.

Discussion

GLOW™ consists of 9 natural ingredients (Niacin, Zinc, Gingko Biloba, L-arginine, Saw Palmetto Berry, Epimodium Herb Extract (Horny goat weed), Tribulus Terrestris, Tongkat Ali, and Avena Sativa) that was designed to alleviate symptoms, such as, inattention, hyperactivity/impulsivity, depression, and sexual dysfunction. Of all the ingredients, gingko biloba has been shown to be beneficial in ADHD [25-27] and depression [29], and effective in treating antidepressant-induced sexual dysfunction [28]. Zinc has been widely used to improve the symptoms of ADHD [23,30,35] and is a potential nutrient for treating depression [31]. Niacin may improve depression and anxiety [32,33]. Other ingredients, including L-arginine, Saw Palmetto Berry, Epimodium Herb Extract (Horny goat weed), Tribulus Terrestris, Tongkat Ali, and Avena Sativa, are potential candidates for improving sexual function [34-43]. However, their combined efficacy has not been evaluated in any previous research.

The findings of this open-label study indicated that, by adding the dietary supplement (GLOW™) into their original disorder medication, patients could effectively alleviate 1) ADHD related symptoms, such as inattention and hyperactivity/impulsivity, 2) depression, and 3) female sexual dysfunction, such as sexual function in desire, arousal, lubrication, orgasm, and satisfaction, and overall satisfaction, as soon as 15 days of GLOW™ consumption. Furthermore, the efficacy of GLOW™ continued to improve 30 days post intervention, except female sexual function in lubrication. However, the analysis results suggested that female participants had no better sexual function in pain over the study period.

The efficacy of GLOW™ on inattention, hyperactivity/impulsivity, and depression found in this study was similar to findings of previous research. For example, 4 weeks of treatment with Gingko biloba (50mg) and ginseng (200mg) significantly improved hyperactivity in a group of 36 children (ages 3–17) [26]. In a 12-week double-blind study, reduced impulsiveness, hyperactivity, and social difficulties were seen in children supplemented with zinc sulfate (150mg).[30] Deficiencies of zinc and niacin levels have been seen in depressed patients, and hence dietary supplements of zinc and niacin could substantially improve symptoms of depression [52-54].

The finding of the improvement of female sexual dysfunction was similar to a qualitative–quantitative study based on hospital records of female patients of reproductive age, treated with 250 mg Tribulus terrestris extract (1 tablet thrice daily for 90 days), where statistically significant (P < 0.005) improvements over the study period were seen in the following FSFI domains, including, desire, arousal, orgasm, and satisfaction, and the overall scores of FSFI [40].

In this study, the sexual desire for male participants was improved significantly only after 30 days of using GLOW™. The overall satisfaction of sexual function for male improved after 15 days of using GLOW™, but the efficacy of GLOW™ deteriorated after follow-up. There was no statistically significant efficacy of GLOW™ on other aspects of male sexual function, including, erectile function, orgasmic function, and intercourse satisfaction over the study period. The mixed findings of improvement of male sexual dysfunction with dietary supplements were also reported in previous research. A small study showed that 40% of the men with erectile dysfunction who were administered 208g L-arginine per day for two weeks reported improvement in erection [55]. On the other hand, a randomized, placebo-controlled, crossover comparison of 1.5 g L-arginine daily versus placebo did not show positive treatment results on treating erectile dysfunction [56]. Similarly, while gingko biloba has been recognized as effective in treating antidepressant-induced sexual dysfunction [28], two randomized placebo controlled trials have found no significant benefit of Gingko extract on sexual function [57,58]. Furthermore, the Saw palmetto for Treatment of Enlarged Prostates (STEP) study, a randomized clinical trial performed among 225 men with moderate-to-severe symptoms of benign prostatic hyperplasia, comparing a standardized extract of the saw palmetto berry (160mg twice daily) with a placebo over a one-year period, had concluded that no statistically significant differences were observed between the saw palmetto and placebo groups in the measured domains of sexual functioning (sexual drive, erectile function, ejaculation, perception of problems) with the exception of the perception of sexual problems domain [59].

No side-effects of regarding GLOW™ were found in this study. However, side-effects of the targeted herbs, minerals, and vitamins have been documented in literature and should not be ignored. For example, reported side effects of Gingko biloba included: more impulsive, hyperactive, aggressive, emotional, and tired, and increased sweating [26]. Initial manifestations of niacin may comprise symptoms like fatigability, headache, and sleep disturbance [60]. Subjects in the STEP study had reported the following adverse-effects about saw palmetto berry: Lumbar laminectomy, gastrointestinal bleeding, vertigo, and elective laminectomy [59]. Although zinc is generally well tolerated, nausea and metallic taste were frequent complaints from participants [61]. Additionally, overdose of zinc can cause gastrointestinal disturbances, tachycardia, shock, and damage to pancreas and liver.[54] Known side-effects for horny goat weed include: fever, increased heart rate, and irritability [62]. Finally, a series of adverse events were documented for the use of Tribulus terrestris extract in the treatment of female sexual dysfunction [40].

The study had a number of limitations. This study is an open-label trial and hence the observed improvement in symptoms cannot be completely attributed to the dietary supplement. The sample size of the study was rather small and the study was conducted in a single site, which may post challenge on the generalization of the results. Short treatment duration and having no drug free follow-up period were other limitations of this study. Finally, based on the recommendation of DSM-IV, the study applied the abbreviated ADHD-SC4 to evaluate ADHD symptoms on adults; while the targeted audiences of abbreviated ADHD-SC4 were children and adolescents. The more commonly used and recommended ADHD instrument for adults may be the Adult ADHD Self-Report Scale (ASRS) Symptom Checklist [63].

Some perspectives for future research can be considered. Randomized clinical trials can be conducted to show improvement in symptoms are completely attributed to the dietary supplement. Moreover, other types of studies could be established to further investigate the clinical effects of GLOW™. For example, cognitive studies can be established to investigate the effects of GLOW™ in improving attention, and neuroimaging studies can be used to show the effects of GLOW™ in brains.

Conclusions

In conclusion, this study found that GLOW™ is an effective and safe dietary supplement to alleviate symptoms, such as, inattention, hyperactivity/impulsivity, depression, and sexual dysfunction. Further trials with larger sample size, various drug dosages, and longer treatment and follow-up duration are warranted. Also, the mechanisms of action of the ingredients of GLOW™ on ADHD and depression related symptoms are needed to be investigated.

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