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Original Article

Pharmacology Section

Evaluation of *Prunus dulcis* as an Adjunct in Major Depressive Disorder: A Randomised Open Label Clinical Study

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ABSTRACT

Introduction: Depression is a common mental disorder affecting over 264 million people worldwide, impacting daily life and overall mental and physical well-being. Commonly used antidepressants often cause significant side effects, creating a need for safer alternatives or adjunctive treatments to existing medications.

Aim: To evaluate the effect of inositol-rich *Prunus dulcis* as an adjunct to standard therapy in individuals diagnosed with Major Depressive Disorder (MDD).

Materials and Methods: An open-label, randomised, parallel-group controlled trial included 61 patients with MDD, divided into two groups: the control group (n=32), which received escitalopram (10-20 mg/day) for eight weeks, and the study group (n=33), which received escitalopram (10-20 mg/day) plus 6g/day of *Prunus dulcis* (eight almonds) for eight weeks. Primary outcomes assessed changes in Hamilton Depression Rating Scale (HDRS) and Beck Depression Inventory (BDI) scores from baseline to weeks 4, 6, 8, and 12. Secondary outcomes included clinical health improvements (weight, blood pressure) and adverse drug reactions. Intergroup comparisons used an unpaired t-test, with $p<0.05$ considered statistically significant.

Results: Most patients were aged 41-50 years, with 59% female and 41% male participants. Mean BDI scores in mild depression patients at the 4th, 6th, 8th, and 12th weeks were 10±12, 8.8±2.1, 7.6±1.2, and 6.9±1.2 in the study group versus 9±13.89, 12.9±1.7, 10.6±1.2, and 8.9±0.9 in the control group ($p<0.05$). Other grades showed no significant differences. Mean HDRS scores in mild depression at the 6th week were 8.0±1.7 (study group) versus 10.3±1.1 (control group, $p=0.003$). HDRS scores for moderate depression at the 8th and 12th weeks also showed significant differences ($p<0.05$). Overall weight comparisons between groups showed significant differences ($p<0.05$) at each assessment point, with the study group consistently having a higher mean weight.

Conclusion: *Prunus dulcis* (almond), when used as an add-on to standard antidepressant therapy, accelerated recovery among patients with mild depression from the 6th week onwards. Furthermore, it also contributed to significant weight gain in patients suffering from MDD.

Keywords: Antidepressant, Beck depression inventory, Depression, Hamilton depression rating scale

INTRODUCTION

Depression is a psychological health disorder characterised by persistent sadness, lack of enthusiasm or interest in previously rewarding or enjoyable activities, and poor concentration. It can also disrupt proper sleep and appetite. Depression differs from normal mood fluctuations and temporary emotional reactions to everyday challenges. When it persists over time, it often reaches moderate to severe intensity and can develop into a significant health concern.

According to Rollo May, "Depression is the inability to construct a future." It can cause affected individuals to suffer greatly and function poorly at work, school, and within the family. At its worst, depression can lead to suicide [1].

Statistically, depression affects more than 264 million people worldwide. Although effective treatments for mental disorders are available, the World Health Organisation (WHO) reports that between 76% and 85% of people in low-and middle-income countries receive no treatment for their conditions [1].

The most commonly used medications for depression include first-generation drugs such as Tricyclic Antidepressants (TCAs) and Monoamine Oxidase Inhibitors (MAOIs), as well as second-generation antidepressants like Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs) [2]. Unfortunately, these treatments are not always effective. Reports indicate that up to one-third of individuals with depression do not experience improvement with their initial antidepressant medication. Moreover, while these medications have significant antidepressant effects, they are often associated with various side effects. Consequently, many studies have focused on developing newer antidepressants with fewer adverse effects. In this context, natural products have recently gained increasing attention due to their demonstrated safety and efficacy, supported by clinical experience [3]. Various natural substances have been explored, including dietary sources such as curcumin, oil seeds, and nuts.

Prunus dulcis (almond) is a type of nut containing a high amount of Inositol Hexakisphosphate (IP6) (0.35-9.42 g/100 g) [4]. Previous studies have reported that inositol possesses antidepressant activity [5-7]. Being a natural product, it has no significant side effects and is commonly consumed as food. Moreover, *Prunus dulcis* has demonstrated antidepressant effects in mice models [8].

Therefore, it is prudent to study the antidepressant effects of inositol-rich *Prunus dulcis* in humans. If *Prunus dulcis* demonstrates positive outcomes, it may serve as a complementary therapy alongside conventional antidepressant medications. Depending on the results, it could potentially allow for adjustments in the dosage of standard antidepressants when used in combination with *Prunus dulcis*, thereby minimising the adverse effects associated with these medications in the treatment of MDD.

Hence, the aim of the present study is to evaluate the effect of inositol-rich *Prunus dulcis* as an adjunct to standard therapy in individuals diagnosed with MDD.

MATERIALS AND METHODS

This was an open-label, randomised, parallel-group controlled trial conducted over 12 months (January 2020 - December

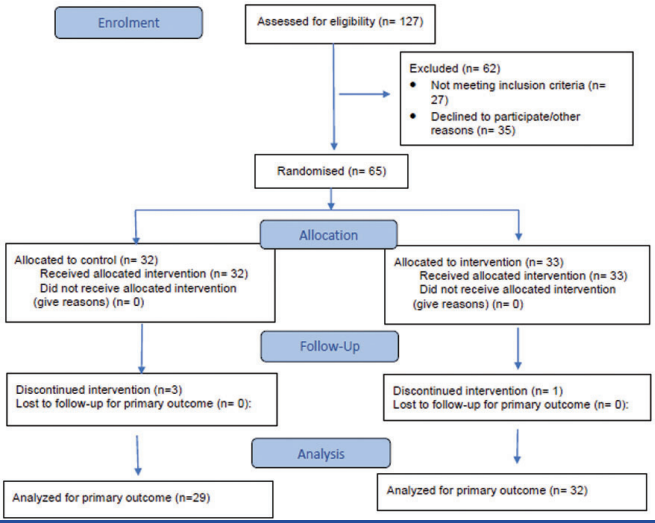
2020) at the Department of Psychiatry, Karpagam Faculty of Medical Sciences and Research (KFMSR), Coimbatore. Ethical clearance was obtained from the Institutional Human Ethical Committee (IHEC/181/Pharmacology/12/2019), and the study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment.

Sample size calculation: The sample size was estimated based on previous literature, with a 95% Confidence Interval (CI), a 5% margin of error, and a 10% dropout rate [9]. The initial target was 100 participants (50 per group). However, due to COVID-19 constraints, the final enrollment included 65 participants (32 in the control group and 33 in the study group). The patients analysed comprised 29 in the control group and 32 in the study group.

Inclusion criteria: Outpatients aged 19-60 years diagnosed with MDD based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria.

Exclusion criteria: Participants with recurrent depression, psychosis, major medical co-morbidities, substance abuse, pregnancy, lactation, concurrent use of herbal medications, or nut allergy were excluded.

Participants were randomly assigned using computer-generated simple randomisation into two groups [Table/Fig-1]:



[Table/Fig-1]: CONSORT 2025 flow diagram.

- Control group (n=32): Received escitalopram (10-20 mg/day) for eight weeks.
- Study group (n=33): Received escitalopram (10-20 mg/day) plus *Prunus dulcis* 6 g/day (equivalent to eight almonds) for eight weeks.

Study Procedure

A detailed history was obtained from each patient regarding the onset and course of illness. A semi-structured proforma was used to assess sociodemographic parameters, baseline assessments (including weight, blood pressure, and illness parameters), and follow-up assessments at weeks 2, 4, 6, 8, and 12. The HDRS and BDI scores were used to quantify depression severity and related features [10,11].

The BDI is one of the most widely used self-reported scales in the world. It is commonly used for screening individuals in the general population who are at risk of developing depression, for selecting subjects for studies, and for evaluating treatment effects. The severity of symptoms is interpreted as follows:

- 0-10: No or minimal depression
- 11-16: Mild mood disturbance
- 17-20: Borderline clinical depression
- 21-30: Moderate depression
- 31-40: Severe depression
- >40: Extreme depression

Primary outcomes: The primary outcomes were changes in HDRS and BDI scores from baseline to weeks 4, 6, 8, and 12. The secondary outcomes included clinical health improvements such as changes in weight, blood pressure, and adverse drug reactions.

Baseline assessments included sociodemographic details, weight, blood pressure, and illness duration. Structured interviews and psychometric evaluations using HDRS and BDI were conducted at baseline, with follow-up visits scheduled at weeks 2, 4, 6, 8, and 12.

STATISTICAL ANALYSIS

Data were analysed using IBM Statistical Package for the Social Sciences (SPSS) Statistics for Windows, Version 23.0 (Armonk, NY: IBM Corp). Descriptive statistics were presented as frequency and percentage for categorical variables, and Mean±Standard Deviation (SD) for continuous variables. The unpaired sample t-test was used to compare continuous variables between independent groups. The Chi-square test was used to assess the significance of categorical data. In all statistical analyses, a p-value<0.05 was considered statistically significant.

RESULTS

A total of 127 patients were assessed for eligibility. After applying the inclusion and exclusion criteria, 62 were excluded, resulting in 65 participants who were randomised into the control (n=32) and study (n=33) groups.

[Table/Fig-2] presents the demographic variables, which were comparable between the two groups. Most participants belonged to the 41-50 years age group. In this study, 59.0% of participants were female, and 41.0% were male.

Variables	Study group (n=32)	Control group (n=29)	χ^2, p-value
Age (years)			
19-30	2 (6.3%)	5 (17.2%)	2.32 (0.51)
31-40	8 (25%)	8 (27.6%)	
41-50	12 (37.5%)	10 (34.5%)	
51-60	10 (31.3%)	6 (20.7%)	
Gender			
Female	19 (59.4%)	17 (58.6%)	0.004 (0.95)
Male	13 (40.6%)	12 (41.4%)	
Grades			
Mild	10 (31.3%)	9 (31%)	0.06 (0.97)
Moderate	14 (43.8%)	12 (41.4%)	
Severe	8 (25%)	8 (27.6%)	

[Table/Fig-2]: Distribution of demographic variables among the study participants (N=61).
Chi-square test used between the groups

[Table/Fig-3] shows the comparison of BDI scores between the control and study groups using the unpaired t-test. Throughout the study period, the BDI scores between the control and study groups showed no statistically significant difference (p>0.05).

Further grade-wise (mild, moderate, and severe) comparisons of BDI scores between the control and study groups, depict highly significant improvement in the study group compared to the control group at the 4th week (p=0.0001), 6th week (p=0.0002), 8th week (p=0.0001), and 12th week (p=0.0009). This indicates that the intervention in the study group significantly reduced BDI scores in mildly depressed individuals. However, the BDI scores for moderate and severe grades between the control and study groups showed a statistically significant difference only at the 4th week (p=0.0001),

Beck's score	Groups	N	Mean	SD	t-value	p-value
1st visit	Study group	32	25.3	8.2	0.319	0.751 #
	Control group	29	24.6	8.1		
2nd week	Study group	32	25.2	8.1	0.308	0.759 #
	Control group	29	24.5	8.1		
4th week	Study group	32	23.7	9.2	0.167	0.868 #
	Control group	29	24.0	8.5		
6th week	Study group	32	21.3	9.9	0.884	0.380 #
	Control group	29	23.4	8.4		
8th week	Study group	32	17.6	7.6	1.120	0.267 #
	Control group	29	19.7	6.9		
12th week	Study group	32	13.4	5.0	1.060	0.293 #
	Control group	29	14.7	4.6		

[Table/Fig-3]: Comparison of BDI score between the groups by unpaired t-test. #No statistical significance at p>0.05 level Unpaired t-test used between the groups

with no statistically significant differences observed thereafter (p>0.05) throughout the study period [Table/Fig-4].

Beck's Score	Mild	N	Mean	SD	t-value	p-value
4th week	Study group	10	10	12.00	4.562	0.0001**
	Control group	9	9	13.89		
6th Week	Study group	10	8.8	2.1	4.642	0.0002 **
	Control group	9	12.9	1.7		
8th Week	Study group	10	7.6	1.2	5.345	0.0001 **
	Control group	9	10.6	1.2		
12th week	Study group	10	6.9	1.2	4.012	0.0009 **
	Control group	9	8.9	0.9		
Beck's Score	**Moderate**	**N**	**Mean**	**SD**	**t-value**	**p-value**
4th week	Study group	14	25.04	2.60	0.58	0.0001**
	Control group	12	24.50	2.80		
6th week	Study group	14	22.9	2.6	1.466	0.156 #
	Control group	12	24.4	2.5		
8th week	Study group	14	20.0	2.9	1.711	0.100 #
	Control group	12	21.8	2.2		
12th week	Study group	14	15.1	2.7	1.299	0.206 #
	Control group	12	16.6	2.9		
Beck's Score	**Severe**	**N**	**Mean**	**SD**	**t-value**	**p-value**
4th week	Study group	8	34.94	2.49	0.25	0.0001**
	Control group	8	35.20	2.30		
6th week	Study group	8	34.0	2.3	0.287	0.779 #
	Control group	8	33.6	2.9		
8th week	Study group	8	25.9	2.5	0.708	0.491 #
	Control group	8	26.9	3.1		
12th week	Study group	8	18.4	1.4	0.000	1.000 #
	Control group	8	18.4	2.3		

[Table/Fig-4]: Grades wise comparison of BDI score between the groups. **Highly Significant at p<0.01 and # No statistical significance at p>0.05 Unpaired t-test used between the groups

[Table/Fig-5] shows the comparison of HDRS scores between the control and study groups using the unpaired t-test. Throughout the study period, the HDRS scores between the overall control and study groups showed no statistically significant difference (p>0.05).

Further grade-wise (mild, moderate, and severe) comparisons of HDRS scores between the control and study groups were performed using the unpaired t-test. As shown in [Table/Fig-5], in mild depression at the 6th week, the study group showed significantly lower HDRS scores (8.0±1.7) than the control group (10.3±1.1; p=0.003).

HDRS score	Groups	N	Mean	SD	t-value	p-value
1st visit	Study group	32	15.6	4.0	0.027	0.988 #
	Control group	29	15.6	3.6		
2nd week	Study group	32	15.6	4.0	0.096	0.924 #
	Control group	29	15.7	3.7		
4th Week	Study group	32	14.8	4.2	0.353	0.726 #
	Control group	29	15.2	3.7		
6th week	Study group	32	13.7	4.7	0.877	0.384 #
	Control group	29	14.7	3.9		
8th week	Study group	32	11.1	3.7	0.870	0.388 #
	Control group	29	11.9	3.8		
12th week	Study group	32	8.8	3.2	1.749	0.085 #
	Control group	29	10.3	3.8		

[Table/Fig-5]: Comparison of HDRS score between the groups by unpaired t-test. # No statistical significance at p>0.05 level Unpaired t-test used between the groups

In moderate depression, no significant difference was observed at the 6th week (p=0.781). However, the study group showed significantly lower scores at the 8th week (p=0.047) and a highly significant reduction at the 12th week (p=0.002). For the severe grade, the HDRS scores showed no statistically significant difference between the groups at any time point (p>0.05) [Table/Fig-6].

HDRS score	Mild	N	Mean	SD	t-value	p-value
4th week	Study group	10	9.80	1.63	0.91	0.375
	Control group	9	10.32	1.64		
6th week	Study group	10	8.0	1.7	3.490	0.003 **
	Control group	9	10.3	1.1		
8th week	Study group	10	6.7	1.4	0.925	0.368 #
	Control group	9	7.2	1.0		
12th week	Study group	10	5.6	1.3	0.758	0.459 #
	Control group	9	6.0	0.9		
HDRS score	**Moderate**	**N**	**Mean**	**SD**	**t-value**	**p-value**
4th week	Study group	14	15.19	1.30	0.42	0.678
	Control group	12	15.10	1.30		
6th week	Study group	14	14.3	1.3	0.281	0.781 #
	Control group	12	14.4	1.0		
8th week	Study group	14	11.5	1.3	2.093	0.047 *
	Control group	12	12.7	1.5		
12th week	Study group	14	8.4	1.4	3.563	0.002 **
	Control group	12	10.5	1.6		
HDRS score	**Severe**	**N**	**Mean**	**SD**	**t-value**	**p-value**
4th week	Study group	8	20.06	1.06	0.38	0.710
	Control group	8	20.25	1.20		
6th week	Study group	8	19.8	0.9	0.247	0.809 #
	Control group	8	19.9	1.1		
8th week	Study group	8	15.9	1.2	0.332	0.745 #
	Control group	8	16.1	1.7		
12th week	Study group	8	13.3	1.3	1.868	0.083 #
	Control group	8	14.9	2.1		

[Table/Fig-6]: Grades wise comparison of HDRS score between the groups. **Highly statistical significance at p<0.01, * Significant at p<0.05 and # No statistical significance at p>0.05 Unpaired t-test used between the groups

[Table/Fig-7] shows the comparison of weight between the control and study groups throughout the study period. The mean weight of the control group was consistently lower than that of the study group throughout the study period, showing a statistically significant difference (p<0.05).

[Table/Fig-8] presents the grade-wise (mild, moderate, and severe) comparisons of weight between the control and study groups using

Visit	Groups	N	Mean	SD	t-value	p-value
1st week	Study group	32	55.7	9.9	2.188	0.032 *
	Control group	29	50.0	10.5		
2nd week	Study group	32	55.6	9.9	2.187	0.033 *
	Control group	29	49.9	10.5		
4th week	Study group	32	55.8	10.0	2.217	0.031 *
	Control group	29	50.0	10.5		
6th week	Study group	32	56.3	10.0	2.352	0.022 *
	Control group	29	50.1	10.4		
8th week	Study group	32	56.8	10.4	2.341	0.023 *
	Control group	29	50.5	10.4		
12th week	Study group	32	57.3	10.2	2.371	0.021 *
	Control group	29	51.0	10.4		

[Table/Fig-7]: Comparison of weight between the groups by unpaired t-test.
*Statistical Significance at p<0.05 level Unpaired t-test used between the groups

Visit	Mild	N	Mean	SD	t-value	p-value
4th week	Study group	10	68.2	5.1	2.674	0.512
	Control group	9	66.8	4.7		
6th week	Study group	10	64.4	8.1	2.714	0.015 *
	Control group	9	53.0	10.2		
8th week	Study group	10	65.4	8.2	2.801	0.012 *
	Control group	9	53.5	10.2		
12th week	Study group	10	65.5	8.0	2.768	0.013 *
	Control group	9	53.9	10.2		
Visit	**Moderate**	**N**	**Mean**	**SD**	**t-value**	**p-value**
4th week	Study group	14	72.3	5.8	0.85	0.403
	Control group	12	70.9	6.1		
6th week	study group	14	54.1	8.7	0.593	0.559 #
	control group	12	51.8	10.6		
8th week	study group	14	54.8	8.6	0.695	0.494 #
	control group	12	52.2	10.5		
12th week	study group	14	55.5	8.5	0.736	0.469 #
	Control group	12	52.8	10.5		
Visit	**Severe**	**N**	**Mean**	**SD**	**t-value**	**p-value**
4th week	Study group	8	69.8	7.2	0.92	0.372
	Control group	8	67.5	6.8		
6th week	study group	8	49.9	8.4	1.287	0.219 #
	control group	8	44.2	9.2		
8th week	study group	8	49.5	9.0	1.055	0.309 #
	control group	8	44.6	9.3		
12th week	study group	8	50.1	9.0	1.088	0.295 #
	control group	8	45.2	9.2		

[Table/Fig-8]: Comparison of weight between grades with groups by unpaired t-test.
*Significant at p<0.05 and # No Statistical Significance at p>0.05 Unpaired t-test used between the groups

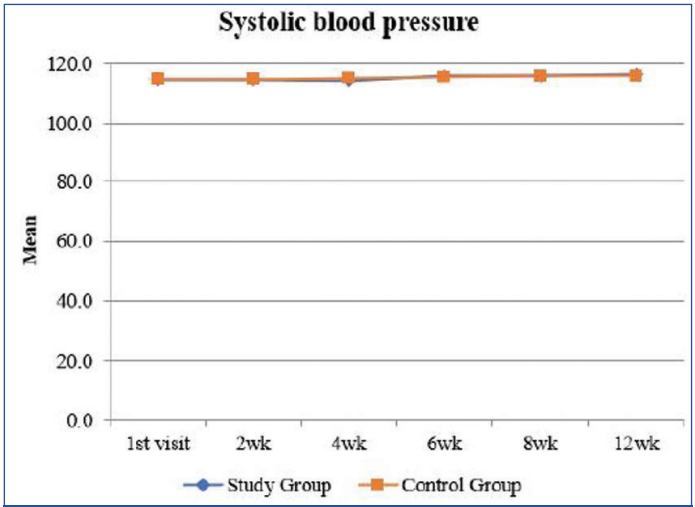
the unpaired t-test. Among participants with mild depression, the study group consistently showed a statistically significant (p<0.05) higher mean body weight compared to the control group across all assessment periods.

Although there was weight gain among participants with moderate and severe depression in both groups, no statistically significant difference was observed (p>0.05). It is evident that the study group recorded proportionately greater weight gain than the control group by the end of the 8th week [Table/Fig-9]. From baseline to the 8th week, the study group exhibited a consistently greater proportional and percentage increase in weight compared to the control group, with all differences being statistically significant.

Visit	Groups	N	Mean	Proportionate increase	%Proportionate increase	SD	t-value	p-value
0 week	Study group	32	55.7	0	0	9.9	2.188	0.032*
	Control group	29	50	0	0	10.5		
2nd week	Study group	32	55.6	-0.0017	-0.18	9.9	2.187	0.033*
	Control group	29	49.9	-0.002	-0.2	10.5		
4th week	Study group	32	55.8	0.0017	0.18	10	2.217	0.031*
	Control group	29	50	0	0	10.5		
6th week	Study group	32	56.3	0.0107	1.08	10	2.352	0.022*
	Control group	29	50.1	0.002	0.2	10.4		
8th week	Study group	32	56.8	0.0197	1.97	10.4	2.341	0.023*
	Control group	29	50.5	0.01	1	10.4		

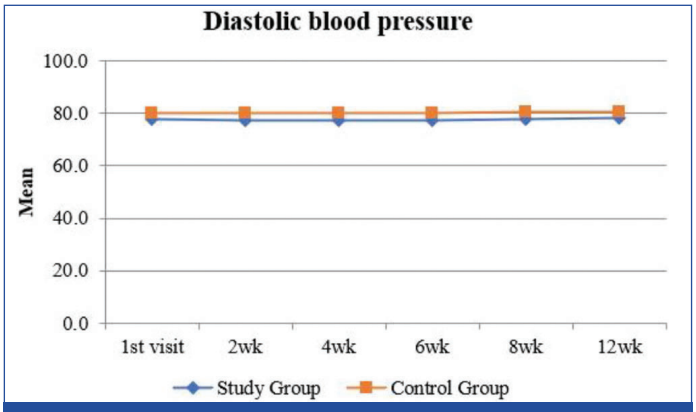
[Table/Fig-9]: Proportionate comparison of weight gain.
*Significant at p<0.05 and # No statistical significance at p>0.05 Unpaired t test used between the groups

The comparison of Systolic Blood Pressure (SBP) between the control and study groups using the unpaired t-test showed no statistically significant difference (p>0.05) throughout the study period [Table/Fig-10].



[Table/Fig-10]: Comparison of SBP between groups.

Similarly, the comparison of Diastolic Blood Pressure (DBP) between the control and study groups by unpaired t-test showed no statistically significant difference (p>0.05) throughout the study period [Table/Fig-11]. No side effects were reported in either group.



[Table/Fig-11]: Comparison of DBP between groups.

DISCUSSION

The present study investigated the potential role of *Prunus dulcis* (almond) as an adjunct to standard antidepressant therapy in patients diagnosed with MDD. The key outcomes assessed included changes in depression severity, measured using the HDRS and the BDI, as well as physiological parameters such as weight and blood pressure. The results suggest promising early benefits for mild-to-moderate depression but limited impact on severe cases.

In the present study, a total of 61 patients were included and randomly assigned to either the study group (receiving *Prunus dulcis* as an adjunct) or the control group. These patients were categorised into different age groups: 11.5% were aged 19-30 years, 26.2% were aged 31-40 years, 36.1% were between 41-50 years, and 26.2% were between 50-60 years.

The severity of depression among participants was classified as mild, moderate, or severe based on depression scores. The present study found that 31.1% of patients were mildly depressed, 42.6% were moderately depressed, and 26.2% were severely depressed. The comparison of depression severity between the study and control groups did not reveal any statistically significant differences.

Studies by Stroud LR et al. and Young EA et al. reported that psychosocial stress stimulates pituitary corticotropin secretion by increasing Corticotropin-Releasing Hormone (CRH) from the hypothalamus [12,13]. This, in turn, activates the adrenal glands to release the stress hormone cortisol. The stress response is also partly gender-specific, with females being more reactive to stress compared to males. This aligns with our study findings, where a higher proportion of participants were female (59%) compared to male (41%).

The study further evaluated BDI and HDRS scores over the study duration. Overall, comparisons of BDI and HDRS scores between the control and study groups showed no statistically significant differences at any assessment point. However, when BDI scores were analysed among patients with mild depression, statistically significant improvements were observed at weeks 4, 6, and 8, while HDRS showed significant improvement at week 6. This indicates that patients with mild depression who received *Prunus dulcis* as an adjunct to antidepressant therapy experienced better outcomes compared to those who received antidepressant therapy alone.

For patients with moderate and severe depression, no statistically significant differences in BDI or HDRS scores were observed between the two groups at any assessment point. These findings are consistent with preclinical research by Kanan G et al. (2019), who demonstrated antidepressant effects of almond extract in mice, as evidenced by reduced immobility in both the forced swim test and tail suspension test. The results indicated that almond extract significantly reduced immobility periods, suggesting potential antidepressant properties [8].

Furthermore, human studies support the mood-enhancing benefits of nuts. Almonds' bioactive components, such as phenolic compounds and monounsaturated fats, are considered neuroprotective. In diabetic populations, almond-enriched diets have been associated with lower depression scores along with metabolic improvements [14-16]. However, authors of these studies have emphasised the need for further research to confirm their efficacy in humans. It is therefore essential to analyse and further explore the role of almonds in modulating neuropsychiatric symptoms, as the findings from the present study remain inconclusive.

The present study also assessed weight changes as a secondary outcome measure. At baseline, the mean weight of participants in the present study group was higher than that of the control group, and this difference remained consistent throughout the study duration. Statistical analysis using the unpaired t-test revealed that the difference in mean weight between the two groups was statistically significant at each follow-up interval ($p<0.05$), suggesting a potential impact of *Prunus dulcis* on weight maintenance or gain.

When subgroup analysis was performed based on depression severity, participants with mild depression in the study group showed statistically significant weight gain at the 6th and 8th-week assessments compared to the control group. This suggests that *Prunus dulcis* may play a supportive role in preventing weight loss or promoting weight gain in mildly depressed individuals. In contrast, no statistically significant differences in weight were observed among participants with moderate or severe depression at any time point.

The nutritional profile of almonds, which includes healthy fats, protein, and micronutrients such as magnesium and vitamin E, may have contributed to improved appetite and better metabolic support, potentially explaining the observed weight gain in the study participants. Nutraceutical reviews highlight almonds' antioxidant, anti-inflammatory, and anxiolytic properties-key biological mechanisms involved in depression management- which may further justify the findings of the present study [17,18].

On the contrary, a few studies have found that including almonds in an energy-restricted diet not only helps with weight loss but also improves cardiometabolic health. This finding suggests that almonds can be part of a weight-loss diet, which may contrast with the weight gain observed in certain populations [19,20].

The present study also assessed blood pressure, including both SBP and DBP. The absence of significant blood pressure changes in both groups aligns with existing literature. Some meta-analyses have shown that almond intake reduces SBP by approximately -0.90 mmHg, with mixed effects on DBP depending on dosage [21,22]. The 6 g/day dosage used in our study may explain the lack of observable blood pressure effects. These findings are consistent with escitalopram's well-established cardiovascular safety profile, as SSRIs are known to have no clinically meaningful effect on blood pressure and are considered safe for patients with cardiovascular disease [23,24]. The neutral effect on blood pressure supports the cardiovascular safety of combining low-dose almond supplementation with escitalopram in patients with MDD.

The findings of the present study suggest that *Prunus dulcis*, when used as an adjunct to standard antidepressant therapy, significantly contributed to weight gain in patients with mild depression. However, this add-on intervention did not produce statistically significant changes in depression severity as measured by the BDI or HDRS scores within this subgroup. Furthermore, no significant differences in weight, BDI scores, HDRS scores, or blood pressure were observed between the study and control groups among patients diagnosed with moderate or severe depression.

Limitation(s)

Although the present study is the first of its kind, it has several potential limitations that can be addressed in future research. Due to the COVID-19 pandemic, the sample size was relatively small, which may have reduced the statistical power and the ability to generalise the findings. The open-label design could have introduced bias; therefore, future double-blind randomised controlled trials are recommended. Additionally, the intervention period of eight weeks may have been insufficient to observe significant or long-term physiological effects, particularly in patients with moderate to severe depression.

CONCLUSION(S)

The results of the present study indicate that the dose of antidepressant drugs may potentially be reduced when used in conjunction with *Prunus dulcis* in the treatment of mild depression, thereby minimising the side effects associated with conventional antidepressants. The study also highlights the potential supportive role of *Prunus dulcis* in enhancing nutritional status or preventing weight loss in individuals with mild depressive symptoms. Nonetheless, the absence of notable antidepressant effects across all depression severity levels underscores the need for larger, more

comprehensive studies to validate these preliminary findings and to investigate the possible physiological mechanisms through which *Prunus dulcis* may exert its influence.

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