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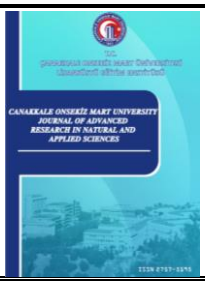

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Effect of Venlafaxine on The Vitamins Contents of *Saccharomyces Cerevisiae* (NRRLY-12632)

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Research Article

Abstract − In this study, *Saccharomyces cerevisiae* (NRLLY-12632) was grown in YPD medium containing different concentrations of Venlafaxine ((RS)-1-[2-dimethylamino-1-(4-methoxyphenyl)-ethyl] cyclohexanol). To counteract the effect of venlafaxine, vitamin C was added to the growth medium, and vitamins content of *S. cerevisiae* were investigated by HPLC. It was found that the amounts of water-soluble vitamins and lycopene concentration in *S. cerevisiae*, decreased with increased venlafaxine concentration compared to the control ($p<0.05$). On the other hand, the amounts of fat-soluble vitamins A, E, and β-carotene concentration were found to be increased ($p<0.05$). The addition of vitamin C to the growth medium containing venlafaxine at different concentrations increased the number of water-soluble vitamins and lycopene content of *S. cerevisiae*, while decreasing the amount of fat-soluble vitamins A, E, and β-carotene, depending on vitamin C concentration. With the addition of vitamin C to the growth medium containing venlafaxine, all the vitamin concentrations get close to the control group. From these findings, it can be said that the negative effect of venlafaxine on *S. cerevisiae* is reduced by adding vitamin C to the growth medium of *S. cerevisiae*.

Keywords − *S. cerevisiae, venlafaxine, vitamins, HPLC*

1. Introduction

The term microorganism describes many living things broadly, including bacteria, yeast, fungi, and algae. Although humans and microorganisms have many genes in common, microorganisms carry some genes that are not present in humans. Yeast is a single-celled and eukaryotic organism widely found in biological systems. It is a highly adaptable organism that manufactures various food products, making it a group of organisms with a high biotechnological importance [1].

From yeasts, especially *S. cerevisiae* is widely used in scientific studies such as eukaryotic biology and the study of human diseases, its worldwide production is higher than that of other microorganisms. Yeast is used in many industries because it reproduces at a high rate quickly by using cheap renewable food sources and providing low cost [2]. Depression, which is a psychiatric disorder, is a complex disease with symptoms such as irritability, insomnia, fatigue, agitation, psychomotor changes, feelings of guilt, and self-devaluation, leading to serious dysfunctions in patients. Since depression, which is frequently seen in societies, brings with it the use of antidepressant drugs. Investigation of the effects of antidepressants on cellular structures has also become an important issue [3].

Like other drugs, antidepressants also cause oxidative stress by affecting cell metabolism, and the resulting

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free radicals can affect many parameters, such as cell membranes, proteins, amino acids, vitamins, total oxidant, and antioxidant capacity. Determining the damage to the cells due to the aforementioned harmful effects is important in preventing this damage [4]. Vitamins are organic molecules that have regulatory functions in the living system, act as a catalyst in metabolic events and help efficiently use nutrients in energy production. Vitamins are divided into two groups: water-soluble and fat-soluble [5]. Vitamin C has a strong antioxidant effect which is effective in releasing some hormones in the event of stress in living organisms [6].

In this study, the microorganism *S. cerevisiae* (NRRLY-12632) was used because of easy to culture, has at least 23% common genes among humans, and is similar to humans in terms of protein [7]. The effect of antidepressants on vitamins in *S. cerevisiae* cells was investigated by adding Venlafaxine, which humans widely use. In addition, it was aimed to examine the effect of vitamin C on the vitamin content of *S. cerevisiae* by adding vitamin C in the growth medium containing Venlafaxine.

2. Materials and Methods

2.1. Material

S. cerevisiae (NRRLY-12632) used in this study was obtained from Fırat University, Department of Chemical Engineering, Biotechnology Laboratory. *S. cerevisiae* produced in yeast peptone dextrose (YPD) broth (10.0 g peptone, 5.0 g yeast extract, 10.0 g Dextrose per liter) was used. Solutions of 1000 ppm venlafaxine chloride and 500 ppm vitamin C were prepared freshly and used. The microorganism was produced in 250 mL flasks containing 50 mL nutrient medium. Experiments were carried out by forming the following groups for the study.

1. Control group: Microorganisms were grown by inoculating S. cerevisiae in the YPD medium.

2. Venlafaxine group: Microorganisms were grown by adding venlafaxine stock solution at desired concentrations (100 - 500 ppm) to the control.

3. Vitamin C group: Microorganisms were produced by adding vitamin C at the desired concentration (10-75 ppm) to the venlafaxine group.

The medium was incubated on an orbital shaker (Selecta Rotabit) for 72 hours at 150 rpm at 30 °C. The concentration of *S. cerevisiae* was determined by measuring the absorbance at 600 nm with a spectrophotometer (CHEBIOS s.r.l.). After centrifugation of the medium containing the microorganism at 8000 rpm at 10 ºC for 10 minutes (Nüve NF 800 R), the supernatant was removed, and the microorganism was washed twice with distilled water for further analysis.

2.2. Determination of Water Soluble Vitamins

The microorganism of known weight was vortexed by adding 3.0 mL of distilled water, and the mixture was sonicated (Wise Clean, WUC-AO3H, 170 W) 10 times for 30 seconds in an ice water bath. 1.0 mL, 0.5 M $HClO_4$ was added to the sonicated samples, the vortexed mixture was centrifuged at 8000 rpm for 10 minutes, and 1.0 ml of the supernatant was taken into HPLC vials. As the mobile phase in HPLC, the sodium salt of 5 mM heptanosulfonic acid was dissolved in methanol, and a solution of (A) and a solution of 0.1% triethylamine (B) were prepared. Then, solutions A and B were mixed at a volume ratio of 25:75, then the pH of the mixture was adjusted to 2.8 with phosphoric acid. Vitamins B and C were determined using a C18-DB column (15 cm x 4.6 mm x 5 µm) at a mobile phase flow rate of 1.0 mL/min [8].

2.3. Determination of Fat-Soluble Vitamins and Lycopene

6.0 mL of ethanol was added to the microorganism of known weight and vortexed; then, the microorganism solution was sonicated in an ice water bath (Wise Clean, WUC-AO3H, 170 W) for 30 seconds 10 times for each sample. The sonicated samples were centrifuged at 8000 rpm for 10 minutes, then 1.0 mL n-hexane was added to each tube and centrifuged again for 6 minutes at 4000 rpm. The n-hexane phase was transferred to a glass tube, and this process was repeated twice. Hexane was removed under vacuum at 30 °C, then 1.0 mL of methanol was added to the residue in the tube, transferred to HPLC vials, and analyzed by HPLC using an ODS-2 (25 cm, 4.6 mm ID, 5 µm) column. [9,10].

Intraday repeatability, linear working range, regression equation, regression coefficient, and % recovery values for water- and fat-soluble vitamins are given in Table 1.

Table 1. Some validation values in the determination of fat- and water-soluble vitamins

Parameters	Intra-day repeatability µg/mL	Range µg/mL	Regression equation	R^2	Recovery %
Vitamin A (1.0 µg/mL)	0.96	0.20 – 20	$y = 142378x$	0.999	98.2
Vitamin E (2.0 µg/mL)	1.90	0.30 – 70	$y = 1594.9x$	0.998	98.4
β-carotene (4.0 µg/mL)	3.90	0.10 – 60	$y = 14504x$	0.996	97.8
Lycopene (1.0 µg/mL)	0.95	0.05 – 50	$y = 5249.3x$	0.996	98.0
Vitamin C (5.0 µg/mL)	4.80	0.25 – 35	$y = 48528x$	0.999	97.6
Vitamin B1 (5.0 µg/mL)	4.90	0.15 – 50	$y = 43129x$	0.999	96.8
Vitamin B2 (2.0 µg/mL)	1.85	0.15 – 10	$y = 82893x$	0.999	96.5
Vitamin B3 (4.0 µg/mL)	3.90	0.30 – 40	$y = 40858x$	0.999	98.0
Vitamin B5 (3.0 µg/mL)	2.90	0.30 – 30	$y = 7435.1x$	0.999	96.5
Vitamin B6 (5.0 µg/mL)	4.85	0.35 – 45	$y = 45099x$	0.994	97.4
Vitamin B9 (5.0 µg/mL)	4.80	0.40 – 50	$y = 1758.9x$	0.993	97.9
Vitamin B12 (5.0 µg/mL)	4.80	0.10 – 30	$y = 19168x$	0.999	95.8

2.4. Statistical Analysis

All measurements were triplicated, and Mean ± Standard Deviation was determined. The results were subjected to one-way ANOVA by SPSS 26.0 for Windows. Differences between the group's means were analyzed for significance using the Tukey HSD test. The level of statistical significance was expressed as $p<0.05$. The superscripts in the table columns are indicated as **a** if the effect of antidepressants compared to the control group is statistically significant ($p<0.05$), **b** if the effect of vitamin C in growth medium containing antidepressants is statistically significant ($p<0.05$), and **c** if it is not statistically significant ($p>0.05$).

3. Results and Discussion

The concentrations of water and fat-soluble vitamins determined in *S. cerevisiae* for different experimental groups are given in Tables 2-4, respectively.

Table 2. Concentrations of vitamins C, B1, B2, and B3 in *S. Cerevisiae* produced in a nutrient medium containing varying concentrations of antidepressants and vitamin C

Application	Vitamin C (µg/g dw)	Vitamin B1 (µg/g dw)	Vitamin B2 (µg/g dw)	Vitamin B3 (µg/g dw)
Control	69.80±1.05	8.02±0.25	39.10±0.85	451.40±7.25
Ven-1	66.75±0.95[a]	7.50±0.22 [a]	37.15±0.82 [a]	430.10±7.00 [a]
Ven-2	64.10±1.10[a]	6.35±0.19 [a]	36.00±0.65 [a]	405.60±6.54 [a]
Ven-3	61.60±1.20[a]	5.50±0.17 [a]	34.15±0.66 [a]	370.00±5.63 [a]
Ven-4	58.10±1.27[a]	4.28±0.15 [a]	32.40±0.63 [a]	335.80±4.86 [a]
Ven-5	55.10±1.32[a]	3.40±0.13 [a]	30.10±0.58 [a]	300.70±4.74 [a]
Ven-1+C10	67.60±0.90[c]	7.65±0.23 [c]	37.50±0.80 [c]	436.80±6.05 [c]
Ven-1+C25	68.30±0.70[c]	7.80±0.24 [c]	38.10±0.72 [c]	441.00±6.00 [c]
Ven-1+C50	69.10±0.68[b]	7.90±0.20 [c]	38.61±0.70 [c]	445.30±6.10 [b]
Ven-1+C75	70.00±0.72[b]	8.05±0.19 [b]	39.02±0.65 [b]	450.00±5.00 [b]
Ven-2+C10	65.60±0.90[c]	6.42±0.18 [c]	36.65±0.68 [c]	410.85±4.50 [c]
Ven-2+C25	67.10±0.70 [b]	6.90±0.15 [b]	37.25±0.66 [c]	420.90±4.58 [b]
Ven-2+C50	68.30±0.66 [b]	7.15±0.17 [b]	38.00±0.70 [b]	428.60±4.61 [b]
Ven-2+C75	69.60±0.70 [b]	7.50±0.18 [b]	38.66±0.67 [b]	435.00±4.65 [b]
Ven-3+C10	63.60±0.86 [c]	5.95±0.14 [b]	35.00±0.56 [c]	378.10±5.06 [c]
Ven-3+C25	64.45±0.80 [b]	6.40±0.15 [b]	35.85±0.57 [b]	387.40±4.50 [b]
Ven-3+C50	65.70±0.75 [b]	6.90±0.17 [b]	36.58±0.60 [b]	395.00±4.65 [b]
Ven-3+C75	67.60±0.70 [b]	7.20±0.19 [b]	37.10±0.63 [b]	402.80±4.70 [b]
Ven-4+C10	60.00±0.92 [c]	4.50±0.15 [c]	33.00±0.55 [c]	341.50±5.00 [c]
Ven-4+C25	62.30±0.83 [b]	4.85±0.16 [b]	33.75±0.54 [b]	349.75±5.05 [b]
Ven-4+C50	64.60±0.80 [b]	5.35±0.18 [b]	34.30±0.56 [b]	359.00±4.86 [b]
Ven-4+C75	66.30±0.85 [b]	6.00±0.17 [b]	35.10±0.55 [b]	369.50±4.80 [b]
Ven-5+C10	57.60±0.81 [c]	3.90±0.14 [b]	31.00±0.50 [c]	308.80±3.95 [c]
Ven-5+C25	59.70±0.78 [b]	4.40±0.15 [b]	31.90±0.45 [b]	317.90±4.00 [b]
Ven-5+C50	62.45±0.75 [b]	5.20±0.17 [b]	32.85±0.48 [b]	328.00±4.08 [b]
Ven-5+C75	64.60±0.80 [b]	5.86±0.16 [b]	33.70±0.51 [b]	340.00±4.15 [b]

Ven-1: 100 ppm venlafaxin, Ven-2: 200 ppm venlafaxin, Ven-3: 300 ppm venlafaxin, Ven-4: 400 ppm venlafaxin, Ven-5: 500 ppm venlafaxin, C10: 10 ppm Vitamin C, C25: 25 ppm Vitamin C, C50: 50 ppm Vitamin C, C75: 75 ppm Vitamin C

It is reported that vitamin C is a good singlet oxygen scavenger that neutralizes reactive oxygen species (ROS), reduces oxidative stress, and eliminates free radicals with its scavenging effect [11].

It is reported that vitamin C has important roles such as tissue repair, protein formation, inactivation of toxic metals, and protection from the harmful effects of oxidants [6].

As shown in Tables 2 and 3, as the concentration of antidepressants increases in the medium, the vitamin C concentration of *S. cerevisiae* decreases. In addition, the vitamin C content of the microorganism increases as the increased vitamin C is added to the growth medium. It has been reported that adding vitamin C to the medium reduces the oxidative stress caused by Cr (III) [12]. A study said that the amount of ascorbic acid in the tissues of mice given CrO_3 was lower than that of the control group [13].

Table 3. Concentrations of vitamins B5, B6, B9, and B12 in *S. Cerevisiae* produced in a nutrient medium containing varying concentrations of antidepressants and vitamin C

Application	Vitamin B5 (µg/g dw)	Vitamin B6 (µg/g dw)	Vitamin B9 (µg/g dw)	Vitamin B12 (µg/g dw)
Control	168.90±2.75	385.00±4.38	21.80±0.45	6.10±0.20
Ven-1	160.20±2.56 [a]	375.40±4.20 [a]	19.50±0.41 [a]	5.70±0.18 [a]
Ven-2	151.35±2.40 [a]	363.85±4.10 [a]	17.00±0.38 [a]	5.00±0.16 [a]
Ven-3	139.50±2.34 [a]	348.70±4.00 [a]	15.10±0.38 [a]	4.15±0.15 [a]
Ven-4	130.75±2.10 [a]	339.10±4.05 [a]	13.35±0.33 [a]	3.60±0.13 [a]
Ven-5	120.68±2.00 [a]	330,25±3.80 [a]	11.90±0.28 [a]	3.30±0.14 [a]
Ven-1+C10	162.55±2.42 [c]	378.60±4.00 [c]	20.10±0.37 [b]	5.80±0.16 [c]
Ven-1+C25	165.10±2.45 [c]	380.50±3.95 [c]	20.70±0.36 [b]	5.90±0.17 [c]
Ven-1+C50	167.35±2.15 [b]	383.20±3.90 [c]	21.20±0.35 [b]	5.94±0.16 [c]
Ven-1+C75	169.40±2.00 [b]	385.80±4.00 [b]	21.75±0.40 [b]	6.05±0.18 [c]
Ven-2+C10	154.00±2.35 [c]	367.30±3.70 [c]	17.85±0.36 [b]	5.35±0.15 [b]
Ven-2+C25	158.45±2.18 [b]	371.20±3.73 [b]	18.95±0.35 [b]	5.60±0.16 [b]
Ven-2+C50	163.20±2.15 [b]	374.80±3.68 [b]	19.50±0.38 [b]	5.85±0.14 [b]
Ven-2+C75	167.10±2.05 [b]	379.00±3.70 [b]	20.60±0.36 [b]	6.00±0.15 [b]
Ven-3+C10	142.40±2.00 [c]	352.10±3.80 [c]	16.50±0.27 [b]	4.45±0.13 [b]
Ven-3+C25	146.10±2.05 [b]	356.85±3.84 [b]	18.00±0.29 [b]	4.82±0.14 [b]
Ven-3+C50	150.00±2.10 [b]	361.20±3.80 [b]	19.45±0.28 [b]	5.15±0.16 [b]
Ven-3+C75	154.60±2.20 [b]	365.85±3.90 [b]	20.90±0.29 [b]	5.60±0.17 [b]
Ven-4+C10	134.10±1.95 [c]	342.45±3.26 [c]	15.00±0.30 [b]	3.85±0.15 [c]
Ven-4+C25	139.25±2.00 [b]	347.80±3.25 [b]	16.20±0.29 [b]	4.10±0.16 [b]
Ven-4+C50	144.20±2.07 [b]	351.20±3.30 [b]	17.25±0.31 [b]	4.65±0.18 [b]
Ven-4+C75	148.34±2.11 [b]	356.40±3.40 [b]	18.40±0.32 [b]	5.00±0.20 [b]
Ven-5+C10	124.50±2.00 [c]	336.00±3.00 [c]	12.68±0.25 [b]	3.55±0.15 [c]
Ven-5+C25	130.05±2.10 [b]	345.05±3.05 [b]	13.35±0.24 [b]	3.90±0.17 [c]
Ven-5+C50	135.90±2.14 [b]	353.30±3.10 [b]	15.00±0.25 [b]	4.30±0.16 [b]
Ven-5+C75	140.80±2.17 [b]	360.00±3.00 [b]	16.45±0.27 [b]	4.80±0.19 [b]

Ven-1: 100 ppm venlafaxin, Ven-2: 200 ppm venlafaxin, Ven-3: 300 ppm venlafaxin, Ven-4: 400 ppm venlafaxin, Ven-5: 500 ppm venlafaxin, C10: 10 ppm Vitamin C, C25: 25 ppm Vitamin C, C50: 50 ppm Vitamin C, C75: 75 ppm Vitamin C

It has been reported that the deficiency of B vitamins, which are involved in all areas of the catabolic process for energy production, adversely affects cells. In particular, the active forms of thiamine, riboflavin, niacin, and pantothenic acid are essential coenzymes in cellular energy production through their role in the electron transport chain [14,15]. Vitamins B1 and B6 are necessary for the health of the nervous system; vitamin B3 regulates blood circulation. Vitamin B6 and B9 play a role in forming red blood cells, while vitamin B12 is important in nucleic acid metabolism and myelin synthesis [16].

As seen in Tables 2 and 3, it was observed that the number of vitamins B1, B2, B3, B5, B6, B9, and B12 in the microorganism decreased depending on the concentration of Venlafaxine added to the medium. In addition, it was found that increased vitamin C concentration in the growth medium containing venlafaxine led to an increase in the amount of B vitamins in the microorganism. As a result of the addition of 100 ppm venlafaxine to the control group, decrease in the amounts of vitamins as percentage 4.37, 6.48, 4.99, 4.49, 5.15, 2.49, 10.55, 6.55 were C, B1, B2, B3, B5, B6, B9, B12 respectively, on the other hand 400 ppm venlafaxine added, the

ratio of the same vitamins was found to be 16.76, 46.63, 17.14, 25.61, 22.58, 11.92, 38.76, 40.98, respectively. As a result of adding 25 ppm vitamin C to the medium containing 300 ppm venlafaxine, the percentage increase in the amounts of vitamins C, B1, B2, B3, B5, B6, B9, B12 was 4.63, 16.36, 4.98, 4.70, 4.73, 2.34, 19.21, 16.14. In comparison, 75 ppm of vitamin C was added to the same medium, and the ratio of increase in the same vitamins was found to be 9.74, 30.91, 8.64, 8.82, 10.82, 4.93, 38.41, and 34.94, respectively.

Table 4. Concentrations of fat-soluble vitamins *in S. cerevisiae* produced in a nutrient medium containing various concentrations of antidepressants and vitamin C

Application	Vitamin A (µg/g dw)	Vitamin E (µg/g dw)	β-Carotene (µg/g dw)	Lycopene (µg/g dw)
Control	4.50±0.16	30.50±0.50	1.35±0.09	0.69±0.05
Ven-1	5.30±0.18 [a]	32.60±0.52 [a]	1.50±0.10 [a]	0.61±0.04 [a]
Ven-2	5.95±0.17 [a]	35.00±0.60 [a]	1.85±0.11 [a]	0.54±0.04 [a]
Ven-3	6.50±0.20 [a]	37.70±0.56 [a]	2.10±0.13 [a]	0.47±0.03 [a]
Ven-4	7.00±0.22 [a]	40.00±0.61 [a]	2.50±0.12 [a]	0.41±0.03 [a]
Ven-5	7.70±0.19 [a]	43.00±0.63 [a]	2.90±0.14 [a]	0.35±0.02 [a]
Ven-1+C10	5.10±0.17 [c]	32.25±0.50 [c]	1.46±0.10 [c]	0.63±0.03 [c]
Ven-1+C25	4.90±0.15 [b]	31.90±0.48 [c]	1.42±0.08 [c]	0.65±0.04 [c]
Ven-1+C50	4.72±0.11 [b]	31.45±0.45 [b]	1.39±0.07 [c]	0.67±0.04 [c]
Ven-1+C75	4.51±0.10 [b]	30.90±0.43 [b]	1.36±0.07 [c]	0.69±0.03 [b]
Ven-2+C10	5.76±0.15 [c]	34.60±0.50 [c]	1.79±0.12 [c]	0.59±0.03 [c]
Ven-2+C25	5.50±0.13 [b]	34.00±0.47 [c]	1.73±0.11 [c]	0.62±0.03 [b]
Ven-2+C50	5.15±0.12 [b]	33.35±0.48 [b]	1.68±0.10 [c]	0.66±0.04 [b]
Ven-2+C75	4.90±0.10 [b]	32.80±0.44 [b]	1.60±0.08 [b]	0.70±0.04 [b]
Ven-3+C10	6.15±0.18 [c]	37.25±0.52 [c]	2.00±0.12 [c]	0.51±0.03 [c]
Ven-3+C25	5.90±0.16 [b]	36.85±0.50 [c]	1.92±0.10 [c]	0.56±0.03 [b]
Ven-3+C50	5.57±0.15 [b]	36.25±0.48 [b]	1.84±0.10 [b]	0.60±0.03 [b]
Ven-3+C75	5.35±0.15 [b]	35.80±0.45 [b]	1.76±0.09 [b]	0.64±0.02 [b]
Ven-4+C10	6.71±0.19 [c]	39.50±0.53 [c]	2.38±0.13 [c]	0.46±0.03 [c]
Ven-4+C25	6.30±0.15 [b]	38.90±0.50 [c]	2.24±0.11 [b]	0.51±0.03 [b]
Ven-4+C50	5.93±0.16 [b]	38.20±0.47 [b]	2.11±0.11 [b]	0.57±0.03 [b]
Ven-4+C75	5.50±0.14 [b]	37.75±0.45 [b]	1.93±0.10 [b]	0.61±0.04 [b]
Ven-5+C10	7.41±0.20 [c]	42.55±0.56 [c]	2.80±0.16 [c]	0.39±0.02 [c]
Ven-5+C25	7.06±0.19 [b]	42.00±0.53 [c]	2.69±0.13 [c]	0.45±0.02 [b]
Ven-5+C50	6.82±0.17 [b]	41.25±0.50 [b]	2.56±0.11 [b]	0.51±0.03 [b]
Ven-5+C75	6.34±0.14 [b]	39.85±0.42 [b]	2.40±0.10 [b]	0.58±0.03 [b]

Ven-1: 100 ppm venlafaxin, Ven-2: 200 ppm venlafaxin, Ven-3: 300 ppm venlafaxin, Ven-4: 400 ppm venlafaxin, Ven-5: 500 ppm venlafaxin, C10: 10 ppm Vitamin C, C25: 25 ppm Vitamin C, C50: 50 ppm Vitamin C, C75: 75 ppm Vitamin C

As seen from these results, the number of water-soluble vitamins decreased. When vitamin C, which has antioxidant properties, is added to the growth medium of *S. cerevisiae*, led to an increase in the number of water-soluble vitamins. As a result, it might be said that the metabolic stress caused by venlafaxine in microorganisms is reduced by vitamin C.

A study reported that cadmium added to the medium of *C. freundii* decreased the amount of water-soluble vitamins C and B in the microorganism. In contrast, vitamin C addition to the same medium increased the

amount of vitamins C and B [17]. A study investigating resistance to oxidative, osmotic, and thermal stress reported that thiamine increased the stress resistance of *S cerevisiae* [18].

It has been reported that lipid peroxidation increases in rats' tissues due to insufficient riboflavin in nutrition [19]. It has been reported that niacin added to the feed of rats caused a significant increase in superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione and zinc levels and a decrease in lipid peroxidation (LPO) levels compared to the control group [20]. It has been reported that when fish under oxidative stress are fed a diet deficient in pantothenic acid, SOD and CAT activities in the liver were found to be low, and there was a positive relationship between pantothenic acid and antioxidant defense [21].

In a study investigating the effect of pyridoxine on oxidative stress on erythrocyte membrane protein, it was shown that pyridoxine can significantly reduce lipid peroxidation and protein carbonylation in the red cell membrane exposed to high concentrations of oxidant agents [22].

Koyama et al. [23] reported that when heat stress was applied to mouse embryos, the curative effects of folic acid on the development of mouse embryos were observed.

Investigation of the effects of different concentrations and application times of vitamin B12 on the antioxidant response of *Physiophora alceae*, conducted by Abdelfattah [24], was reported that administered that vitamin B12 reduced superoxide anion radical (O2 •-) and hydrogen peroxide (H_2O_2) levels. At all venlafaxine concentrations, while vitamin B1 concentration decreased significantly ($p<0.05$), the addition of vitamin C to a medium containing 200, 300, 400, and 500 ppm venlafaxine significantly increased the amount of vitamin B1 ($p<0.05$).

Vitamins B3, B5, and B12 were significantly decreased ($p<0.05$) at 200, 300, 400, and 500 ppm with the increased venlafaxine concentrations. When 25, 50, and 75 ppm of vitamin C were added to the growth medium containing the same concentrations of venlafaxine, the number of vitamins B3, B5, and B12 increased significantly ($p<0.05$). The decrease in vitamins B2 and B6 was significant at all venlafaxine concentrations ($p<0.05$). The increase in vitamin B2 and B6 amounts was significant, adding 25, 50, and 75 ppm of vitamin C to media containing 300, 400, and 500 ppm of venlafaxine ($p<0.05$). The amounts of vitamin C and B9 were significantly reduced ($p<0.05$) at all concentration values of venlafaxine added to the medium. Adding vitamin C to the growth medium containing venlafaxine at 25, 50, and 75 ppm led to significantly increased vitamins C and B9 in the microorganism ($p<0.05$).

In a study conducted to investigate the effect of vitamin A treatment on yeast strains with SOD deficiency, it was observed that the addition of vitamin A to the medium at certain concentrations increased CAT and GSH Px activities and GSH levels in yeast [25].

Vitamin E has been found to reduce free radicals in the plasma, lungs, and brains of mice exposed to arsenic. It has also been determined that vitamin E supplementation facilitates the work of stress enzymes in animals [26]. Finaud et al. [27] reported that β-carotene deactivates ROS and reduces lipid peroxidation. In a study on cats with kidney failure, it was reported that the concentration of 8-hydroxy 2-deoxygenase, which is a marker of oxidative stress, in the blood serum decreased as a result of the administration of vitamins E, C, and β-carotene [28].

Investigation of the role of lycopene in oxidative stress: various forms of lycopene were reported to reduce markers of lipid peroxidation and oxidative stress [29]. It was reported that applying heavy metal stress on *C freundii* decreased lycopene concentrations due to stress. At the same time, the addition of vitamin C increased the amount of lycopene concentration [17]. It was found that vitamin A increased significantly ($p<0.05$)

depending on the concentration of venlafaxine added to the medium, and the amount of vitamin A observed decreased significantly ($p<0.05$) at all concentrations except 10 ppm of vitamin C. While vitamin E concentration increased significantly with the increase of venlafaxine added to the medium ($p<0.05$), it was found that 50 and 75 ppm of vitamin C added to the medium decreased vitamin E ($p<0.05$) (Table 4).

The amount of β-carotene was significantly increased at all venlafaxine concentrations ($p<0.05$); the addition of vitamin C to the medium containing 100 and 200 ppm venlafaxine did not cause a significant change in the concentration of β-carotene ($p>0.05$) (Table 4).

It was observed that Lycopene concentration was decreased significantly ($p<0.05$) at all venlafaxine concentrations. On the other hand, the addition of vitamin C to the growth medium (25, 50, and 75 ppm) containing 200, 300, 400, and 500 ppm venlafaxine increased lycopene concentrations significantly ($p<0.05$).

A study reported that cadmium added to the growth medium of *S. cerevisiae* increased the amount of vitamin E [30]. A survey conducted by [17] said that adding vitamin C to the nutrient medium containing cadmium increases the concentration of fat and water-soluble vitamins by reducing cadmium's toxic and negative effects on the metabolism of microorganisms.

4. Conclusion

It has been observed that the addition of Venlafaxin to the YPD medium of S. cerevisiae led to decreased water-soluble vitamins and lycopene concentration while increasing the A, E vitamins, and β-carotene concentrations. The addition of vitamin C to the growth medium of S. cerevisiae containing Venlafaxin caused the opposite effect on the concentration of all the parameters studied. It can be concluded that vitamin C reduced the negative effect of all the parameters studied caused by Venlafaxine.

Author Contributions

All the authors equally contributed to this work. They all read and approved the final version of the paper.

Conflicts of Interest

All the authors declare no conflict of interest.

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