



Bee Venom an Ingredient to Be Added to Honey to Feel Energetic

Suzanne Fouad^{1*}, Rasha Monir², Fatma A. Ibrahim³, Ahmed G. Hegazi⁴, Aliaa El Gendy²

¹Nutrition and Food Science Department, National Research Centre, Dokki, Giza, Egypt.

²Complementary Medicine Department, National Research Centre, Dokki, Giza, Egypt.

³Biochemistry Department, Genetic Engineering & Biotechnology Institute, National Research Center, Giza, Egypt.

⁴Department of Zoonotic Diseases, National Research Centre, Dokki, Giza, Egypt

(Affiliation ID: 60014618) (Postal Code PO: 12622)



CrossMark

Abstract

The effect of honey fortified with bee venom was assessed on patients complaining of fatigue and exhaustion. 123 women aged 32- 35 years participated as volunteers in the study, Sixty-two subjects participated in group (A), they consumed 30 ml clover honey fortified with bee venom with a mean age of 32.86 ± 12.07 years while sixty-one volunteers enrolled in group (B) as a control group, they consumed 30 ml clover honey with a mean age of 34.75 ± 12.26 years. After two months of dietary supplements consumption, subjects in group (A) showed a statistically significant improvement in the calculated fatigue scores, the anti-inflammatory marker (IL-10), catalase enzyme, MDA and SOD ($p < 0.05$). While participants in group (B) consuming clover honey unfortified showed an improvement in the MDA serum level and FSS fatigue score ($p < 0.05$). Furthermore, the haemoglobin level increased numerically in both group but without statistical significance difference ($p > 0.05$), moreover, there was no effect on fasting blood sugar level in both groups ($p > 0.05$).

Conclusion: clover honey fortified with bee venom can alleviate fatigue and exhaustion.

Keywords: bee venom; clover honey; fatigue; exhaustion; functional foods.

1. Introduction

Fatigue and lack of energy can damage health and well-being in human. They may feel a surge of energy when they need to be most productive at work. Simply exhausted people don't have the motivation to do anything which can lead to even more feeling of fatigue. [1]

Feeling energetic makes you more likely to be happy and productive at work. Maintaining a certain level of physical energy by such as regular snack and exercise can make a big difference and by reducing the dependence on caffeine through the day. [2,3]

Apitherapy is the use of bee stings for treatment of inflammatory diseases, rheumatologic diseases, neurologic disorders, vascular diseases, and gastrointestinal disorders. Bee venom (BV) is administered by direct bee sting or by manual

injection (intramuscular or intradermal injection). When used directly by worker bees sting, bees leave their stingers and sac containing the venom implanted in the patient. [4]

Analysis of a drop of Bee venom consists of eighty-eight per cent water and only 0.1 microgram of dry venom; the dry venom is mainly composed of melittin (40-50% dry wt), phospholipase A (12-15% dry weight), hyaluronidase (1.5-2% dry weight), minerals and less than 1% of acid phosphatase, histamine and adrenaline. [5]

Previous study demonstrated the great value of usage of fresh bee venom (BV) for medical purposes. BV was documented to affect the release of cortisone and to stimulate the function of immune system, as cortisone has a powerful anti-inflammatory property.

*Corresponding author e-mail: suzannefouad6161@yahoo.com

Receive Date: 22 February 2023, Revise Date: 10 April 2023, Accept Date: 12 April 2023

DOI:10.21608/EJCHEM.2023.195717.7632

©2023 National Information and Documentation Center (NIDOC)

BV must be sheltered from humidity and light and must be stored in a cool and dry place. [6]

The objective of this study was to study and evaluate the consequence of consumption of honey fortified by bee venom on young females complaining of fatigue and exhaustion.

2. METHODOLOGY

2.1. Design of the study

This case control study was conducted in National Research Centre in Cairo after Ethical Committee approval (NRC Registration Number 19/178). Volunteers signed consent to participate in the study after told them all the information about the steps of the study. Subjects suffering from unexplained fatigue or exhaustion relieved by rest and/or sleep were recruited from NRC Complementary medicine clinic to participate as volunteers in this study. The objective of the study was discussed with the volunteers.

Selection of participants was based on nonexistence of medical illness (acute or chronic eg. hypertension, ischemic heart disease, diabetes mellitus, thyroid dysfunctions, hypercholesterolemia, joints complains, fatty liver, history of food or drug allergy and no parenchyma diseases) and no history of antipsychotic drugs or other medical or supplements therapies. We told the participants not to take analgesics or vitamins for 60 days. The volunteers were clinically evaluated carefully. Presence of history of medical illness or getting non steroidal anti-inflammatory preparations or vitamins was debarred from the study. No special advice concerning their nutrition intakes.

Each patient was subjected to general examination. Detailed medical and pharmaceutical drugs histories were taken. Anthropometric and body composition parameters were reported by BC-418MA-Japan [7]. Full clinical examination and weekly follow up during the study period were performed. Evaluation and diagnosis of fatigue was performed by the tiredness questionnaire and Fatigue Severity Scale, reevaluation was done at the end of the study. Fatigue Severity Scale (FSS) depends on nine questionnaires in easy comprehensive words to assess the extent of fatigue and how it affects people performance. We asked about the motivation to do anything after exhaustion, if onset of fatigue was rapidly than before, and if has an effect on their physical routine or work. Calculated total score more than or equal to thirty-six suggests that subjects suffer from exhaustion and fatigue. [8,9]

Trudie Chalder research team at King's College at London created a score to evaluate the severity of fatigue in general practice settings. The tiredness questionnaire which consists of different substance (if there is rapid tiredness; change in thinking that it become difficult and get pathetic as you go on; lack of energy to do anything; have you lost your interest to do your preferable thing) [10]

2.2. Preparation of the food supplements:

Preparation of the food supplements was carried out in the Plant Protection Research Institute at Agriculture Research Center, during the 2021 summer season. Venom was collected from the *Apis mellifera* L Carniolan pure bee workers by latex [11]. Collection of bee venom was done by electric shock apparatus (VC-6F Apitronic Services, Canada), using wire electrodes placed in parallel to each other. So that, electrical current moved as impulses to stimulate the bees to sting from side to side the latex sheet, which was placed on a glass plate as containers of the collected venom. The venom odour stimulates other *Apis mellifera* to sting over the latex sheet to collect more venom. After collection of the bee venom, we transferred it using Fakhimzaden manoeuvre [12] to the laboratory and stored it in dark jars in dry cool place [13]. Analysis of the bee venom contents and estimation of its median lethal dose were estimated according to Akhila procedure [14] at the department of immunology at NRC, by diluting ten mg of the collected BV venom with twenty mL purified water to be filtered for HPLC analysis [15]. AOAC method was used for determination of moisture content in the sample using an infrared heated moisture analyzer [16]. 30 mg Bee venom was mixed with one kg clover honey.

2.3. Subjects:

Volunteers' participants were erratically divided into two groups using a computer 1:1 generated randomized number. The subjects in group A consumed bee clover honey enriched with bee venom (30 µg bee venom added per gram of honey). They received one spoonful (30 ml) fortified honey dissolved in 150 ml water per day for each subject. The subjects in group B (as a control group) consumed one spoonful (30 ml) clover honey dissolved in 150 ml water per day.

2.4. Biochemical parameters:

5 ml venous blood samples were collected in heparinised tubes to assess different biochemical parameters among the two groups twice; at 1st day of the study and 2 months later after consumption of the supplements. Quantitatively Determination of glucose Concentration in plasma using Bio STC Kit by colorimetric method according to Weissman procedure [17]. Colorimetric Hemoglobin Determination using Drabkin's solution [18]. Determination of Malondialdehyde level (MDA) as an oxidative stress marker according to Satoh [19]. Determination of the antioxidants enzymes, *Superoxide dismutase* according to the method of Nishikimi [20], and catalase enzyme according to Aebi procedure [21]. Human Interleukin 10 as an anti-inflammatory marker was determined quantitatively in plasma by Sino Gene Biotech Kit No.28 District 311112, China).

2.5. Statistical analysis

The obtained data were analyzed statistically by Independent-samples t tests or Mann-Whitney U tests for comparison results among the same group and in-between the studied groups using the Statistical Package for Social Sciences, version 17), and the statistical compare means with Confidence Interval Percentage was 95% using SPSS program. The data were presented as mean \pm standard Deviation. The difference between the groups and in the same group before and after supplements consumption was statistically evaluated. "P" value less than 0.05 was considered significant.

3. RESULTS

One hundred twenty-three Egyptians' volunteers complaining of fatigue and/or exhaustion without medical diseases participated in the study which lasted for 60 days. Subjects were females aged range was (31-35 years) who had similar socioeconomic status. All anthropometrics parameters, education level and calculated fatigue scales among both groups were comparable at the beginning of the study. [Table 1]

Sixty-two participated in group (A), they consumed 30 ml clover honey fortified with bee venom with a mean age of 32.86 ± 12.07 years while sixty-one volunteers shared in group (B) as a control group, they consumed 30 ml clover honey with a mean age of 34.75 ± 12.26 years. Clinical data and biochemical parameters values from first and last visits among the groups are shown in table (2). After two months of dietary supplements consumption, results in group (A) consuming the fortified clover honey demonstrated statistically significant improvement on the calculated fatigue scores, the anti-inflammatory

marker (IL-10), catalase enzyme, MDA and SOD. Whereas subjects in the control group consuming clover honey revealed significant improvement in serum MDA and FSS fatigue score. Performing the statistical significances in-between groups, there were significant differences in the effect of consumption of the two supplements in the calculated fatigue scales, the anti-inflammatory marker and in their effect in the antioxidants markers. improvement was significant more in the fortified clover honey consumption group. The haemoglobin level increased numerically in both group but without statistical significance difference. There was no effect on fasting blood sugar level in both groups at the end of the study.

The result of the content analysis of the dried bee venom used for fortification of the honey is shown in (Tables 3), *Apis mellifera* beekeepers venom revealed that the humidity content of the sample was 7.73%, bee venom has an adequate content of sugars, mellitin, apamin and phospholipase A2 . the median lethal dose of adult was estimated at 2.8 mg bee venom per kg human body weight (eg. adult of weight 70 Kg can consume up to 196mg/day).

4. Discussion

"I'm tired rapidly" is a common complaint. Fatigue, tiredness and exhaustion are common problems; in many cases, it's not a medical problem, but it's something that can be reversed with lifestyle changes and healthy foods [22]. Fatigue can negatively affect performance at work, home life, and social relationships. Tiredness and fatigue are important topics in applied occupational medicine, there is a growing understanding of their relevance to employee performance, health, safety and overall work capacity [23].

Consumption of healthy foods aids the persons to perform their duty perfectly [24]. Lifestyle modification and functional foods can help people complaining of fatigue or tiredness to combat these symptoms and to feel more active [25].

Honey, in addition to being food, it has many pharmacological properties and several health benefits. The health benefits of different bee products documented such as antimicrobial, antifungal, wound healing, antigastric ulcer, anticancer, antiaging, immunomodulatory properties and protective functions on neurodegenerative disorders [26].

Due to bee products efficacies, there is increasing demand of functional food from these products. Bee

venom one of the valuable bee products, produced by the glands of *Apis Mellifera*, it is a rich source of peptides and amines. Bee race, feeding supplies, season, age and method of bee venom collection are factors affecting its production. [27,28]

From the obtained results, the study demonstrated that consuming the clover honey fortified with bee venom demonstrated an improvement in the fatigue scores, the anti-inflammatory marker (IL-10), the antioxidants biomarkers (catalase enzyme and SOD), the oxidative stress marker (MDA), and the hemoglobin level more than consuming the non-fortified honey. Bee venom is a good source of proteins, mast cell degranulating peptide, biogenic amines (examples of them are melittin, noradrenaline, histamine, serotonin, dopamine, histidine, phospholipase and hyaluronidase) and enzymes [29].

Bee venom has many biological benefits; of them are pain reliever, anti-bacterial, anti-inflammatory, immune-modulator, improve blood circulation, lowers cholesterol levels and stimulates secretion of endogenous cortisone. Melittin can suppress inflammation by inhibiting the activity of the enzyme phospholipase which when released can lead to tissue degradation and organ dysfunctions. In addition, melittin can block the release of neutrophil superoxide. [30]

Fatigue and exhaustion evaluations could be assessed by short questionnaires written in simple terms and need a simple straightforward response to provide a concise tool for measuring physical, mental and psychological fatigue. FSS was valid in large sample size studies as a dependable reliable method to

evaluate fatigue for clinical purpose [31]. Moreover, FSS is an excellent psychometric property in healthy and diseased people and can be used in the scientific research and medical settings evaluating fatigue [32].

Catalase and SOD are antioxidant enzymes that act as the body's defense system against H₂O₂, a powerful oxidant that can cause intracellular damage. Assessing these enzymes is a useful tool in oxidative stress research and is considered an antioxidant biomarker. [33,34]

Bee Venom was approved by United Nation Food and Agriculture Organization (FAO) and by South Korean food and drug administration (FDA) as a biotherapeutic medication [35]. Several preparations and products are available in markets in the form of tablets, capsules, chewable tablets, cream and ointments. Moreover, there is an approved dry lyophilized injection form of bee venom in North American and European countries. In addition, in China and Europe, bee venom sterile solutions are used with electrophoresis [36]. Examples of the pharmaceutical products available in markets, Bee venom Capsules from Deep blue health company and ApiVENZ Chewable tablets (ApiHealth NZ Ltd company) to support joint health [37]. These pharmaceutical products became famous in the last decade as well as the venom acupuncture which was approved to have high efficacy as a complementary medicine for relieving pain resulted from chronic arthritis and lumbo-sacral pain [38].

Table 1 Basic characteristic of both groups

Parameter	Group A	Group B
	mean± standard deviation	mean± standard deviation
Age (years)	32.86 ± 12.07	34.75 ± 12.26
Education	Highly educated	Highly educated
Work status	Employed	Employed
Socioeconomic level	middle	middle
Height (cm)	161.28 ± 8.47	158.8 ± 5.93
Weight (Kg)	74.87 ± 18.48	73.55 ± 17.23
Body Mass Index (BMI kg/m ²)	29.23 ± 5.79	29.1 ± 6.04
Basal metabolic rate (kcal / day)	3932.28 ± 1236.18	3998.8 ± 750.3
Body Fat%	36.34 ± 7.64	34.9 ± 7.9
Free Fat Muscle (Kg)	45.8 ± 9.86	46.7 ± 5.6
Hip circumference (cm)	111 ± 12.84	109.2 ± 13.1

Waist circumference (cm)	92.85 ± 12.75	93.6 ± 13.3
Tiredness' questionnaire score	31± 5.37	34.65 ± 6.7
Fatigue Severity Scale	54.5 ± 7.01	53.3 ± 10.03

Table 2: Clinical data and biochemical parameters among two groups

Items	Group A: Fortified honey N: 62			Group B (control) N: 61		
	1 st day (Mean ± SD)	Last day (Mean ± SD)	P value	1 st day (Mean ± SD)	Last day (Mean ± SD)	P value
Hb (g/l)	11.66 ± 0.82	12.0 ± 0.77	P > 0.05	11.7 ± 0.72	12.5 ± 1.27 ^{*y}	P > 0.05
FBS (mg/dL)	75.69 ± 12.16	73.93 ± 10.42	P > 0.05	71.9 ± 8.9	75.15 ± 8.2	P > 0.05
MDA(nmol/mL)	4.83 ± 0.82	2.34 ± 0.58	P < 0.05	5.41 ± 0.56	4.1 ± 0.7 ^{*y}	P < 0.05
SOD (U/mL)	189.16 ± 12.1	91.06 ± 13.74	P < 0.05	184.45 ± 15.07	180.45 ± 16.5 ^{*y}	P > 0.05
Catalase (U/L)	70.6 ± 10	102.38 ± 12.15	P < 0.05	56.6 ± 11.6	56.5 ± 11.5 ^{*y}	P > 0.05
IL10 (ng/L)	44.29 ± 9.42	20.66 ± 4.9	P < 0.05	51.1 ± 6.9	50.3 ± 7.1 ^{*y}	P > 0.05
Tiredness' questionnaire	31± 5.37	14 ± 3.06	P < 0.05	34.65 ± 6.7	31.9 ± 6.6 ^{*y}	P > 0.05
<i>Fatigue Severity Scale</i>	54.5 ± 7.01	19.09 ± 6.8	P < 0.05	53.3 ± 10.06	42.6 ± 11.2 ^{*y}	P < 0.05

Hb: hemoglobin; FBS: Fasting blood sugar, MDA: Malondialdehyde. SOD: Superoxide dismutase ; IL: interleukin. ^{*y} Significant at $p < 0.05$ between both group. $p < 0.05$: Significant; $p > 0.05$: Non significant.

Table 3: Content analysis of collected dried Apis mellifera Bee Venom

	Moisture %	Glucose (%)	Sucrose (%)	Maltose (%)	Fructose (%)	Melittin (%)	Phospholipase A2 (%)	Apamine (%)
dried Bee Venom	7.73±0.33	5.77±0.04	1.88±0.51	0.29±0.05	2.94±0.13	45.61±0.73	10.47±0.15	2.63±0.07

5. Conclusion

Bee venom has been licensed for human therapy; when added to honey, this natural product has an impressive effect to alleviate fatigue and rapid exhaustion. This fortified honey has antioxidant and antiinflammatory effects. There was significant difference among the two studied groups concerning their effect on the calculated fatigue scales, anti-inflammatory marker, oxidative stress marker and the antioxidants parameters. Improvement was noticed more in the fortified clover honey.

6. Conflicts of interest

There are no conflicts to declare.

7. Funding

This study was funded by National Research Centre, Egypt. The project number "12060123" entitled "Food habits and dietary intervention to fight chronic fatigue and rapid tiredness as symptoms affecting the efficiency in work and production capacity"

8. Acknowledgments

The authors would like to thank the female volunteers who participated in this study, more to the National Research Center.

9. Ethics approval

The research was given ethical approval from Ethical Committee of the National Research Centre (Registration Number is 19/178).

10. References

- [1] Vaes AW, Goërtz YMJ, van Herck M, Beijers, van Beers M, Burtin C, Janssen DJA, Schols AM, Spruit MA. Physical and mental fatigue in people with non-communicable chronic diseases. *Ann Med*. 2022; 54(1):2522-2534. doi:10.1080/07853890.2022.2122553.
- [2] Chekroud SR, Gueorguieva R, Zheutlin AB, Paulus M, Krumholz HM, Krystal JH, Chekroud AM. Association between physical exercise and mental health in 1.2 million individuals in the USA between 2011 and 2015: a cross-sectional study. *Lancet Psychiatry*. 2018; 5(9):739-746. doi:10.1016/S2215-0366(18)30227-X.
- [3] Codella R, Chirico A. Physical Inactivity and Depression: The Gloomy Dual with Rising Costs in a Large-Scale Emergency. *Int J Environ Res Public Health*. 2023; 20 (2):1603. doi: 10.3390/ijerph20021603.
- [4] Trumbeckaite S, Dauksiene J, Bernatoniene J, Janulis, V. Knowledge, attitudes, and usage of apitherapy for disease prevention and treatment among undergraduate pharmacy students in Lithuania. *Evidence-Based Complementary and Alternative Medicine*, vol. 2015, Article ID 172502, 9 pages, 2015. <https://doi.org/10.1155/2015/172502>
- [5] Wehbe R, Frangieh J, Rima M, El Obeid D, Sabatier JM, Fajloun Z. Bee Venom: Overview of Main Compounds and Bioactivities for Therapeutic Interests. *Molecules*. 2019; 24(16): 2997. doi: 10.3390/molecules24162997.
- [6] Kekecoglu, Meral & Samanci, Taylan. Comparison of commercial and Anatolian bee venom in terms of chemical composition. *Uludag Bee Journal* 2019, 19 (1): 61-68.
- [7] Jelliffe DB. The assessment of the nutritional status of the community. World Health Organization Monograph, Geneva. (1966) Series No 53:50–84
- [8] Valko PO, Bassetti CL, Bloch KE, Held U, Baumann CR. Validation of the fatigue severity scale in a Swiss cohort. *Sleep*. 2008 Nov;31(11):1601-7. doi: 10.1093/sleep/31.11.1601.
- [9] Cella M and Chalder T. "Measuring fatigue in clinical and community settings." *J Psychosom Res* 2010; 69(1): 17-22.
- [10] De Vries J, Michielsen HJ, Van Heck GL. Assessment of fatigue among working people: a comparison of six questionnaires. *Occup Environ Med*; 2003; 60 (Suppl. 1): i10–i15.
- [11] Brandeburgo MA. A Safe Device For Extracting venom from honeybees. *Bee world* 1992, 73(3); 128-130.
- [12] Fakhimzaden K. Improved device for venom extraction. *Bee world*. 1998; 79 (1); 52-56.
- [13] Hegazi AG, EL-Feel MA, Eman H, and Abed Al-Fattah MA.: Antibacterial activity of bee venom collected from *Apis mellifera* Carniolan pure and hybrid races by two collection methods. *Int. J. Curr. Microbiol. App. Sci*, 2015; 4(4): 141-149.
- [14] Akhila, J. S., Shyamjith, D., & Alwar, M. C. (2007). Acute toxicity studies and determination of median lethal dose. *Current Science*, 93(7), 917–920. <http://www.jstor.org/stable/24099255>
- [15] Zenon, J., Kokot, J.M. (2009). Simultaneous Determination of Major Constituents of Honeybee Venom by LC-DAD. GWV Fachverlage GmbH. 2009, Department of Inorganic and Analytical Chemistry, Poznan university of Medical Sciences, Poland.
- [16] AOAC. Official methods of analysis of AOAC International. 2000. (17th Ed.) by Horwitz, W. Suite 500, 481 North Fredric avenue Gaithersburg, Maryland 20877-22417, USA.
- [17] weissman M, kien B. Evaluation of glucose determination in untreated serum samples. *clin chem* 1958.
- [18] Drabkin DL, Austin JH. Spectrophotometric studies I. Spectrophotometric constants for common hemoglobin derivatives in human, dog and rabbit blood. *J Biol Chem*. 1932: 98:719-733
- [19] Satoh K. Serum lipid peroxide in cerebrovascular disorders determined by a new colorimetric method. *Clin Chim Acta* 1978; 90 (1): 37-43.
- [20] Nishikimi M, Appaji N, and Yagi K: The occurrence of superoxide anion in the reaction of reduced phenazine methosulfate and molecular oxygen. *Biochem Biophys Res Commun*. 1972: 46 (2): 849-854.
- [21] Aebi H: Catalase in vitro. *Methods Enzymol*. 1984; 105:121-126.
- [22] Gawron, Valerie. Overview of Self-Reported Measures of Fatigue. *The International Journal of Aviation Psychology*; 2016: 26(3-4):120-131. DOI:10.1080/10508414.2017.1329627
- [23] Fouad S, El Gendy A, Monir R, Abdel-Wahhab KA, Shafei HF, Hegazi AG. Bee Products for Relieving Menopausal Symptoms. *Open Access Macedonian Journal of Medical Sciences*. 2022; 15; 10(B):632-638. doi.org/10.3889/oamjms.2022.8191.
- [24] Rico-Campà A, Martínez-González MA, Alvarez-Alvarez I, de Deus Mendonça R, de la Fuente-Arrillaga C, Gómez-Donoso C, Bes-Rastrollo M. Association between consumption of ultra-processed foods and all cause mortality: SUN prospective cohort study. *BMJ*. 2019; 365:l1949. doi: 10.1136/bmj.l1949
- [25] Suksatan W, Moradi S, Naeini F, Bagheri R, Mohammadi H, Talebi S, Mehrabani S, Hojjati Kermani MA, Suzuki K. Ultra-Processed Food Consumption and Adult Mortality Risk: A Systematic Review and Dose-Response Meta-Analysis of 207,291 Participants. *Nutrients*; 2021: 14(1):174. doi: 10.3390/nu14010174

- [26]Pasupuleti VR, Sammugam L, Ramesh N, Gan SH. Honey, Propolis, and Royal Jelly: A Comprehensive Review of Their Biological Actions and Health Benefits. *Oxid Med Cell Longev*. 2017;1259510. doi: 10.1155/2017/1259510.
- [27]Hussein, A. E. ; M. K. El-Ansari and A. A. Zahra. Effect of the Honeybee Hybrid and Geographic Region on the Honey Bee Venom Production; *J. Plant Prot. and Path*. 2019;10 (3):171 - 176.
- [28]Zidan, Hind & Mostafa, Zahia & Ibrahim, Mahmoud & Haggag, S. & Darwish, Doaa & Elfiky, Abir. (2018). Venom Composition of Egyptian and Carniolan Honeybee, *Apis mellifera* L. Affected by Collection Methods.. *Egyptian Academic Journal of Biological Sciences. A, Entomology*. 2018: 11. 59-71. 10.21608/eajbsa.2018.17733.
- [29]Scaccabarozzi D, Dods K, Le TT, Gummer JPA, Lussu M, Milne L, Campbell T, Wafujian BP, Priddis C. Factors driving the compositional diversity of *Apis mellifera* bee venom from a *Corymbia calophylla* (marri) ecosystem, Southwestern Australia. *PLoS One*. 2021 Jun 30;16 (6):e0253838. doi: 10.1371/journal.pone.0253838.
- [30]Ali, M.A.M. Studies on Bee Venom and Its Medical Uses. *Int. J. Adv. Res. Tech*. 2012: 1(2):1-15
- [31] Sobayel, H.I. Ranyah M. Albawardi N, Alnahdi A and Daif A. Validation of an Arabic version of Fatigue Severity Scale. *Saudi Medical Journal* 2016, 37 (1): 73 -77.
- [32] Naik H, Shao S, Tran KC, Wong AW, Russell JA, Khor E, Nacul L, McKay RJ, Carlsten C, Ryerson CJ, Levin A. Evaluating fatigue in patients recovering from COVID-19: validation of the fatigue severity scale and single item screening questions. *Health Qual Life Outcomes*. 2022 Dec 27;20(1):170. DOI: 10.1186/s12955-022-02082-x
- [33] Nandi A, Yan LJ, Jana CK, Das N. Role of Catalase in Oxidative Stress- and Age-Associated Degenerative Diseases. *Oxid Med Cell Longev*. 2019 Nov 11;2019:9613090. doi: 10.1155/2019/9613090.
- [34] Pizzino G, Irrera N, Cucinotta M, Pallio G, Mannino F, Arcoraci V, Squadrito F, Altavilla D, Bitto A. Oxidative Stress: Harms and Benefits for Human Health. *Oxid Med Cell Longev*. 2017: 8416763. doi: 10.1155/2017/8416763.
- [35] Alalawy, A.I.; El Rabey, H.A.; Almutairi, F.M.; Tayel, A.A.; Al-Duais, M.A.; Zidan, N.S.; Sakran, M.I. Effectual Anticancer Potentiality of Loaded Bee Venom onto Fungal Chitosan Nanoparticles. *International Journal of Polymer Science*, vol. 2020. Article ID2785304, 9pages. doi.org/10.1155/2020/2785304.
- [36] Khalil A, Elesawy BH, Ali TM, Ahmed OM. Bee Venom: From Venom to Drug. *Molecules*. 2021 15;26(16):4941. doi: 10.3390/molecules26164941.
- [37] Singh, D. Bee venom. In *Commercial Beekeeping (Production, Processing and Value Addition of Beehive Products for Income and Employment Generation)*; Scientific Publishers: Jodhpur, India, 2020; pp. 257–262.
- [38] El Gendy A, Saber M, Daoud E, Abdel-Wahhab K, Abd el-Rahman E, Hegazi A. Role of bee Venom Acupuncture in improving pain and life quality in Egyptian Chronic Low Back Pain patients. *Journal of Applied Pharmaceutical Science*. 2017: 7 (08), 168-174. DOI: 10.7324/JAPS.2017.70823