v. 4, n. 2, 2024

International Journal of Biological and Natural Sciences

"ANTIDEPRESSIVE AND ANSIOLYTIC ACTION OF OPUNTIA FICUS - INDICA L. MILL IN RATTUS NORVEGICUS"

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Abstract: Anxiety and depression disorders can affect spatial memory. In this article, the anxiolytic and antidepressant effects of macerated pulp and peel of *Opuntia ficus-indica L. Mill* were evaluated. This function was studied in an animal model of depression. *Rattus N.* (n:12) males, were divided according to the administration of the hydroalcoholic extract into a control group, a group which pulp was administered (concentration of 223.4 mg/dl at a dose of 60 mg every 12h/8d) and a group to which the peel was administered (concentration of 730 mg/dl at a dose of 180 mg every 12h/6d). After treatment, depression was measured by forced swimming, anxiety by gripping technique and spatial memory by the Morris water maze, which was designed by R.G. Morris. In forced swimming, the control group had an average of 705,750s, while the pulp group had 1260,750s and the peel group had 768,750s; in the grip test, the control group had an average of 6,250s, while the pulp group had 17,000s and the peel group had 12,750s; in the Morris water maze test, the control group had 266,000s, the pulp group had 116,250s and the peel group had 142,250s. Through the t-student test, the control group, pulp group and peel group were compared. These results suggest that the pulp has, in fact, an effect as antidepressant, anxiolytic and also on spatial memory. On the other hand, the peel only had effects on the spatial memory.
Keywords: Depression, Anxiety, Spatial memory, Disorders, rats

INTRODUCTION

Stress, anxiety, or depression can cause difficulty concentrating and an inability to retain that disrupts daily activities.

Stress and anxiety is when the body becomes very alert to face a crisis, producing a series of biochemical changes to enhance the flight response system. This increases the brain chemical cortisol, for example, mobilizing energy and alertness. When stress and anxiety become chronic, such as with work or family problems, the system becomes overloaded with substances intended for emergency use. As a result, the brain loses cells and struggles to form new neurons. This creates problems with cognitive thinking, especially when it comes to retaining new information. (1)

Depression is often related to low levels of serotonin, a neurotransmitter connected to the arousal system. Concentration and concentration are affected, impairing the ability to correctly store new memories (memory). (1)

Many people consume prickly pear for its pleasant flavor, without knowing the benefits it can provide to their health. This fruit, in all its varieties (white, red and orange) has nutritional properties: having vitamins, such as thiamine, niacin and riboflavin, as well as essential minerals, such as calcium, iron, selenium, phosphorus, potassium, copper, zinc, magnesium and sodium. (2)

Peru is the largest producer of prickly pears in South America, with 72,500 hectares dedicated to *prickly pears and* ten thousand five hundred to *nopales*. There are plantations in the Andes of Peru: the largest wild production is in the inter-Andean valleys in regions such as: Ayacucho, Huancavelica, Apurímac, Arequipa, Ancash, Lima and Moquegua, among others. (2)

Opuntia ficus-indica has medicinal, nutritional, antioxidant properties and a quantity of fibers that have health effects such as weight control, cholesterol and diabetes. (3)

From this, the anxiolytic or antidepressant effect will be evaluated in the use of *Opuntia ficus-indica* L. Mill. macerate in *Rattus* N., which could have an effect on memory by reducing anxiety and stress levels. With the specific objectives of Evaluate the activity, anxiolytic, antidepressant and cognitive activity in Rattus Norvegicus. Compare the

anxiolytic, antidepressant and cognitive activity in fruit and peel of *Opuntia ficus-indica L. Mill.*

So this work is important because the anxiolytic or antidepressant effect of the *Opuntia ficus-indica L.* Mill macerate generates new knowledge about natural treatments for anxiety and depression, and this way improve cognitive ability.

Akkol, E. Ilhan, M. Karpuz, B. Genç, Y. mention us in their scientific article on "Sedative and anxiolytic activities of Opuntia ficus indica (L.) Mill.: an experimental evaluation in mice". In this work they tell us about the use of the fruits of the "prickly pear" as an anxiolytic, as well as for the treatment of diabetes, burns, constipation and even bronchial asthma. Focusing on anxiolytic effects, they used a pull test, chimney test, pegboard test, maze test, and open field test. They also emphasize that the EtOAc subextract showed more anxiolytic and sedative effects, where within its structure there are components such as isorhamnetin, isorhamnetin 3-O -glucoside, isorhamnetin 3- O -rutinoside and kaempferol 3- O -rutinoside. This article confirms that an anxiolytic effect is evident in the plant. [4]

Yasser, E. Marwa, I. Ezzat M mention that Opuntia - Indica, better known as "prickly pear" has a large number of functional, nutraceutical and biological activities. Furthermore, they mention that various parts of the plant (such as its pulp, peel, stem) have certain therapeutic potential, highlighting effects on the cardiovascular system, neuroprotective, sedative, analgesic, anxiolytic, antimicrobials and effects on cognitive function and memory. [5]

Silva MA, Albuquerque TG, Pereira P, Ramalho R, Vicente F, Oliveira MBPP, et al. They emphasize that the prickly pear is "multipurpose" due to its high content of polyphenols, as well as its antioxidant, anxiolytic and anti-inflammatory properties. [6]

DEPRESSION

Disorder that causes feelings of sadness and loss of interest in carrying out activities, among the symptoms it causes are: irritation, lack of interest in personal appearance, sleep disturbance, intention to attack the person, fatigue, difficulty socializing and physical problems in case this disorder is advanced. Can cause cognitive problems. [7]

ANXIETY

Disorder that generates excessive worry and fear in the person, involving sudden episodes that cannot be controlled in situations that generate insecurity. The cause of this condition can be due to different factors such as: trauma, accumulation of stress, other mental disorders and hereditary. [8]

Scientific Classification of Opuntia Ficus - Indica L. Mill

Class: Equisetopsida

Subclass: Magnoliidae

Superorder: Caryophyllanae

Order: Caryophyllales

Family: Cactaceae

Gender:

Species: *ficus-indica*

Scientific name: *Opuntia ficus-indica* (L.) Mill.

Popular name: "tuna"

Properties of Opuntia Ficus - Indica L. Mill

Among some properties already studied of this species, we have:

HYDROALCOHOLIC EXTRACT

➔ Anti-inflammatory that is tested through the red blood cell membrane stabilization technique. [9]

➔ Antioxidants that can be given by 3 methods: Method of scavenging the free radical 1,1 - diphenyl - picryl - hydrazyl (DPPH), Method of sequestering the radical cation of the acid 2,2´- azinobis - (3- ethylbenzothiazoline) - 6-sulfonic acid (ABTS. +) and Iron Reducing Antioxidant Potential (FRAP) Method) [10]

MUCILAGE

➔ Alternative Natural Coagulant to treat cloudy waters, in this a mucilage coagulation process occurs with doses capable of removing the turbidity of the waters. [11]

HYPOTHESIS

NULL HYPOTHESIS

The use of macerated *Opuntia ficus-indica L. Mil* has no effect as an anxiolytic or antidepressant in rattus norvegicus.

ALTERNATIVE HYPOTHESIS

The use of macerated Opuntia ficus-indica L. Mil has anxiolytic or antidepressant effect in rattus norvegicus.

MATERIAL AND METHOD

SAMPLE

For the present investigation, 3 kg of the fruit of the Opuntia Ficus plant were used, it was acquired in a food market in the city of Trujillo, Peru, where a random sampling of different stalls was done, based on information from the person who provided the fruit to the plants. They come from the city of Huaraz located in the department of Ancash, Peru located approximately 3000 meters above sea level.

MATERIALS

Biosafety material

- Gloves
- Apron
- Mask

Experimental material

- 12 Albino rats: 12 male rats of the species *Rattus norvegicus* weighing 250 to 300 g each, acquired from the Lima vivarium, were experimented with a diet that came from the same vivarium, in an environment and in a dark place. (Appendix 1)
- 3 kilos of purple prickly pear
- Blender
- Aluminum

Laboratory materials

- Bisturí
- Test tube
- Decanting equipment
- Test tubes
- Beakers of 1000 ml, 400 ml and 600 ml.
- Glass funnel
- Kitchen
- Petri dish
- Filter paper
- Graduated pipette
- Scale
- Glass shaker
- Electric kitchen
- Alcohol at 96º
- Distilled water
- 50ml amber bottles
- 3 and 2 liter amber bottles
- Flask
- Wire mesh

- Morris Maze

PREPARATION OF THE HYDROALCOHOLIC EXTRACT

Separate pulp and peel from the purple prickly pear. With the 96º alcohol, convert it to 76º, acquiring a hydroalcohol, with the alcohol at 70º and liquefy pulp on one side and peel on the other. Place the extract in the two amber bottles, let it rest and see the separation between sediment and precipitate. Add twice the amount of alcohol to the sediment and let it rest for 5 days with shaking every 12 hours and protected from sunlight, then apply filtration with Whattman No. 40 paper, with beaker bottles, evaporate the rest of the alcohol, decant for 1 day. and finally obtain the metabolites. The modified methodology used by Herrera et all in 2015 was used for both pulp and peel. [12]

ADMINISTRATION OF THE HYDROALCOHOLIC EXTRACT

The dose to be administered to each rat was calculated, where in the pulp extract with a concentration of 223.4 mg/dl at a dose of 60 mg every 12 hours for 8 days. And from the peel extract with a concentration of 730 mg/dl at a dose of 180 mg every 12 hours for 6 days.

DEPRESSION INDUCTION

A rat is placed in a tank of water where it is made opaque with milk or some non-toxic substance, in this case cornstarch, so that it cannot stand at the bottom and has to swim to breathe. The test is carried out over two days: a first 15-minute session and another 5-minute session the next day at the same time. In the two sessions, the times that the rodent spends performing 4 different behaviors (swimming, climbing on the walls of the cylinder, diving and immobility) are recorded. The time that the rodent spends immobile (that is, only making the movements necessary to keep its head above water) has been used as an indicator of "hopelessness" because the animal has learned that it is impossible to escape; the modified technique was used that was mentioned by Steimer et all. [13]

ANXIETY ASSESSMENT

Using the grip technique where a wire mesh was used, the rat was placed, once it was grabbed, the mesh was turned over and the time it lasted until it was released was measured. The technique was used modified that was mentioned by Ruiz et all. [14]

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SPATIAL MEMORY ASSESSMENT

The water maze was designed by R.G. Morris to evaluate spatial memory in rats [15]. It consists of a circular pool filled with water in which a platform is located that must be located by the animal, depending on whether rats or mice are used. In the traditional procedure, the water is made opaque with milk or some non-toxic substance, preventing you from seeing the platform. In the acquisition phase, the animal is introduced with its snout pointing towards the walls of the pool so that it searches for the platform for 60 or 120 seconds. If it is not found, it is placed on the platform for 20 or 30 seconds. An animal is considered to have found the platform when it remains on it for 5 or 10 seconds. The animal is then removed from the platform and allowed to rest briefly before starting the next trial. This procedure is repeated in the different trials and throughout the training, this modified technique that was mentioned by Prados et all. [16]

ANALYSIS OF RESULTS

All tables are compiled and evaluated in Excel and then in SPSS with **ANOVA and T-STUDENT** tests**.**

RESULTS

Statistical results			
Evidence	**Groups**	**Average**	**Significance**
Forced Swim	**Control**	705.750 ±44.932	0.000*
	Pulp	1260.750 ± 22.232	
	Peel	768.750 ± 46.615	
Grip Test	**Control**	6.250 ± 2.872	0.005*
	Pulp	17.000 ± 2.582	
	Peel	12.750± 4.573	
morris test	**Control**	266.000 ± 10.985	0.000*
	Pulp	116.250 ± 5.188	
	Peel	142.250± 15.283	

* There was a significant difference

** There was no significant difference

Time in seconds			
Evidence	**Groups**	**Average**	**Significance**
Forced Swim	**Control vs shell**	705.750 ±44.932 vs 768.750±46.615	0.100**
	Control vs Pulp	705.750 ±44.932 vs 1260.750 ± 22.232	0.000*
	Pulp vs. Peel	1260.750 ± 22.232 vs 768.750±46.615	0.000*
Grip Test	**Control vs shell**	6.250 ± 2.872 vs 12.750 ± 4.573	0.053**
	Control vs Pulp	6.250 ± 2.872 vs 17.000 ± 2.582	0.001*
	Pulp vs. Peel	17.000 ± 2.582 vs 6.250 ± 2.872	0.157**
morris test	**Control vs shell**	266.000± 10.985 vs 142.250 ± 15.283	0.000*
	Control vs Pulp	266.000± 10.985 vs 116.250 ± 5.188	0.000*
	Pulp vs. Peel	116.250 ± 5.188 vs 142.250 ± 15.283	0.036*

* There was a significant difference

** There was no significant difference

Comparison t-student test control vs shell: there is a statistically significant difference in the morris test, there is no difference in forced swimming and grip test

Comparison t-student test control vs pulp: there is a statistically significant difference in forced swimming, grip and morris test.

Comparison t-student pulp and peel test: it was found that there is a statistically significant difference in forced swimming and the Morris test, however there is no such difference in the grip test.

DISCUSSION

In the present work it was shown that the maceration of the pulp of the fruit of Opuntia Ficus - Indica L. Mill has antidepressant and anxiolytic effects when administered in rattus norvegicus, this way the hypothesis proposed in this research is confirmed. Examining the results shows that the peel maceration of Opuntia Ficus - Indica L. Mill had no effect on the control group of rattus norvegicus, the opposite happened with the group of rattus norvegicus to which the pulp maceration was administered. which proved to have differences with respect to the control group.

Linking the results obtained with the maceration of the pulp of the fruit of Opuntia Ficus - Indica L. Mill in the present investigation, the similarity described by the results obtained by Akkol et all is evident, thus generating a solid base that demonstrates the antidepressant and anxiolytic activity. of the plant in question.

CONCLUSIONS

The Opuntia Ficus - Indica L. Mill, commonly known as "prickly pear" is a cactus which contains a wide variety of beneficial properties for humans, corroborating in this project its anxiolytic and antidepressant effects.

The results obtained in the different tests considered in the evaluation showed us a significant difference. This is because in the

group that was administered peel, there was only a difference in spatial memory, unlike the group that received pulp, which met the 3 criteria.

RECOMMENDATIONS

If you wish to delve into further research on the anxiolytic effect of Opuntia Ficus - Indica L. Mill, it is recommended to isolate the metabolite "EtOAc", also known as ethyl ethanoate. because it has a greater amount of anxiolytic effects.

GRATITUDE

We thank the Faculty of Human Medicine of the Antenor Orrego Private University, our advisors Dr. Dan Altamirano and Dr. Karyn Olascuaga, as well as our parents, who supported us financially to be able to carry out this research. Special thanks are made to Mrs. Ori Salazar, the author's mother, for her unconditional support in being able to meet the author's personal and academic objectives. Furthermore, she motivated and promoted this research, and that thanks to this this work is published.

REFERENCES

1. Vargas V. Causas de la pérdida de memoria que no son Alzheimer [Internet]. Cuidum. 2019 [citado el 7 de julio de 2022]. Disponible en: https://www.cuidum.com/blog/perdida-de-memoria/

2. Nopal de Castilla (Opuntia ficus-indica) [Internet]. NaturaLista Mexico. [citado el 9 de julio de 2022]. Disponible en: https://www.naturalista.mx/taxa/64119-Opuntia-ficus-indica

3. Enciso Roca EC, Aguilar Felices EJ, Común Ventura PW, Tinco Jay JA. ACTIVIDAD ANTIINFLAMATORIA Y ANTIOXIDANTE DE TRES VARIEDADES DE Opuntia ficus-indica "TUNA". Rev Soc Quím Perú [Internet]. 2021 [citado el 9 de julio de 2022];87(3):207–16. Disponible en: http://www.scielo.org.pe/scielo.php?pid=S1810-634X2021000300207&script=sci_arttext

4. Akkol EK, Ilhan M, Karpuz B, Genç Y, Sobarzo-Sánchez E. Sedative and Anxiolytic Activities of Opuntia ficus indica (L.) Mill.: An Experimental Assessment in Mice. Molecules [Internet]. 2020 [citado 5 de julio de 2022];. Disponible en: https://pubmed.ncbi.nlm.nih.gov/32316321/

5. Abbas EY, Ezzat MI, El Hefnawy HM, Abdel-Sattar E. An overview and update on the chemical composition and potential health benefits of Opuntia ficus-indica (L.) Miller. J Food Biochem [Internet]. 2022 [citado 5 de julio de 2022]. Available in: http://dx.doi.org/10.1111/jfbc.14310

6. Silva MA, Albuquerque TG, Pereira P, Ramalho R, Vicente F, Oliveira MBPP, et al. Opuntia ficus-indica (L.) Mill.: A multi-benefit potential to be exploited. Molecules [Internet]. 2021 [citado 5 de julio de 2022];. Disponible en: https://www.mdpi.com/1420-3049/26/4/951

7. Mayo Clinic - Mayo Clinic [Internet]. Depresión (trastorno depresivo mayor) - Síntomas y causas - Mayo Clinic; 2021 [consultado el 8 de julio de 2022]. Disponible en: https://www.mayoclinic.org/es-es/diseases-conditions/depression/symptoms-causes/syc-20356007#:~:text=Sentimientos%20de%20tristeza,%20ganas%20de,los%20pasatiempos%20o%20los%20deportes

8. Mayo Clinic - Mayo Clinic [Internet]. Trastornos de ansiedad - Diagnóstico y tratamiento - Mayo Clinic; 2021 [consultado el 6 de julio de 2022]. Disponible en: https://www.mayoclinic.org/es-es/diseases-conditions/anxiety/diagnosis-treatment/drc-20350967

9. DSpace Home [Internet]. Evaluación de la penca de tuna (Opuntia ficus-indica (L.) Mill) como coagulante natural alternativo para la purificación de muestras de agua provenientes del canal de San Fernando, Nuevo Imperial - Cañete; [consultado el 6 de julio de 2022]. Disponible en: https://repositorio.cientifica.edu.pe/handle/20.500.12805/1405?show=full

10. SciELO - Scientific Electronic Library Online [Internet]. Actividad antiinflamatoria y antioxidante de tres variedades de Opuntia ficus-indica "Tuna"; [consultado el 7 de julio de 2022]. Disponible en: http://www.scielo.org.pe/scielo.php?pid=S1810-634X2021000300207&script=sci_arttext

11. RiuNet repositorio UPV [Internet]. EFECTO DEL MÉTODO DE EXTRACCIÓN EN LAS CARACTERÍSTICAS QUÍMICAS Y FÍSICAS DEL MUCÍLAGO DEL NOPAL (Opuntia ficus-indica) Y ESTUDIO DE SU APLICACIÓN COMO RECUBRIMIENTO COMESTIBLE; [consultado el 8 de julio de 2022]. Disponible en: https://riunet.upv.es/bitstream/handle/10251/3794/tesisUPV2920.pdf

12. Herrera-Calderon Oscar, Chinchay-Salazar Rosa, Palomino-Ormeño Estela, Arango-Valencia Evelyn, Arroyo Jorge. Efecto hipoglucemiante del extracto etanólico de Geranium ruizii Hieron. (pasuchaca) en la hiperglucemia inducida por aloxano en ratas. An. Fac. med. [Internet]. 2015 Abr [citado 2022 Jul 10] ; 76(2): 117-122. Disponible en: http://www.scielo.org.pe/scielo.php?script=sci_arttext&pid=S1025-55832015000300002&lng=es. http://dx.doi.org/dx.doi.org/10.15381/anales.v76i2.11135

13. Steimer T, la Fleur S, Schulz PE. Neuroendocrine correlates of emotional reactivity and coping in male rats from the Roman high (RHA/Verh)- and low (RLA/Verh)-avoidance lines. Behav Genet. 1997 Nov;27(6):503-12

14. Ruiz P, Calliari A, Genovese P, Pautassi R. La memoria espacial, y los niveles de BDNF en el hipocampo, disminuyen en ratas adolescentes deprimidas farmacológicamente con reserpina. Rev psicol [Internet]. 2021 [citado el 10 de julio de 2022];39(1):35–57. Disponible en: http://www.scielo.org.pe/scielo.php?pid=S0254-92472021000100035&script=sci_arttext&tlng=pt

15. Morris R. Developments of a water-maze procedure for studying spatial learning in the rat. J Neurosci Methods [Internet]. 1984;11(1):47–60. Disponible en: http://dx.doi.org/10.1016/0165-0270(84)90007-4

16. Prados J, Trobalon JB. Locating an invisible goal in a water maze requires at least two landmarks. Psychobiology (Austin, Tex) [Internet]. 1998;26(1):42–8. Disponible en: http://dx.doi.org/10.3758/bf03330589