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TO EVALUATE THE ANTIDEPRESSANT EFFECT OF APPLE AND ORANGE PULP IN MICE

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ABSTRACT

Brain recession is one of the most extensive, persistant diseases determining temper, view, physical health and actions of a human being.The following research was done in order to investigate the anti-anxiety effects of severe and persistant use of apple and orange pulp in group of animals for experiment. We administered the juice from the fresh fruits of Malus domestica and citrus sinensis (1 ml and 2 ml per kilogram of weight). Dibenzoazepine (10 mg per kilogram per oral). Three series of animals were prepared, and one animal was in each series. Drugs and vehicles were administered before 60 min of experiments in acute study. Drugs and vehicles were provided in chronic study prior 60 mins for 15 days and on the fifteenth day last dose was administered. FST and TST for evaluation of anti-anxiety effects were done. **(1)**

INTRODUCTION:
Determined feeling of rejection and lack of interest in things and activities you would normally enjoy is called Depression. This condition may initiate problem in thought process, memorizing things and events, eat and sleep habits.It is okay to be mourn on a tough situation in your life, like depreciating career or losing a loved one. However, depression is unique in that it occurs nearly daily for a symptoms. **(2)(13)(14)(16)(17)**

Depression Types:

Among all types of depressions Clinical depression is the most prevalent type of depression. Presence of major depressive disorder means a person is feeling dejected, or dishearted for many days more than 15 days. Moreover, issues in sleeping habits, loss of appetite are indictive of seriousness of depression.
The symptoms of persistant depressive disorder are mild but may persist for more than 2 years. It is denoted by PDD. **(18)**
Disruptive mood dysregulation disorder (DMDD): DMDD is abbreviated by disruptive mood disorderconsequently leads to chronic irritation, mood swings and short temperament in children appering at the age of ten years
With PMDD (premenstrual dysphoric disorder) diagnosed with premenstrual syndrome (PMS) and swings in mood, such as irritation, stress or feeling low. Such indications may resolve soon but will badly effect the quality of life.
Depressive disorder due to another medical condition: Certain medical problems may initiate abnormality in body leading to dejection and depression. Such as hypothyroidism, heart disease, Parkinson's disease and cancer.
Medicines For Depression:
Antidepressants:
Anti-depressants are drugs need prescription that may cure dejection like illnesses such as stress and OCD. There exist many classes of anti-depressants. **(4) (15) (19)**
Antidepressants Types:
Following are various kinds (classes) of antidepressants, including:

1. Selective serotonin reuptake inhibitors (SSRIs):
- They are frequently prescribed category of antidepressant.

2. Serotonin/norepinephrine reuptake inhibitors (SNRIs)
3. Tricyclic antidepressants (TCAs):
- TCAs are the long known generation of anti-depressants usually used for treating resistant type of depression and anxiety because there are higher rates of complications.

4. Atypical antidepressants
5. Serotonin modulators

6. Monoamine oxidase inhibitors (MAOIs):
- These render most senior of the antidepressants. Although very effective, they're usually held in reserve for anxiety and treatment-resistant depression. The reason is that it's necessary to make dietary changes to prevent hypertensive reactions due to interactions with the amino acid tyramine, which is found in large amounts in certain foods.

7. N-methyl-D-aspartate (NMDA) antagonists:
- There are also a number of types of medications (and brands) within each category.

(19) (20) Apple origination
Apple is significant fruit crop fertilized in temperate regions like Asia and Europe (Janick et al., 1996). The genus of apple is Malus. Fertilized apple is a consequence of hybridization. The combination of Malus x domestica is registered as its biological name (Korban and Skirvin, 1984).
(10) (11)

Common name

In recent time, Malus pumila and Malus domestica are significant names, by far M. pumila is quite historic but M. domestica is

originated in the 21st century among western world.

Traditional uses.

Traditionally, they have been used to treat digestive issues like diarrhea and constipation, as well as for their cleansing and cooling properties in inflammatory conditions.

- **Apple Tea:** A drink made with apples and boiling water was used for colic, digestive problems, and colds.
- **Digestive Issues:** Unripe apples were used for diarrhea, and ripe apples for constipation.
- **Cleansing and Cooling:** Apples were traditionally used to cleanse the body and soothe inflammation related to conditions like indigestion, arthritis, and gout.
- **Desserts:** They are a key ingredient in pies, crumbles, cakes, and other baked goods.
- **Beverages**: Apples are processed into juice, cider (alcoholic and nonalcoholic), and even wine.
- **Preserves**: Apples can be made into jams, jellies, applesauce, and apple butter.
- **Cooking**: They are used in savory dishes, such as with pork or sausage.
- : Historically, apples were dried for preservation.
- **Invalid Food**: Stewed apple was considered a nourishing food for invalids and children.

Pharmacological Activities:

- **Anti-obesity:** Eating apples is associated with a decreased risk of obesity, potentially through mechanisms such as inhibition of enzymes and alterations to metabolic pathways.
- **Cardiovascular Health:** Apple consumption is also associated with cardiovascular disease risk reduction through mechanisms such as fiber, antioxidants, and other bioactive components.
- **Antioxidant**: Apples contain large amounts of antioxidants like flavonoids and phenolic acids which neutralize harmful free radicals in the body.
- **Anticancer**: Studies suggest apples may help to suppress cancer cell growth due to the active ingredients such as triterpenoids.
- **Enzyme Inhibitor:** Apples have substances capable of inhibiting certain enzymes, including those related to carbohydrate digestion, which could potentially help manage blood glucose levels.

Antimicrobial:Some apple extracts have antimicrobial effects on certain pathogens.

Anti-inflammatory: Some apple compounds (i.e. phloretin) have also shown anti inflammatory properties**. (12)**

INTRODUCTION TO ORANGES:

The juicy orange (Citrus sinensis (L.) Osbeck), which accounts for nearly half of the global orange production, is one of the most important members of the large Citrus family. This family is cultivated in numerous tropical and subtropical areas around the world that are roughly located along the 35 degree centigrade at north and 35 degree centigrade at south parallels. In reference with 2020 FAO data, the sweet orange is grown around the globe at about 3.8 million
hectares, producing 75.5 million tons of equivalent fruit. The top producers of oranges are Brazil, India, and China, with outputs of 16 million tons seven million tons and 9.8 million tons separately. The United States comes next with 4.8 Mt (FAOSTAT 2020). Huanglongbing (HLB), a bacterial disease, has inexplicably caused a decline in the production of high-quality oranges in Brazil and the United States over the past few years. One of the most serious threats to citrus plants is the infection brought on by the phloem-limited Gram-negative bacterium “Candidatus Liberibacter spp.” Although C. Liberibacter was reported for a long time in China, its origin and early spread are unknown. The HLB disease initially appeared on the mainland of America less than 20 years ago. After being introduced in Sao Paulo, Brazil, in 2004, it was first released in Florida in 2005, where it caused significant economic harm. Despite the discovery of Diaphorina citri in Israel, one of the two reported transporters of this disease (Trioza erytreae) in Portugal & Spain, HLB is now being proclaimed In the Mare Magnum nations.

Using mice modeled after chronic

unpredictable mild stress (CUMS), the current study examined the antidepressant-like properties of navel orange [Citrus sinensis (L.) Osbeck] essential oil (OEO) and its primary ingredients, as well as potential mechanisms. The findings showed that inhaling OEO considerably improved the depression-like symptoms of CUMS mice, including lessened immobility time, dyslipidemia, and reduced body weight, sucrose preference, curiosity, and mobility. Limonene, the compound that constituted the majority of the mice's brains after breathing the OEO, was not quickly metabolized there. Furthermore, limonene inhalation effectively reversed the depressive behavior caused by CUMS, the hyperactivity of the hypothalamic pituitary adrenal axis, the reduction in monoamine neurotransmitter levels, and the degeneration of brain isolated neuro-trophic entity and its receptors effects in the hippocampus. As a result, the study suggests that limonene's antidepressant effects are related to improvements in the neuroendocrine, neurotrophic, and monoaminergic systems. **(3)**

Combination of apple and orange juice:

Citrus fruits and citrus drinks, in particular, can have an impact on drug metabolism. It has been noted that the juices of grapefruits, oranges, apples, cranberries, pomegranates, purple grapes, and pomelos interact. However, it is still often hard to evaluate whether a particular product of fruit can interact, even with extensive research in this area.

This is caused by environmental factors such as the climate in which the fruit is grown and differences between fruit varieties. The chemical makeup of citrus juices can also be changed by commercial juicing techniques. For example, mechanical pressing improves the interaction between the peel and the fruit's pith, which has a significantly higher amount of naringin than the juice vesicles. Bergamottin and 6',7 '-dihydroxybergamottin are furanocoumarins, while naringin and hesperidin are flavonoids, which are examples of the pharmacologically active substances present in fruit drinks.

Juice concentration may also have an impact on the chemicals. Which substances interact with drugs is unknown. Grape-fruit, orange and apple juice have potential to inhibit organic aniontransport mechanism of polypeptides OATPs, which are responsible for transporting protein across membrane that helps in the absorption of compounds across barriers such the gastrointestinal tract. The impacted medications will be absorbed less efficiently as a consequence of this inhibition.

Requirements:

Apple
Orange
Tap water
Knife
Electric juicer blender machine
Strainer / filter paper
Beaker / jars
Ph meter
Gavage needle
Mice

Method:

Wash the apples thoroughly to remove any dirt, bacteria, or chemical residues. They are cut into tiny pieces to make it easier to extract the juice. When the apple slices are processed in a juicer, the fruit is macerated and juice is generated. Alternatively, the oranges can be blended in a blender, and then the mixture can be strained through cheesecloth or a fine-mesh filter to remove the pulp and sediment from the juice. The extracted juice can become clearer after centrifugation removes any leftover particles.

The segments of the orange are ready for juicing once the skins have been gently stripped off. The oranges are then juiced using an electric or manual juicer, which removes the juice from the skin and pulp. To remove any pulp and sediment, the juice is filtered in cheesecloth or a filter. Like apple juice, orange juice can be centrifuged to achieve greater clarity. Both juices undergo quality control

procedures after extraction, including pH testing to assess acidity and microbial analysis to confirm they are contaminant-free.

Source of apple and orange:

To assess the antidepressant qualities of apple and orange juice, we obtained half a kilogram of apples and half a kilogram of oranges from a local shop. The juices are then put in clean jars and either refrigerated or frozen to maintain their quality for future analysis and testing.

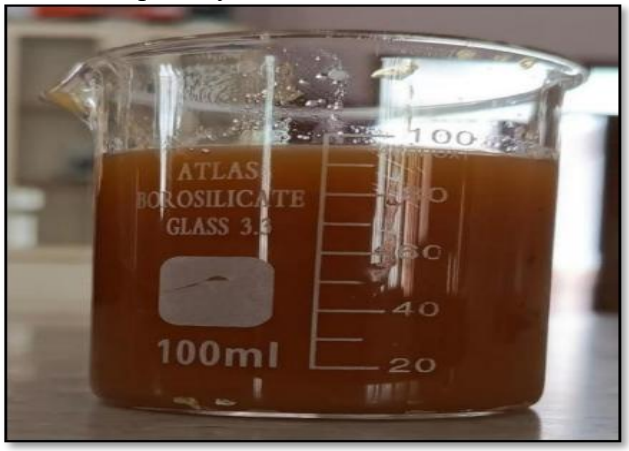
Chemicals in Apple and Oranges due to which depression may be decreased:

There are various chemicals in these citrus fruits, some of them are below:

- Carbohydrates
- Dietary fibers
- Vitamin C
- Potassium
- Phytochemicals

Method to Prepare Apple and Orange Juice

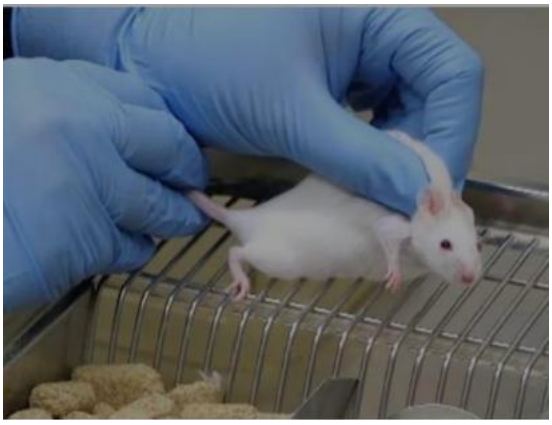
- First, take fresh apples and oranges to make juice
- Wash the apples and oranges with warm water.
- After washing peel the apples and oranges, cut them into small pieces, and remove the seeds and core.set the blender or juicer properly and plug it in. Place the glass first, add apple pieces into the chute. Use the pusher to press them gently.
- Collect the juice and strain it.
- Use same step for orange juice.
- After preparing the juices mix both juices in same quantity.



First, we took six mice and divided them into three groups, each group containing two mice. Then we induced depression in every group using the cage tilt method as a part of the Chronic Mild Stress (CMS) protocol.

CAGE TILT METHOD

In this method, mice were placed in cages tilted at an angle of approximately 45 degrees for several hours daily, typically ranging from 6 to 12 hours, over a period of 5 days. The tilted position disrupted their normal environment and caused stress. This stressor can contribute to inducing depression-like behaviors in mice, such as changes in behavior, sleep, or sucrose preference, which are used to model human depression.



Drug Administration:

In acute study, drugs and vehicle was provided 60 minutes before test. In the chronic study drugs and vehicles was provided for 15 days and final dose was adminitered on the 15 day. FST and TST were chosen in order to evaluate antidepressant activity.

FST:

The forced swim test is a rodent test for screening of antidepressant drugs, antidepressant activity of new compounds, and behavioral effects of experimental manipulations that produce or prevent depression-like syndromes. Mice are placed in a transparent tank that cannot be escaped which contains water and tested for their escape

related mobility behavior.

The forced swim test is a simple, reproducible procedure that can be implemented with limited special instrument. Forced swim test should be properly conducted with some procedural details, and some stress for mice should be avoided. Here in the protocol and accompanying video, we

describe how to perform the mouse version of this test and focus on what could be the pitfalls affecting the interpretation of the results and how to get around them**. (5) (7)**

each group, take readings from the recorded video to measure their mobility and immobility time periods. **. (5) (7)**

TST: The tail-suspension test (TST) is a commonly used test for the analysis of potent anti- depressant drugs. It is a rapid, low-cost, prognostic, and high output analysis for the acute

behavioral actions of anti-depressants. The test is based on the fact that when mice are subjected to the short-term, inescapable stress of being suspended by their tail, they will enter an immobile posture. Antidepressant treatment, with various mechanisms of action, decreases the time spent immobile by increasing escape-oriented behavior.

Researchers frequently employ the tail-suspension test (TST) to screen potential antidepressant drugs. The test provides quick cost-effective predictions and handles many samples to determine immediate antidepressant behavioral responses. The test operates on the idea that mice exposed to the short-term, unavoidable stress of tail suspension develop an immobile posture. Various antidepressant medications lead to a reduction in immobility duration for mice through the enhancement of escape-oriented actions regardless of their main mechanism. **(6) (8)**

PROCEDURE:

Place the camera in position. The optimal distance for the camera placement should be the shortest possible to ensure maximum animal resolution. Prepare tape fragments for the session by cutting them and applying necessary

PROCEDURE:

- Male and female mice, were kept in groups of 3 per cage (33 cm × 40 cm × 18 cm) under controlled lighting (12 h light/dark cycle with lights on at 07:00 am) and temperature (22 ± 2 C) conditions with free access to food and water, except during the behavioral test.
- First, use a transparent cylindrical container (height: 18.5 cm, diameter: 12.5 cm) for mice swimming.
- Fill the container with water at 25°C to a depth of 13.5 cm to prevent the mice from touching the bottom.
- Set the camera in position to record the test, then gently place one mouse into the water-filled cylinder and let it swim for 5 minutes.
- The same is done to all mice in the experimental and control groups to produce consistent results.
- After performing the test on every mouse in

marking

- The experiment is well controlled on a wooden or metal shelf above the floor about 50cm. The adhesive tape is engaged to hang the mouse by the tail. A layer of a soft material is placed below to cushion in case of any fall.
- Handle the mouse carefully, and placed the tap close to the tip of its tail (1–2 cm from the tip). The mouse is suspended in air by attaching the tape to a hook or bar. The height of suspended mouse above the surface should b approximately
- Suspend the mouse by its tail with the help of tape. Throughout this time, the animal first attempts to free itself, illustrated active movement, and ultimately becomes motionless. The behavior is recorded for analysis.
- The time of immobility is recorded, especially for the last 4 minutes of the test (the first 2 minutes are an acclimatization phase). Immobility is the absence of any movement of limbs or body except those needed for balancing and breathing.
- Following the test, the mouse was carefully removed from suspension, and the tape slowly peeled away from the tail. The mouse was returned to its home cage and was observed for signs of stress or injury.
- The same is done to all mice in the experimental and control groups to produce consistent results. **(6) (8)**

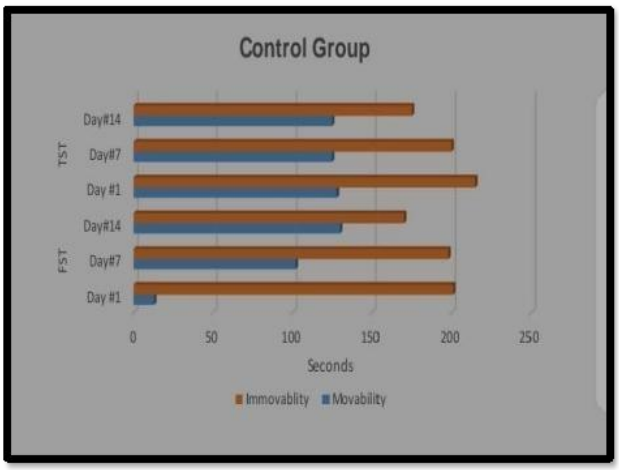
Conclusion:

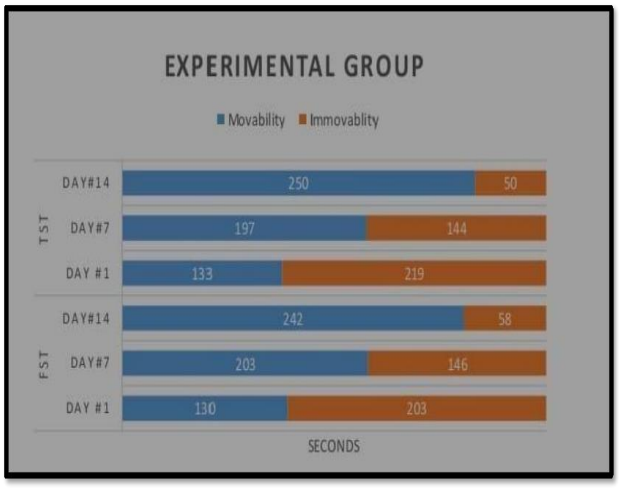
The findings of this study show that orange as well as apple fruit juice can aid people with depression in the modern world.

Result:

When compared to depression control, the dosage of fruit juice demonstrated a dose-dependent significant decrease in depression and an increase in physiological parameters such as dopamine as well as drop mono amino oxidase. The outcome had similarities with that of the common medication imipramine.

Graphical Results:





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