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DYNAMIC EVALUATION OF CUCUMIS MELO ON NEURODEGENERATIVE MODEL OF RATS

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ABSTRACT

Objectives: *Neurodegenerative disorders (NDDs) are the most concerned health issues, because of high percentage of mortality. Elderly patients mostly suffer from these diseases. Neurodegenerative disorders cause progressive damage to nervous system. Parkinson's disease, depression, Huntington's disease and Alzheimer's disease are the most prevalent neurodegenerative disorders.*

Materials and methods: *Natural products have shown significant effects in the treatment of such neuronal disorders. These natural products have improved neuronal cellular survival, growth, differentiation and activities in in-vivo/ invitro experimental models.*

Cucumis melo (Melon) is one of the most popular crops worldwide which belongs to the Cucurbitaceae family. Many studies were performed on different plants of this family due to their nutritional, medicinal and pharmacological values. It also shows anti-ulcer, analgesic, anti-inflammatory, anti-diabetic and diuretic activities.

This study is based on evaluating the neuronal activities of natural seed extracts of Cucumis melo in in-vivo/ invitro experimental models.

The ethanolic extracts of Cucumis melo seeds was investigated for evaluating the neuronal effects in Wistar albino rats and albino mice. Experiments were performed to analyze the effects of the extracts on genetic marker (IL-6) involved in neuromodulation. In-vitro neuronal activity was carried out through anti-oxidant scavenging activity method, cell viability test, anti-microbial activity and anti-inflammatory activity and ELISA on neonatal hippocampal cells. Results were calculated by means of ANOVA (One way, Tukey's - Post hoc test)

Results: *Results of the study have demonstrated the extract have shown significant reduction in neurodegeneration and neuroinflammation. It has also provided significant reduction in in-vitro free radical scavenging activity and enhanced neuronal cell proliferation.*

Conclusion: *This study suggested that the extract had shown an important consideration about the pharmacological effects of Cucumis melo as an alternative therapy to conventional drugs for treatment of neurological disorders.*

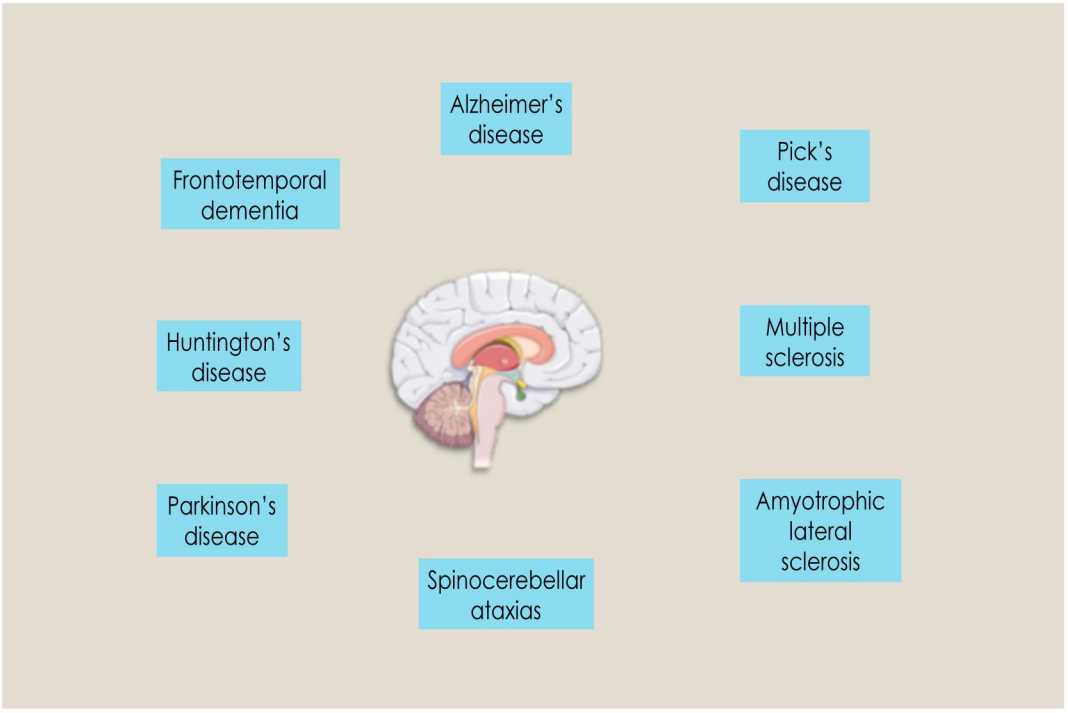
Keywords*: Cucumis melo, Neurological disorders, Neurodegeneration, Neuro-inflammation*

INTRODUCTION

Neuro-inflammatory

Neuro-inflammation is the term used to describe inflammatory conditions which are generated in the brain and spinal cord. Neuro-inflammation plays a dynamic role in development of neurodegenerative disorders for instance Parkinson's disease (PD), Alzheimer's disease (AD), traumatic brain injury (TBI) and Amyotrophic lateral sclerosis (ALS) as in fig 1.

Figure 1. Most common types of neurodegenerative diseases.

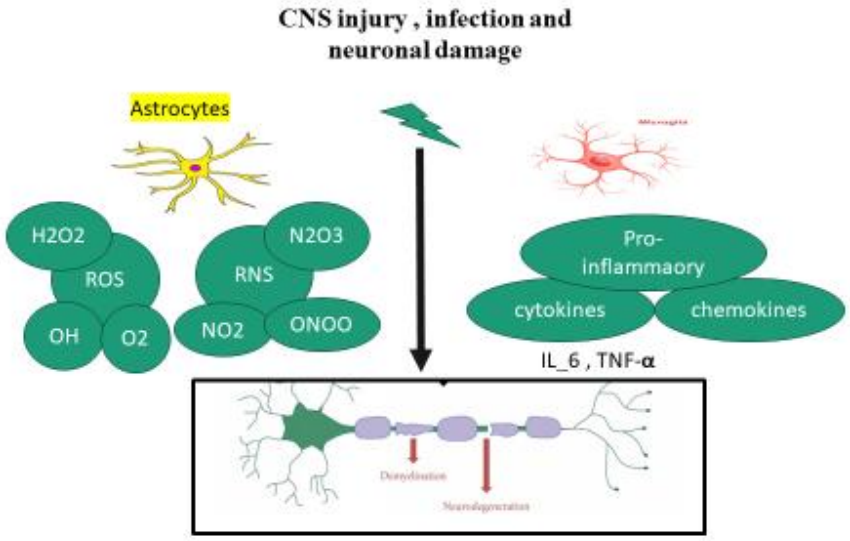


The generation of cytokines, chemokines, reactive oxygen species, and secondary messengers mediates this inflammation. Endothelial cells, peripherally derived immune cells, and resident CNS microglial cells and astrocytes, all generate these inflammatory mediators. These neuro-inflammatory reactions have severe immunological, physiological, metabolic, and psychological effects [(1)].

Proinflammatory cytokines including interleukin-1 (IL-1), interleukin-6 (IL-6), is an eminent in the distressed regions of brain because of the ongoing activation of microglia and astrocytes. Elevated levels of interleukins have been linked to the development and progression of neurodegenerative diseases.

The cytokine interleukin-6 (IL-6) has a major impact on nerve cell activity and is essential for neuroinflammation. Moreover, IL-6 is known as a potent biomarker of neurodegenerative illnesses as elevated levels of the protein have been regularly linked to a number of these conditions [(2)]. Numerous cell types, including T cells, B cells, monocytes, fibroblasts, and endothelial cells, produce and release IL-6. In healthy circumstances, skeletal muscle and adipocytes can also generate IL-6. In chronic diseases, such as tumors and persistent intracellular infections, IL-6 plays a crucial role in triggering both mucosal humoral responses against infection and cellular immune responses to afflicted cells. It also acts as an inducer of acute phase reactions [(3)].

Figure 2. Representation of the CNS cell mediated demyelination and neurodegeneration due to release of Reactive oxygen species and proinflammatory cytokines. Neuroinflammation through these factors promotes demyelination and axonal damage, finally leading to neurodegeneration.



The renowned neurodegenerative diseases such as Alzheimer's disease, involves neuroinflammation which cause changes in brain structure and functions. It starts with minor cognitive impairment and progresses to serious brain damage [4]. Alzheimer disease is the common type of dementia and nearly fifty-five million human beings are encountering with different dementias. This figure will be almost doubled every twenty years, reaching seventy-eight million in 2030 and 139 million in 2050 (global Alzheimer report 2022) [5]. Another neurodegenerative disease influencing millions of individuals is Parkinson's disease, which results from the disruption with in the nerve cells in substantial nigra, a dopamine rich center. The pathogenesis involves inadequate protein deposition and lack in their clearance [6]. There's no such treatment for Parkinson's; however, drug treatments are available to improve the symptoms. Dopamine agonists (levodopa and carbidopa) and monoamine oxidase inhibitors (selegiline and phenelzine) are typically suggested drugs for the treatment. Depression is a common illness which adversely affects the routine behavior. The symptoms are emotions of unhappiness and lack of physical activities. The disease involves low levels of monoamines including dopamine, serotonin, epinephrine and norepinephrine [7].

Natural drugs in the treatment of Neuroinflammatory disorders

Neurodegenerative disorders can be treated with both traditional drug treatments and natural based products. *Cucumis melo* (C. melo, melon) is one of the most popular garden plants around the world and belongs to the Cucurbitaceae family. Several researches have been done on different plants of this family due to their nutritional, medicinal, ethnoveterinary and ethnomedicinal values [8]. The fruits of melon plant are used as first aid agents in treatment of abrasion and burns [9]. The other parts of plant are used for digestive, antitussive [10] and diuretic [11] purposes.

Materials and Methods

Plant material collection and authentication:

The seeds of *Cucumis melo* was purchased from the local herbal stores of Karachi (Pakistan) in 2021. The seeds were deposited for identification in the botanical department of PCSIR and provided with voucher

specimen numbers FMRC/Herb. /0128/23. The seeds were first washed, cleaned, and dried at room temperature before being grounded into powder at a low temperature.

Preparation of extract

The ethanolic extract were prepared by simple extraction technique. The seeds of *Cucumis melo* (1000g) washed, then shade dried and indelicately powdered and extracted with the solvent 70% ethanol for 2 weeks at room temperature. Extract of seeds were dried by using a Soxhlet apparatus. Rotary vacuum (Rota vapor) was used to evaporate the solvent at 50°C temperature and 30 rpm. For subsequent drying the extract was placed in drying hood. The residual extract was stored at 2-8 °C till further use.

Drugs and chemicals

All chemicals used were of an analytical grade and purchased from different companies. These include drug Donepezil (Atco), 2, 2-diphenyl-11picrylhydrazyl (Sigma Aldrich) Ascorbic acid (BDH Laboratory Supplies, England) and Dimethyl sulfoxide (Sigma Aldrich).

In vitro testing of Protein denaturation assay on egg albumin:

Protein denaturation analysis is an in-vitro anti-inflammatory activity of the compounds. The albumin was extracted from fresh hen's egg. The test tubes were first filled with egg albumin and centrifuged it for 3-4 minutes at 5000 rpm, then supernatant was collected in the test tubes. After the collection of proteins from egg, prepared the reagent mixture at different concentrations (10, 20 and 50 ug/ml) of the both extracts and a standard drug diclofenac (10, 20 and 50 ug/ml).

Incubated at 37ºC for 15 minutes after mixing it gently and then kept in water bath at 70 ºC for 5 minutes. The mixture was then cold and plate wells of 96 were observed on multiskan at 620 nm. The percentage inhibition of anti-inflammatory activity was estimated by using the formula:

% inhibition= Absorbance control – Absorbance sample / Absorbance control *100

Anti – oxidant analysis:

Qualitative evaluation of DPPH free radical scavenging activity:

DPPH scavenging test is a delicate approach to analyze anti-oxidant activity of a particular compound or plant extract. The inhibition activity was compared with the vitamin C (Ascorbic acid). The concentrations of the plant extracts used in this activity were 10, 20, 50 µg/ml. DPPH solution (0.1 Mm, 2 ml) was mixed with 1.5ml of different serial diluted concentrations (10, 20, 50 µg/ml) of both extracts. The mixture was incubated at temperature for 20 min in dark. The reduction of the free radical was measured by reading the absorbance at 517 nm by a UV- Spectrophotometer. Solution only having DPPH with ethanol was considered as control and the solution with ascorbic acid was taken as positive control. The investigation was replicated twice. The percentage inhibitory activity and IC50, of every sample were calculated. The capability of scavenging DPPH radicals was calculated using the following equation.

$$\% \text{ Scavenging} = [(AbsC - AbsT) / AbsC] \times$$

Wherein,

AbsC= Absorbance of control

AbsT = Absorbance of Extract (reaction mixture)

Cell Proliferative assay:

The MTT 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide assay was used to determine cell proliferation and viability through cellular metabolic activity. This colorimetric assay is based on live cells activity for converting yellow tetrazolium salt to purple formazan crystals

After 90% confluence, the cells were trypsinized and incubated at a concentration of 1 × 105 cells/ml in 96 well plate. Treatment was completed with various concentrations of given extract of Cucumis melo and Cucurbita pepo l. (5,10 and 50 ug/ml) for 24 and 48 hrs. MTT dye (10 µl; final concentration 0.5 mg/ml) was

added to each well and then cells were incubated at 37° C for 3 hrs. The MTT-formazan product was dissolved in DMSO and absorbance was measured at 570 nm using a spectrophotometer (Shimadzu). The assay was repeated in triplicates for confirmation of results.
The percentage inhibition and IC_{50} was calculated by the following formula;
Percentage mobile inhibition= (Atest- Ablank) /Acontrol- Ablank) * one hundred
Wherein,
ATest comprising of cellular media plus drug,
Ablank containing handiest media plus drug.
Acontrol containing cellular media plus vehicle.
IC50 = (X2 - X1) * (50 - Y1) / (Y2 - Y1) + X1
Wherein,
X1: better concentration is used
X2: decrease awareness is used
Y1: suggest percentage of viable cells at higher awareness (X1) used
Y2: suggest percent of viable cells at decrease awareness (X2)

Determination of antimicrobial activity:
Broth dilution method and agar well diffusion was used for the determination of antimicrobial activity of the extracts .

Broth dilution method and Diffusion method by agar
Cultures of bacteria against E. coli was obtained from microbiology lab of Jinnah university for women. The broth of E. coli was taken and strain it into the agar plates carefully besides the fire flame. Different concentrations (5,10,20 and 50 ug/ml) of melon, pumpkin and combination of both were pipetted into the agar plates. The plates were then incubated for 24 hours at 37 °C. The antibacterial activity against E.coli was quantified by determining the zone of growth inhibition and number of colonies present around the samples.

ELISA (Enzyme-linked immunosorbent assay)
Protein IL-6 levels can be readily measured in serum, plasma, and other areas using commercially available enzyme-linked immunosorbent assay (ELISA) kits. The evaluation was done on serum IL-6 levels by using a sandwich enzyme immunoassay ELISA kit (SEA011Ra). Animals were anesthetized and blood was drawn through cardiac puncture. Then serum was separated by centrifugation and then frozen at-40°C till assays were performed. ELISA kit contains a microplate which were pre-coated with IL-6 specific antibodies. Freshly prepared dilutions of standard and sample were added to the microplate wells along with a biotin-conjugated antibody specific for IL-6. This results in the binding of IL-6, present in the sample and standard to the IL-6 antibody. Then avid in conjugated to C (HRP) was pipetted to the wells and incubated, followed by the addition of TMB (tetramethylbenzidine) substrate. Only those wells of microplate that contains biotin conjugated antibody, enzyme conjugated avidin, and IL-6 showed a color change. Finally, a solution of sulphuric acid was added to cease the reaction, and the change in color was estimated through a spectrophotometer at a wavelength of 450 nm.

Results
Phytochemical analysis:
Qualitative analysis of *Cucumis melo* extract:
The phytochemical components of ethanolic extract of *C. melo* seeds were tested and are summarized in the (Table 1). All the given results show presence of broad range of phytochemical constituents like alkaloids, glycosides, terpenoids, flavonoids, phenols, tannins and coumarin. While carbohydrates, proteins, steroids, sterols, saponins and quinones are found to be absent in *C. melo* seeds. These results indicate medicinal importance of *C. melo* seeds in treatment of neurological disorders.

Table 1. Qualitative photochemical screening of C. melo seeds extract

NO	Test	Observation	Results Presence (+ve)/ Absence (-ve)
1	Fehling's Test	Brick red precipitate	+ve
2	Benedict's Test	Greenish color appears	-ve
3	Molisch's Test	Brick red ring appear	-ve
4	Iodine test	Orange color	-ve
5	Ninhydrin Test	Orange color	-ve
6	Alkaline Reagent Test (Flavonoids)	Dirty white color	+ve
7	Test for Saponins	White color no foam	-ve
8	Test for Phenols and Tannins	Blue-green coloration	+ve
9	Test for Steroids	Black-green color	-ve
10	Test for Quinones	Yellow lemon coloration	-ve
11	Salkowski's Test (Glycoside)	Reddish brown	+ve
12	Test for Coumarin	Yellow	+ve
13	Test for Terpenoids	Reddish – brown	+ve
14	Test for Sterol	Black color	-ve
15	Test for Alkaloids	No precipitate	-ve

***In-vitro* protein denaturation analysis on egg albumin:**

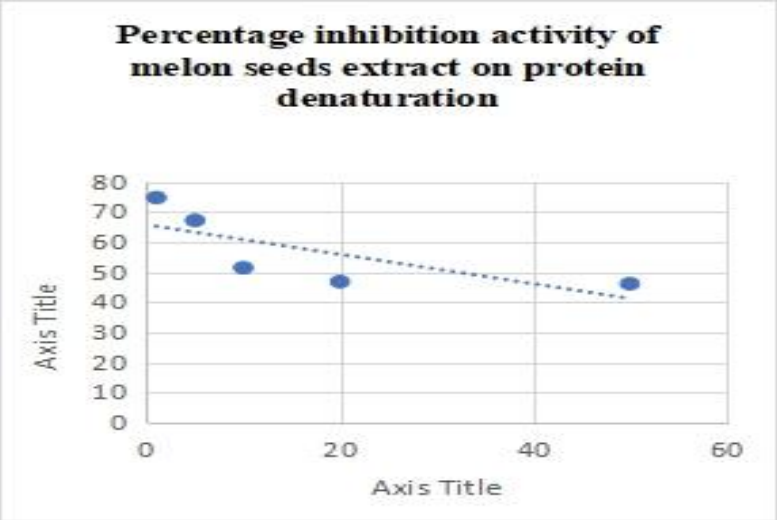
Protein denaturation assay (% inhibition) of the melon seeds extract:

Protein denaturation assay was performed on egg albumin for evaluating melon seeds extract at different concentrations and percentage inhibition was calculated. The melon extract has shown potential ability to inhibit the protein denaturation at lower concentration when compared to the higher concentrations and the maximal activity was observed as 74.815 % at 1 ug/ml.

Table 2. Percentage inhibition capability of melon seeds extract

Concentration ug/ml	Percentage inhibition activity of melon
1	74.815
5	67.224
10	51.468
20	46.854
50	46.165

Figure 3. Percentage scavenging capability of melon seeds extract on protein denaturation



***In-vitro* anti-oxidant activity**

DPPH (2,2-diphenyl-1-picrylhydrazyl) assay determines presence of anti-oxidants in a seed extract by decolorization of DPPH methanolic solution. The dose reaction curve of DPPH radical scavenging activity of extract of melon seeds was analyzed by comparing with standard drug ascorbic acid.

Melon seeds extract's antioxidant activity was evaluated at concentrations of 10, 20 and 50ug/ml. It has shown maximum inhibition 76.468 % at dose of 50 µg/ml The IC_{50} dose of melon seeds extract was observed at 16.106 ug/ml as plotted in figure 3.

Table 3. DPPH assay (% scavenging activity) of the melon seeds extract

Concentration ug/ml	Percentage Free Radical Scavenging activity of Melon seeds extract
10	43.5 %
20	70.873 %
50	76.468 %

Figure 4. Percentage scavenging activity of melon seeds extract.

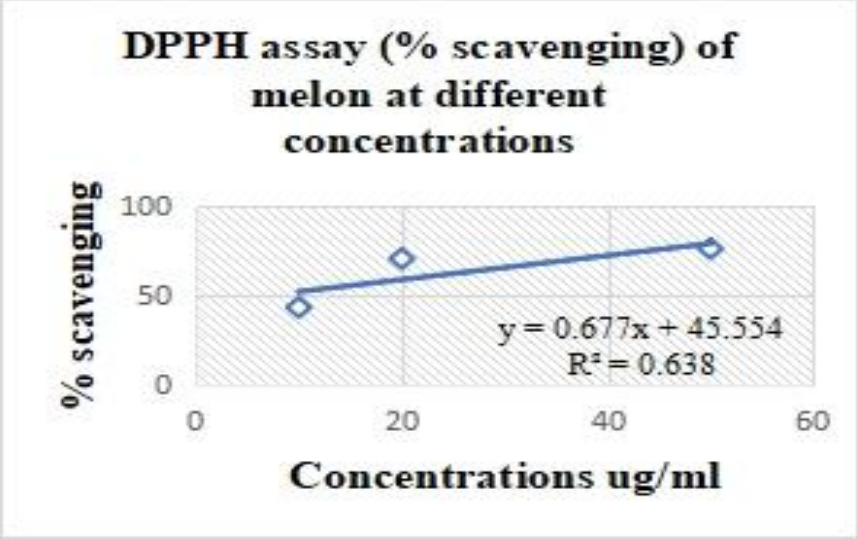
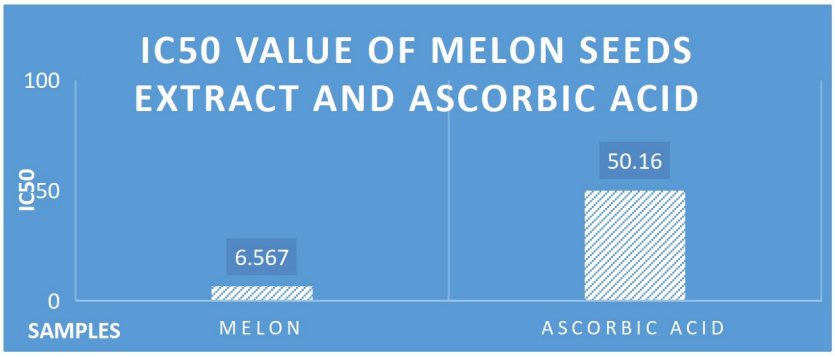


Figure 5. IC_{50} values of melon seeds extract in comparison with standard drug ascorbic acid. The bar chart represents the hydrogen donation and anti-oxidant property of melon compared to standard drug



***In-vitro* cell proliferative activity on neuronal cell culture:**

MTT assay (% cell viability assay) of different concentrations seeds extract of melon.

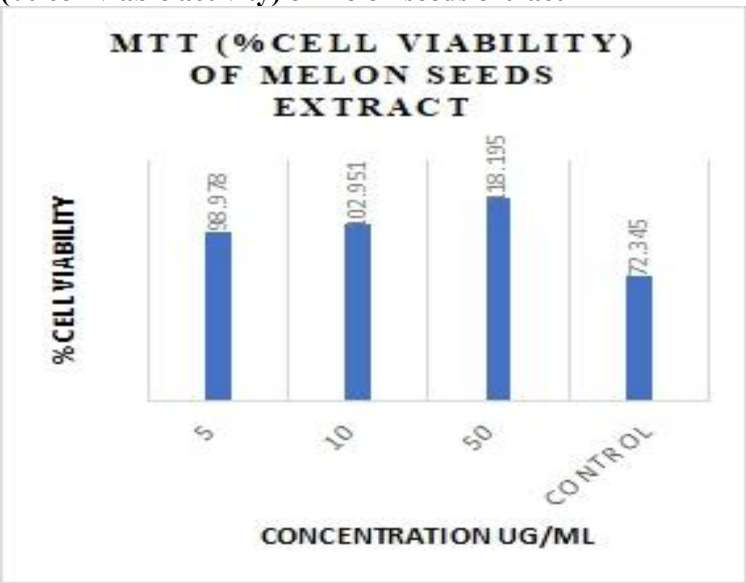
Different concentrations (5, 10, 50) ug/ml of melon seeds extract was analyzed for evaluating the percentage viability of cells. For this purpose, neuronal hippocampal cells were isolated from rat's brain and cultured.

MTT assay was performed for evaluating melon seeds extract at different concentrations to check the percentage viability of cells. The melon has shown potential ability to grow and maintain cell cultures at higher concentration when compared to lower concentrations and the maximal activity was observed 118.195 % at 50ug/ml. An overall increase in absorbance indicates greater proliferative activity. The IC_{50} value was found to be 12ug/ml.

Table 4. Percentage cell viability of neuronal cells treated with melon seeds extract.

Concentration ug/ml	Percentage cell viability of melon
Control	72.345
5	98.978
10	102.951
50	118.195

Figure 6. MTT assay (% cell viable activity) of melon seeds extract



Anti-microbial activity:
Antimicrobial assay was performed through agar plate method for evaluating melon seeds extract at different concentrations to check the % inhibition of *E. coli* culture. The maximum activity was observed at 50ug/ml which was 100 %, whereas pumpkin extract has shown potential microbial inhibiting ability at 10ug/ml by 70 %.

Table 5. Evaluation of melon seeds for its antimicrobial potentials

Concentration ug/ml	% inhibition of microbes Melon
5	83.33
10	83.33
20	96.66
50	100

Evaluation of melon seeds extract for its antimicrobial potentials
Figure7. Graphs represents percentage inhibition activity of melon seeds extract

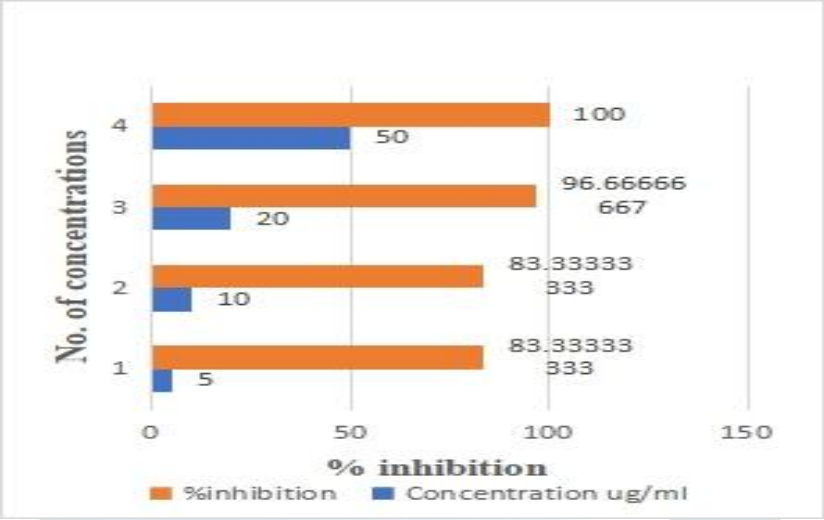
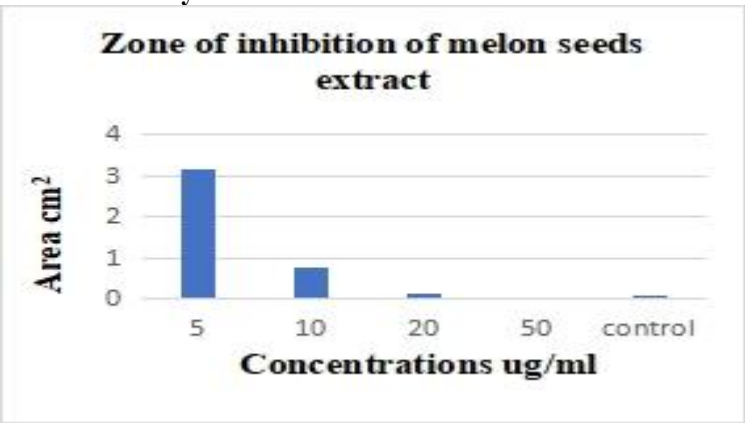


Table 6. Zone of inhibition of melon seeds extract

Concentration ug/ml (melon)	Zone of inhibition	Area (cm2)
5	0.5 cm	0.78
10	0.5 cm	0.78
20	1 cm	3.14
50	2 cm	12.56
Control	0.1 cm	0.03

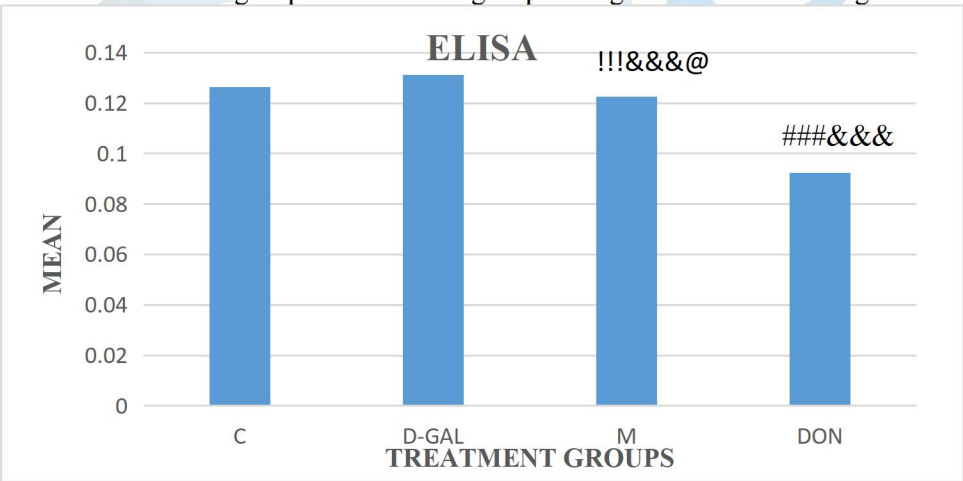
Figure 8. Graph shows the inhibitory area of melon seeds extract in anti-microbial activity



Effects of melon extracts on IL-6 protein expression through ELISA technique

Effect of melon seeds extract on rat's serum samples on interleukin-6 (IL-6) biomarker in rats treated groups compared with D-galactose group. Values are expressed as in the figure 9.

Figure 9. Effect of melon extract on brain interleukin-6 (IL-6) in rats treated with D-galactose. Values are expressed as means ± SD in each group. M and DON group are significant with the D-galactose group.



Discussion:

Neurodegenerative diseases (NDD) are characterized by continuing loss of neurons, glial cells and the neural networks in the brain and spinal cord. It involves selective dysfunctions of the brain. This causes various problems such as movement disorders (ataxias), mental dys-functioning (dementia) and can damage person's ability to move, speak and breathe properly. NDD are incurable and debilitating conditions, that are becoming widespread due to global population ageing.

Clinically Neurodegenerative diseases can be classified as Alzheimer's disease (AD), Dementia, Parkinson's disease (PD), Huntington's disease (HD) and Motor Neuron Disease [(12)].

Cucumis melo (melon) is the most important members of family Cucurbitaceae. The delicious fruit of this Cucurbita family has enormous nutritive and medicinal significance and is widely consumed in many countries.

The phytochemical analysis has proved that the functional properties of C. melo seeds make them useful in improving their functions of brain. The results of different phytochemical tests have shown the presence of alkaloids, glycosides, phenols, terpenoids, flavonoids, tannins and coumarin. All these

important bioactive components have shown neuroprotective properties in various studies, which is in accordance with our results of phytochemical screening. The neuroprotective ability of these biochemical is typically due to presence of antioxidant activity [13].

Terpenoids are the greatest applicants as a natural neuroprotective agent [14].

The presence of antioxidants, polyphenols, and tocopherols can prevent oxidative stress. Phenolic compounds are beneficial in neurological health conditions[15].

Depression like behavior is associated with reduce neurogenesis and increased neuronal degradation. Anti-oxidation activity and cell proliferation growth in neural cells was evaluated using different doses of melon 50 and 100 mg/kg [16].

Protein denaturation assay was performed on egg albumin for evaluating melon seeds extract at different concentrations to check the percentage inhibition of cells. The extracts have shown potential ability to grow and inhibit the cells at concentrations (1, 5, and 20 ug/ml) and the maximal activity was observed 74.815 % at 1 ug/ml [17].

The presence of antioxidant activity indicates that extracts interacted with electron donating systems to minimize the attack of free radicals. The ethanol extract of melon seeds showed the highest activity (76.468 %) at concentration of 50 ug/ml. IC_{50} of Cucumis melo extract were found 16.106 while the IC_{50} of standard (Ascorbic acid) was 5.16 [18].

MTT assay was used to assess the metabolically viable cells and their anti-proliferative activity pumpkin and melon has shown our concentration dependent increase in percentage cell viability which indicates that this drug can be useful in increasing the anti-proliferative action of neuronal cells in neurodegeneration diseases. Melon seeds extract was shown significantly higher proliferative activity against degenerative neuronal cells in high concentrations (50 ug/mL) with inhibition percentage of around 118.195%, respectively. IC_{50} of Cucumis melo extract was found at 12.67 ug/mL.

Antimicrobial analysis was performed for evaluating melon seed extract at different concentrations to check the % inhibition of microbes. This method presents a good outcome of antibacterial testing against broth E. coli bacteria. The extract has shown potential ability to inhibit microbial activity was observed 100% at 50ug/ml [19].

It has been observed that D-galactose exposure has increased expressions of inflammatory biomarkers. Estimation of pro-inflammatory markers including IL-6 by ELISA in the serum samples of rats treated with extract and standard drug, has shown a decrease in the concentration of the protein marker in comparison with disease group [20] [21].

Conclusions

Neurodegenerative diseases have high prevalence in elderly population worldwide. Conventional therapies including drugs like galantamine, levodopa/ carbidopa and fluoxetine are used for managing symptoms of multiple neurodegenerative disorders. In this perspective, our study concludes that *Cucumis melo* seeds extract are useful in treating the neurodegenerative diseases as they have produced improved results in D-galactose induced neuro-degenerative animal model. The extract has shown no toxic effects in acute and chronic studies and exhibits significant therapeutic value by delaying the process of neuronal cell death.

While in Eliza in-vitro technique it shows that melon extract has considerably reduced IL-6 expressions of protein.

Acknowledgments

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Declaration of Interest statement

The author declare that she has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

REFERENCES

DiSabato DJ, Quan N, Godbout JP. Neuroinflammation: the devil is in the details. Journal of neurochemistry. 2016 Oct;139:136-53.

Shan C, Zhang C, Zhang C. The Role of IL-6 in Neurodegenerative Disorders. Neurochemical Research. 2024 Apr;49(4):834-46.

Gabay C. Interleukin-6 and chronic inflammation. Arthritis research & therapy. 2006 Jul;8:1-6.

Simon DK, Tanner CM, Brundin P. Parkinson disease epidemiology, pathology, genetics, and pathophysiology. Clinics in geriatric medicine. 2020 Feb 1;36(1):1-2.

Noreen Z, DeJesus J, Bhatti A, Loffredo CA, John P, Khan JS, Nunlee-Bland G, Ghosh S. Epidemiological investigation of type 2 diabetes and Alzheimer's disease in a Pakistani population. International journal of environmental research and public health. 2018 Aug;15(8):1582.

Zeng XS, Geng WS, Jia JJ, Chen L, Zhang PP. Cellular and molecular basis of neurodegeneration in Parkinson disease. Frontiers in aging neuroscience. 2018 Apr 17;10:109.

Husain N, Chaudhry IB, Afridi MA, Tomenson B, Creed F. Life stress and depression in a tribal area of Pakistan. The British Journal of Psychiatry. 2007 Jan;190(1):36-41.

Kathayat K, Rawat M. Production technology of underutilized crops of cucurbitaceae family. InProduction technology of underutilized vegetable crops 2023 Apr 21 (pp. 101-112). Cham: Springer International Publishing.

Malathi G, Vadivelu J. In-vitro antioxidant, anti-inflammatory and cytotoxic activity of Cucumis melo L. of ethanolic extract. Biomedicine. 2021 Sep 7;41(2):439-42.

Vishwakarma VK, Gupta JK, Upadhyay PK. Pharmacological importance of Cucumis melo L.: An overview. Asian Journal of Pharmaceutical and Clinical Research. 2017 March1:8-12.

Ibrahim DS. Neuroprotective effect of Cucumis melo Var. flexuosus leaf extract on the brains of rats with streptozotocin-induced diabetes. Metabolic brain disease. 2017 Feb;32(1):69-75

Gitler AD, Dhillon P, Shorter J. Neurodegenerative disease: models, mechanisms, and a new hope. Disease models & mechanisms. 2017 May 1;10(5):499-502.

Bellavite P. Neuroprotective potentials of flavonoids: Experimental studies and mechanisms of action. Antioxidants. 2023 Jan 27;12(2):280.

Mondal S, Hossain I, Islam N. Phytochemical screening of ethanolic extract of leaves and stems of Cucubita pepo Linn. International Journal of Chemistry Studies. 2017;1(2):32-4.

Perez Gutierrez RM. Review of Cucurbita pepo (pumpkin) its phytochemistry and pharmacology. Med chem. 2016;6(1):12-21.

Wahid S, Alqahtani A, Khan RA. Nootropic Effects of C. melo and C. lanatus seed extracts. BioMed Research International. 2020;2020(1):8823038.

Amin MZ, Rity TI, Uddin MR, Rahman MM, Uddin MJ. A comparative assessment of anti-inflammatory, anti-oxidant and anti-bacterial activities of hybrid and indigenous varieties of pumpkin (Cucurbita maxima Linn.) seed oil. Biocatalysis and agricultural biotechnology. 2020 Sep 1;28:101767.

Rolim PM, Fidelis GP, Padilha CE, Santos ES, Rocha HA, Macedo GR. Phenolic profile and antioxidant activity from peels and seeds of melon (Cucumis melo L. var. reticulatus) and their antiproliferative effect in cancer cells. Brazilian Journal of Medical and Biological Research. 2018 Mar 1;51:e6069.

Abd El-Maksoud MA. Effect of Cucumis melo var. flexuosus leaves extract on renal oxidative injury and inflammation in diabetic male albino rats. Egyptian Journal of Zoology. 2019 Jun 1;71(71):13-20.

Sanadgol N, Najafi S, Ghasemi LV, Motalleb G, Estakhr J. A study of the inhibitory effects of Citrullus colocynthis (CCT) using hydro-alcoholic extract on the expression of cytokines: TNF-α and IL-6 in

high fat diet-fed mice towards a cure for diabetes mellitus. Journal of pharmacognosy and phytotherapy. 2011 Jul;3(6):81-8.

Abd El-Maksoud MA. Effect of Cucumis melo var. flexuosus leaves extract on renal oxidative injury and inflammation in diabetic male albino rats. Egyptian Journal of Zoology. 2019 Jun 1;71(71):13-20