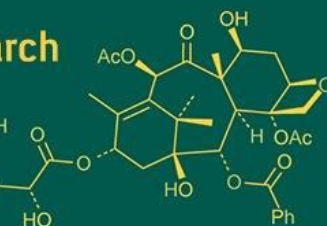


International Journal of Advanced Biochemistry Research



ISSN Print: 2617-4693
ISSN Online: 2617-4707
NAAS Rating (2026): 5.29
IJABR 2026; 10(2): 868-873
www.biochemjournal.com
Received: 02-12-2025
Accepted: 05-01-2026

Gehad Abdelkader Abdelfatah Moustafa

M.B.B.Ch., Demonstrator of Medical Biochemistry Faculty of Medicine, Tanta University, Tanta, Egypt

Dr. Hala El Said Metwally Hamooda

Professor of Medical Biochemistry, Faculty of Medicine, Tanta University, Egypt

Dr. Reham Abd Al Salam Mostafa

Professor of Medical Biochemistry, Faculty of Medicine, Tanta University, Egypt

Dr. Amira Kamel El-Tokhy
Assistant Professor of Medical Biochemistry Faculty of Medicine, Tanta University, Egypt

A Study of The Relation Between Mitochondrial Syntaxin-17, Oxidative Stress and Inflammation Through Targeting mTOR Pathway in Induced Parkinsonism in Experimental Rats

Gehad Abdelkader Abdelfatah Moustafa, Hala El Said Metwally Hamooda, Reham Abd Al Salam Mostafa and Amira Kamel El-Tokhy

DOI: <https://www.doi.org/10.33545/26174693.2026.v10.i2k.7741>

Abstract

Background: Parkinsonism is a chronic neurodegenerative disorder that is distinguished by impaired motor function. It is caused by the degeneration of dopaminergic neurones in the substantia nigra and a deficiency of dopamine in the brain. The aim of this study was to determine relationship between the mitochondrial Syntaxin-17, oxidative-stress and inflammation via the mammalian target of rapamycin (mTOR) pathway in induced parkinsonism in a rat model of rotenone-induced parkinsonism.

Aims: This experimental study was designed to shed light on investigating the relationship between mitochondrial Syntaxin-17, oxidative stress, and inflammation via the mammalian target of rapamycin in experimentally induced parkinsonism in rats.

Materials and Methods: 40 male albino rats were employed for the test, while being allocated randomly to two equal groups as follows: Control group (group I), rotenone-administered group (group II). Total antioxidant capacity tissue homogenate level was measured using spectrophotometric assay. Syntaxin-17 tissue homogenate and mammalian target of rapamycin (mTOR) tissue homogenate levels were measured by Enzyme-linked immunosorbent assay.

Results: Syntaxin-17, mammalian target of rapamycin and total antioxidant capacity levels in rotenone-administered group were significantly decreased than control group.

Conclusion: There is a significant relationship between Syntaxin-17, mammalian target of rapamycin (mTOR) and oxidative stress.

Keywords: Parkinsonism, rats, Syntaxin-17 (STX17), Mammalian target of rapamycin (mTOR), Total antioxidant capacity

Introduction

Parkinsonism is one of the most prevalent neurodegenerative diseases [1]. There are various experimental animal models for parkinsonism among them, the rotenone induced model [2]. Rotenone, a pesticide, selectively impedes mitochondrial complex-I, resulting in the degradation of dopaminergic neurones [3].

One of the major causes of parkinsonism is reactive oxygen species (ROS), mitochondrial dysfunction and inflammation [4]. ROS lowers the level of Syntaxin-17 (STX17), a protein associated with autophagosomes and essential for fusion of autophagosome and lysosome and autophagy completion [5]. ROS also reduce the level of mammalian target of rapamycin (mTOR), a conserved serine/threonine protein kinase [6]. mTOR inhibits autophagy, leading to the induction of inflammation [7]. Total antioxidant capacity (TAC) is an assay used to evaluate the ability of the body to neutralize free radicals [8].

Materials and Methods

Chemicals

Unless otherwise noted, all solvents and chemicals utilised in this study were of high analytical grade and were purchased from Sigma-Aldrich (Sigma, St. Louis, USA). Rotenone (99% purity, CAS No. 83-79-4) was employed in the experiment.

Corresponding Author:
Gehad Abdelkader Abdelfatah Moustafa

M.B.B.Ch., Demonstrator of Medical Biochemistry Faculty of Medicine, Tanta University, Tanta, Egypt

Immediately prior to subcutaneous administration, rotenone was dissolved in 1% dimethyl sulfoxide (DMSO).

Animals: The current study included a sample of 40 albino male rodents, with a mean body weight of 120 to 150 grams. These rodents were obtained from the animal colony that is utilised for research at Tanta University. Throughout the investigation, rats were housed in wire mesh enclosures and were granted unrestricted access to Water. The rats were maintained in a controlled-environment with consistent circumstances, including a temperature of 25 °C and a lighting regimen of 12-h dark/12-h light cycle. The rats underwent regular weekly weighing. This investigation had been performed in the Medical Biochemistry Department, Faculty of Medicine, Tanta University, Egypt, in adherence to the guidelines provided by the ethics committee of Medical Research, Faculty of Medicine, Tanta University, Egypt. (Approval code: 36264MS670/8/24).

Design of the experiment: Randomly, 20 rats were assigned to each of two groups after acclimatisation for one week, as follows:

Group I (control group): A vehicle solution containing 1% dimethyl sulfoxide was administered to the animals in this group at a dosage of 0.1 mL/100 grams/day, S.C., for a period of three weeks.

Group II (Rotenone-administered group): Animals in this group received 11 subcutaneous injecting of rotenone every other day at a dosage of 1.5 mg/kg dissolved in 1% DMSO for 3 weeks [9].

The rats were subjected to a neurobehavioral assessment by hanging wire test at the conclusion of the 21st day of the experiment.

The experimental rats' motor coordination and equilibrium were evaluated using the hanging wire test. A horizontally extended steel wire, which was approximately 80 cm in length and 2 mm in thickness, was suspended between two supports at a height of 1 m above the floor. Each rat was placed so that its forepaws grasped the wire, then released to hang freely. The duration the animal was able to remain suspended before falling (latency to fall) was measured in seconds [10].

Tissue sampling: Rats were sacrificed under anaesthesia, and their brains were promptly dissected with precision and rinsed with ice-cold saline to eliminate any foreign matter present. Blotting the excess saline with filter paper was implemented. The brain tissues were cooled using ice. The brain tissues were wrapped in aluminum foil and stored at -80°C till used for preparation of brain tissue homogenates for assessment of biochemical parameters.

Preparation of brain tissue homogenate: In a 50 mM cold potassium phosphate buffer saline pH 7.4 solution, the brain tissue specimens were homogenised and weighed using a Potter-Elvehjem tissue homogeniser (20-30 up and down strokes) at a 1/5 w/v ratio. A 20-minute centrifugation at 4000 rpm at 4°C was performed on the crude homogenate. Once separated, the supernatant was stored at -80°C until it was required.

Biochemical Laboratory investigations included

Measurement of total antioxidant capacity (TAC) level in brain tissue using spectrophotometric assay: Using a spectrophotometric commercial kit supplied by Sunlong, China, TAC level was determined. TAC values for brain tissue homogenates and was calculated in $\mu\text{mol/mL}$ and $\mu\text{mol/mg}$, respectively.

Measurement of Syntaxin-17 and mTOR levels in brain tissue using ELISA: Syntaxin-17 level and mTOR level were measured in brain tissue homogenate by double antibody sandwich enzyme linked immunosorbent assay kits (Catalogue number #: 201-11-1822 and #: DL-FRAP-Ra) obtained from Wuhan Fine Biotechnology Co., Ltd, Shanghai, China. Values were expressed in pg/mg protein and ng / mg protein.

Statistical analysis: The findings were revealed after statistical analysis, and the information was shown as the average plus or minus the standard deviation (SD), percentage, or raw numbers. The results of the unpaired t-test were computed using SPSS V.20, a statistical program for the social sciences. An important p-value was one that was less than 0.05.

Results: Behavioral assessment of the effect of rotenone on experimental rats.

Rats administered with rotenone exhibited a significant decrease in latency to fall ($p < 0.005$). (Figure 1).

Brain tissue homogenate STX-17 and mTOR levels were significant different among the two studied groups. There was significant reduction in group II than group I. (Figures 2, 3).

Brain tissue homogenate TAC was significant reduce in group II when than group I (Table 1).

Brain tissue homogenate level of STX17 showed a significant positive correlation with brain tissue homogenate mTOR level. ($r = 0.43$, $P = 0.037$) (Figure 4).

Brain tissue homogenate level of STX17 showed a significant positive correlation with brain tissue homogenate TAC. ($r = 0.39$, $P = 0.047$).

Discussion

The pathological definition of parkinsonism is the degeneration of dopaminergic neurones in the nigrostriatal pathway, which is a chronic neurodegenerative disorder [11].

Rotenone is a naturally derived compound obtained from plants and is widely used as a broad-spectrum pesticide and insecticide [12]. It can easily cross the blood-brain barrier and induce neurotoxic effects by inhibiting complex I of the electron transport chain. This disrupts oxidative phosphorylation and reduces ATP production [13].

Furthermore, impaired electron transfer to oxygen within the electron transport chain can result in excessive generation of ROS, leading to increased oxidative stress, inflammation, glial cell damage, and degeneration of dopaminergic neurons in the substantia nigra pars compacta [14].

It has been documented that, induction of parkinsonism using rotenone was verified by change in biochemical and neurobehavioral performance in rats similar to in other mammals [15] vonWrangel C, 2015.

Numerous pathogenic mechanisms have been affiliated with nigral cell damage, including, oxidative stress, mitochondrial dysfunction, neuroinflammation, microglial

triggering, specific nigrostriatal dopaminergic damage, motor impairments, α -synuclein aggregation with formation of Lewy body-like inclusions, and impairment of protein degradation pathways, such as autophagy-lysosome system and ubiquitin-proteasome system [16].

Hence, the current study aimed to examine relationship between syntaxin-17, oxidative-stress and inflammation through targeting mTOR pathway in induced parkinsonism in experimental rats. In Parkinsonism, dopaminergic neuronal degeneration is significantly influenced by oxidative stress, as disruption of redox homeostasis in neurons interferes with multiple cellular processes and ultimately leads to neuronal death [17].

To investigate the possible involvement of oxidative stress in the development of parkinsonism, this study assessed total antioxidant capacity (TAC) levels as an indicator of oxidative stress status, indicating overall antioxidant defense vs. oxidative damage [18].

The present study consistently demonstrated a decrease in TAC in the brain tissue of the rotenone-administered group compared to the control group. This suggests that the antioxidant buffering capacity of the rotenone rats was overpowered by the development of oxidants.

In agreement with the present results, Mbiydenyuy *et al.*, 2018 [19], showed that rotenone differentially enhanced the levels of oxidative markers *in vivo* model of parkinsonism with subsequent decrease in TAC level in brain tissue homogenates.

Syntaxin-17 is a key soluble N-ethylmaleimide-sensitive attachment receptor (SNARE) protein involved in the fusion of autophagosomes with lysosomes, its inactivation leads to autophagy dysregulation [20].

The current study showed a significant decrease in STX17 level in brain tissue homogenates of rotenone administered group suggesting the important role of STX17 against neurodegeneration. These results are in agreement with Wang *et al.* (2024) [21], who reported that the accumulation of immature autophagosomes and endosomes, autophagic dysfunction, and ultimately neuronal injury and cognitive impairment were the result of reduced STX17, which was

mediated by a variety of neurodegenerative factors.

The mammalian target of rapamycin (mTOR) signaling pathway has a complex, dual role in parkinsonism, exerting either neuroprotective or neurotoxic effects depending on the cellular context, environmental conditions, and level of pathway activation [22]. The current study showed a significant decrease in mTOR level in brain tissue homogenates of rotenone administered group compared with control groups, this is suggesting the key regulatory role of mTOR in: dopaminergic cell growth, protein synthesis, and metabolism.

In consistence with the present study, Zhao *et al.*, 2024 [23], reported decreased mTOR levels in brain tissue homogenates of rotenone administered group. Also, they revealed that, mTOR is sensitive to cellular energy status, oxidative stress resulting from rotenone-induced mitochondrial dysfunction and inhibition of mTOR signaling.

Positive correlation was found in this study between mTOR and STX17 in brain tissue homogenate. Also positive correlation was found in this study between Syntaxin-17 and TAC in brain tissue homogenate.

Under normal energy conditions, mTOR is activated, which results in the suppression of autophagy, but in low energy conditions, caused by rotenone, induces mitochondrial dysfunction and oxidative stress lead to suppressing mTOR and activate autophagy in an attempt to remove damaged mitochondria [24]. But the reduction in STX17 disrupts the fusion of autophagosomes with lysosomes, causing autophagy to remain incomplete [25]. This disrupted autophagy can lead to a buildup of autophagosomes and increased cellular stress, eventually promoting cell death [26]. Huang X, *et al.*, 2025.

Thus, from these results, it could be concluded that, the potential role of mTOR signaling and STX17 level in the pathophysiology of parkinsonism in rats. Understanding the crosstalk between these two pathways may provide valuable insights into disease mechanisms and open new avenues for therapeutic interventions targeting autophagy in parkinsonism [27].

Table 1: Comparative statistics of brain tissue homogenate mTOR, Syntaxin-17 and TAC levels among the two studied groups

	Brain tissue homogenate mTOR level ng/mg. protein		Brain tissue homogenate Syntaxin-17 level pg/mg. protein		Brain tissue homogenate TAC μmol/mg. protein	
Group I (n=20)	1.61±1.40		82.51± 29.14		7.31 ± 5.29	
Group II (n=20)	0.84±.49		42.59±10.64		4.29 ±2.07	
T- test						
	t	P-value	t	P-value	t	P-value
	2.25	0.034*	6.04	0.000083*	2.32	0.029*

*Significant at p value (< 0.05), Group I: (control group), Group II: (rotenon administered group), n: number of rats in groups.

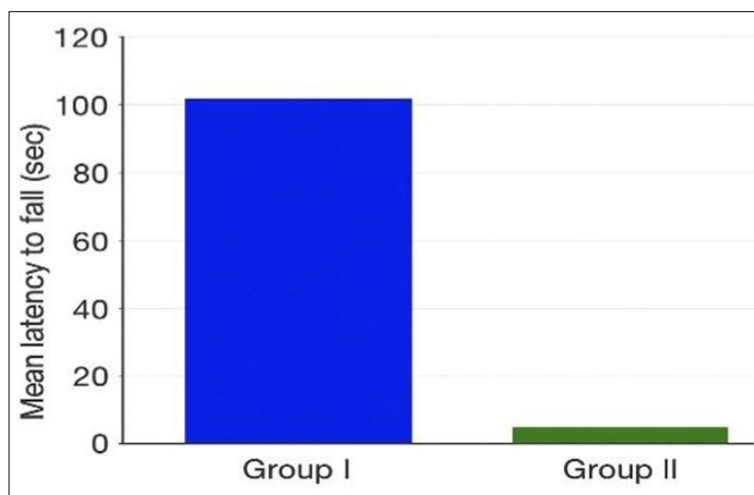


Fig 1: Statistical comparison of latency to fall (sec.) among the two studied groups. (Hanging wire test)

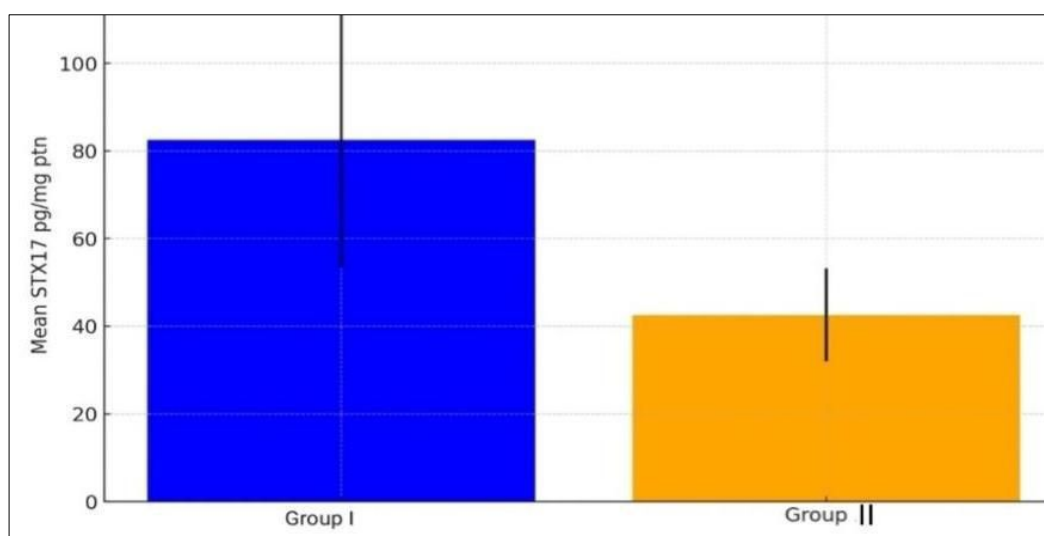


Fig 2: Statistical comparison of STX17 level (pg/mg protein) among the two studied groups

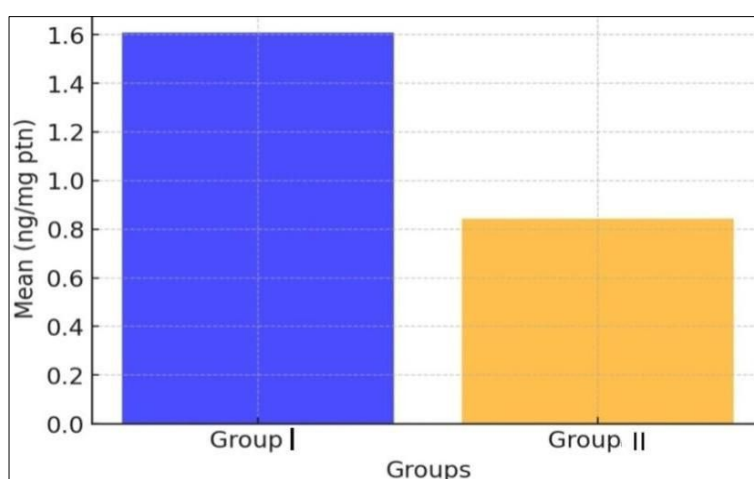


Fig 3: Statistical comparison of mTOR level (ng/mg protein) among the two studied groups

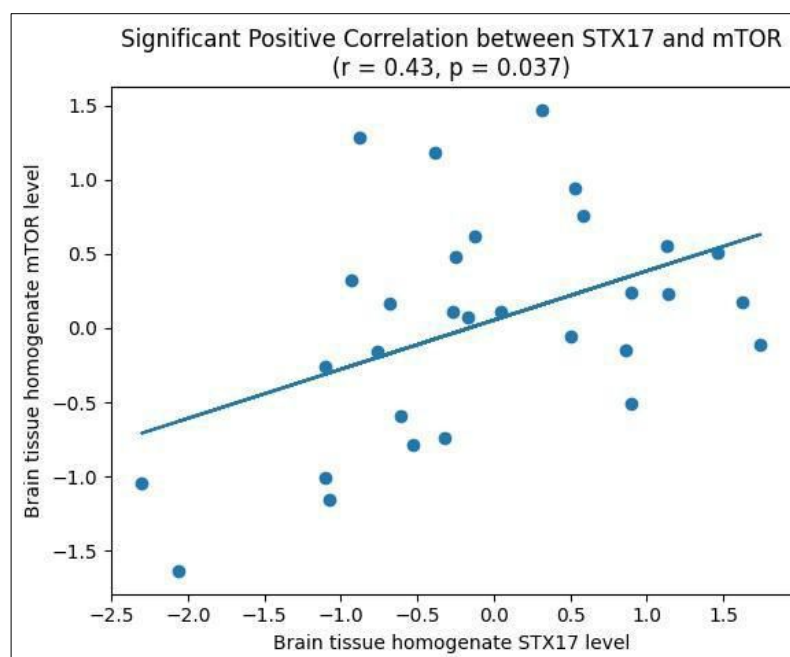


Fig 4: Pearson correlation between mTOR level and STX17 level in brain tissue homogenates. $R = 0.43$, P value = 0.037

Conclusion

There is a well-established connection between Syntaxin-17 and mTOR, indicating that their interplay may serve as a crucial regulatory pathway linking autophagy, mitochondrial dynamics, and cellular stress responses in parkinsonism. Since mTOR is a key regulator that suppresses autophagy, its inhibition can lead to α -synuclein, a hallmark of parkinsonism accumulation. High doses of Oxidative stress suppress mTOR and Syntaxin-17 leading to autophagy dysfunction.

Financial support and sponsorship

Nil.

Conflicts of Interest

There are no conflicts of interest.

References

- Keener AM, Bordelon YM. Parkinsonism. *Semin Neurol*. 2016;36(4):330-334.
- de Souza Nascimento T, Oliveira AV, de Oliveira Bélem M, Bezerra JR, do Carmo MRS, da Silva ME, *et al*. The rotenone-induced sporadic parkinsonism model: Timeline of motor and non-motor features. *Eur J Neurosci*. 2025;61(3):e16669.
- Miyazaki I, Asanuma M. Rotenone toxicity and mitochondrial complex I inhibition in models of Parkinson's disease. *Acta Neuropathol Commun*. 2025;13:234.
- Choi EH, Kim MH, Park SJ. Targeting mitochondrial dysfunction and reactive oxygen species for neurodegenerative disease treatment. *Int J Mol Sci*. 2024;25(14):7952.
- Rojas-Sanchez G, López JA, Davizon-Castillo P, *et al*. TNF- α impairs platelet function by inhibiting autophagy and disrupting metabolism via syntaxin 17 downregulation. *J Clin Invest*. 2025;135(15):e186065.
- Shi B, Chen J, Guo H, *et al*. ACOX1 activates autophagy via the ROS/mTOR pathway to suppress proliferation and migration of colorectal cancer. *Sci Rep*. 2025;15:2992.
- Lang J, Luo J, Lang J, *et al*. Electroacupuncture alleviated post-stroke cognitive impairment via the mTOR/NLRP3-mediated autophagy-inflammatory pathway. *Eur J Med Res*. 2024;29:532.
- Tran MT, Gomez SV, Alenicheva V, Remcho VT. A paper-based assay for the determination of total antioxidant capacity in human serum samples. *Biosensors (Basel)*. 2024;14(11):559.
- Abhangi KV, Patel JJ. Neuroprotective effects of linagliptin in a rotenone-induced rat model of Parkinson's disease. *Indian J Pharmacol*. 2022;54(1):46-50.
- Akinrinde A, Adigun K, Mustapha O. Cobalt-induced neuro-behavioural alterations are accompanied by profound Purkinje cell and gut-associated responses in rats. *Environ Anal Health Toxicol*. 2023;38(2):e2023010.
- Bologna M, Truong D, Jankovic J. The etiopathogenetic and pathophysiological spectrum of parkinsonism. *J Neurol Sci*. 2022;433:120012.
- Smith J, Doe A, Lee K. Rotenone-induced dopaminergic neurotoxicity: Inhibition of mitochondrial complex I, oxidative stress, and ATP depletion in Parkinson's disease models. *Acta Neuropathol Commun*. 2025;13:234.
- Haider S, Madiha S, Batool Z. Amelioration of motor and non-motor deficits and increased striatal ApoE levels highlight the beneficial role of pistachio supplementation in rotenone-induced rat model of Parkinson's disease. *Metab Brain Dis*. 2020;35(7):1189-1200.
- Lucchesi M, Biso L, Bonaso M, Longoni B, Buchignani B, Battini R, *et al*. Mitochondrial dysfunction in genetic and non-genetic Parkinson's disease. *Int J Mol Sci*. 2025;26(9):4451.
- Von Wrangel C, Schwabe K, John N, Krauss JK, Alam M. The rotenone-induced rat model of Parkinson's

- disease: Behavioral and electrophysiological findings. *Behav Brain Res.* 2015;279:52-61.
16. Pitton Rissardo J, McGarry A, Shi Y, Fornari Caprara AL, Kannarkat GT. Alpha-synuclein neurobiology in Parkinson's disease: A comprehensive review of its role, mechanisms, and therapeutic perspectives. *Brain Sci.* 2025;15(12):1260.
 17. Bej E, Cesare P, Volpe AR, d'Angelo M, Castelli V. Oxidative stress and neurodegeneration: Insights and therapeutic strategies for Parkinson's disease. *Neurol Int.* 2024;16(3):502-517.
 18. Kiani A, Li X, Arabuli D, Duarte-Jurado A, Mota S, Oderinu O. Pesticide exposure, oxidative stress and total antioxidant capacity in Parkinson's disease: Implications for redox balance and antioxidant biomarkers. *Cell Mol Neurobiol.* 2024;45(8):2203-2215.
 19. Mbiydzanyuy NE, Ninsiima HI, Valladares MB, Pieme CA. Zinc and linoleic acid pre-treatment attenuates biochemical and histological changes in the midbrain of rats with rotenone-induced parkinsonism. *BMC Neurosci.* 2018;19:29.
 20. Laczko-Dobos H, Bhattacharjee A, Asha Kiran M, *et al.* Phosphatidylinositol 4-phosphate promotes recruitment of syntaxin 17 to autophagosomes and autophagosome-lysosome fusion. *Autophagy.* 2024;20(5):1125-1138.
 21. Wang X, Hu M, Chen J, Lou X, Zhang H, Li M, Cheng J, Ma T, Xiong J, Gao R, Chen X, Wang J. Key roles of autophagosome/endosome maturation mediated by syntaxin 17 in methamphetamine-induced neuronal damage in mice. *Mol Med (Cambridge).* 2024;30(1):4.
 22. Narayanan L, Thekkekkara D, Kondaveeti SN, Babu A, Sailen BA, Chidambaram SB, Manjula SN. Deciphering the intricate role of mTOR signaling and autophagy in Parkinson's disease and therapeutic prospects. *J Appl Pharm Sci.* 2024;14(3):001-010.
 23. Zhao N, Wu M, Velu P, Annamalai V, Zhang J. Sanggenol L alleviates rotenone-induced Parkinson's disease and inhibits mitochondrial complex I by apoptosis via PI3K/AKT/mTOR signalling. *Comb Chem High Throughput Screen.* 2024;1-12.
 24. Noda S, Hattori N. Unraveling the mystery: How autophagy deficiency in dopaminergic neurons drives human Parkinson's disease. *Mol Brain.* 2025;18:66.
 25. Xu H, Zhu Y, Chen X, Yang T, Wang X, Song X, Xie X, Hu M, Jiang L, Cheng J, Gao R, Wang J. Mystery of methamphetamine-induced autophagosome accumulation in hippocampal neurons: Loss of syntaxin 17 in defects of dynein-dynactin driving and autophagosome-late endosome/lysosome fusion. *Arch Toxicol.* 2021;95(10):3263-3284.
 26. Huang X, Lu W, Yao J, *et al.* The inducible role of autophagy in cell death: Emerging evidence and future perspectives. *Cell Commun Signal.* 2025;23:151.
 27. Liang X, Yu C, Tian Y, Xiang X, Luo Y. Inhibition of STX17-SNAP29-VAMP8 complex formation by costunolide sensitizes ovarian cancer cells to cisplatin via the AMPK/mTOR signaling pathway. *Biochem Pharmacol.* 2023;212:115549.