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(71)**Name of Applicant :**
1)Amit Kumar
Address of Applicant :Assistant Professor, School of Pharmaceutical Sciences, Faculty of Pharmacy, IFTM University, Moradabad-244102 Uttar Pradesh India
2)Kashish Maurya
3)Dr. T. Deborah Paripuranam
4)Baisnabdas Pathak
5)Dr. Neha Ronald William
6)Dr. Arpan K Tripathi
7)Dr. Neha R Pathak
8)Prof (Dr.) Reena Nashine
9)Dr. Sweety Lanjhiyana
10)Dr. Sanjay Kumar Lanjhiyana
11)Priti Singh
12)Dr. Sonia Kukreti
(72)**Name of Inventor :**
1)Amit Kumar
2)Kashish Maurya
3)Dr. T. Deborah Paripuranam
4)Baisnabdas Pathak
5)Dr. Neha Ronald William
6)Dr. Arpan K Tripathi
7)Dr. Neha R Pathak
8)Prof (Dr.) Reena Nashine
9)Dr. Sweety Lanjhiyana
10)Dr. Sanjay Kumar Lanjhiyana
11)Priti Singh
12)Dr. Sonia Kukreti

(57) Abstract :
The present invention the invention relates to heterocyclic compounds for treatment of neurodegenerative diseases, particularly Alzheimer's disease and Parkinson's disease, by targeting mitochondrial homeostasis. The compounds modulate mitochondrial calcium uptake and release, reduce ROS/RNS generation, stabilize mitochondrial membrane potential, enhance mitochondrial biogenesis, and regulate signalling pathways including PINK1/Parkin mitophagy, AMPK/mTOR, and Nrf2 antioxidant defense. The heterocyclic scaffolds include nitrogen-containing (pyridine, quinoline, indole), oxygen-containing (furan, coumarin), and sulfur-containing (thiophene) derivatives. A generalized structure Ar–X–Het–R is disclosed, wherein X is an amide/ether linker and R comprises antioxidant and/or metal-chelating moieties to improve blood–brain barrier penetration and reduce iron-induced oxidative stress. Pharmaceutical compositions are provided as tablets, capsules, injectables, or nanoparticle delivery systems, with oral, intravenous, or intranasal administration. Illustrative results show ROS reduction, improved mitochondrial potential, reduced neuronal apoptosis, improved cognition/motor outcomes, reduced amyloid-β/α-synuclein aggregation, Nrf2 upregulation, and Bax/Caspase-3 downregulation. (Accompanied Figure No. 1)

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