NATIONAL INSTITUTE OF UNANI MEDICINE, BENGALURU Extramural Research Projects (Last Three Years)- Sponsored by Other Agencies (Public and Private)

Sl. No.	Name of the Project/ Endowments	Year (Completed/ in progress)	Fund provided
Prof. Mo	phammad Zulkifle		
1	Establishment & Maintenance of small nursery centre at NIUM, Bangalore Principal Investigator: Prof Mohd Zulkifle Dept. of Kulliyat, NIUM, Bengaluru	Approved (2019)	National Medicinal Plant Board, Ministry of AYUSH, Govt. of India, Sanctioned amount: Rs. 10, 25, 500/-
	Co-Investigator: Dr. Shariq Shamsi		
	Assistant Professor, Dept. of Ilmul Saidla NIUM, Bengaluru		



MINSIRTY OF AYURVEDA, YOGA & NATUROPATHY, UNANI, SIDDHA AND HOMEOPATHY

APPLICATION FOR GRANT-IN-AID OF EXTRA MURAL RESEARCH PROJECTS IN AYUSH

Section-A

- 1. Title of the Research Project: Insight into the effect of extracts from Boswellia serrata on transferrin and ferritin: A possible therapeutics for Alzheimer's therapy.
- 2. Details of the Institution submitting the research project

Name: Jamia Millia Islamia, New Delhi & National Institute of Unani Medicine, Bengaluru Postal Address: Jamia Millia Islamia, Jamia Nagar, New Delhi

Telephone: 011-26981717

Fax:

3. In case of individuals submitting the research project" (Name of the collaborating institute may be cited in S.No. 2 above)

Name of the individual: Dr. Asimul Islam

Postal Address: R. No. 19, Centre for

Interdisciplinary Research in Basic Science, Gate No. 23, Ramanujan Block, Jamia Millia

Islamia, New Delhi.

Telephone: 09312812007

Fax:

4. Name and Designation of

Principal Investigator:

Co-Investigator(s):

Consultant: NA

Dr. Asimul Islam, Assistant Professor

CIRBSc, Jamia Millia Islamia, New Delhi.

Dr. Shariq Shamsi **Assistant Professor**

Department of Ilmul Saidla,

National Institute of Unani Medicine

Kottigepalaya, Magadi Main Road, Bangalore-560091

- 5. Duration of Research Project:
 - Period required for pre-trial preparations: 0-6 Months
 - ii. Period that may be needed for collecting the data: 6-12 Months
 - iii. Period that may be required for analyzing the data: 2-3 Years

6. Amount of Grant-in-Aid asked for: Central sector Scheme for Extra Mural Research Program for Non-Communicable Diseases (NCD)-2019

	Total	1 st	2 nd	3 rd	Remaining	Withheld
		Installment	Installment	Installment	Amount	Amount
					(10 %)	(10 %)
Salary	31,30,560	10,43,520	10,43,520	9,39,168	1,04,352	1,04,352
Equipment	15,00,000	15,00,000	0	0	0	0
Books	1,50,000	50,000	50,000	45,000	5,000	5,000
Other Non- recurring expenditure	0		0	0		0
Recurring Expenditure	12,00,000	4,00,000	4,00,000	3,60,000	40,000	40,000
TA/DA	1,50,000	50,000	50,000	45,000	5,000	5,000
Institutional Support	2,53,278	H E OWN III			2,53,278	2,53,278
Fee of PI and Col	1,35,000	n or ma	pearly dust a	lity and g	1,35,000	1,35,000
Miscellaneous Expenses	3,00,000	1,00,000	1,00,000	90,000	10,000	10,000
Total	68,18,838	31,43,520	16,43,520	14,79,168	5,52,630	5,52,630



7. DECLARATION AND ATTESTATION

Certified that:

We have read the provisions, terms and conditions, mentioned in the Extra-Mural Scheme along with its Annexure, Guidelines formulated by the Ministry of AYUSH and we shall abide by the relevant provisions contained under EMR Scheme and General Financial Rules of Govt. of India.

Name and Signature of the:

a)Principal Investigator

Dr. Asimul Islam (Assistant Professor) Centre for Interdisciplinary Research in Basic Sciences Jamia Millia Islamia, New Delhi-25

Dr. Asimul Islam

b) Co-Investigator

Dr. Shariq Shamsi

c) Director of the Centre

Professor Shafeeque Ahmed Ansari

Signature of the Head of the Institution

कुरासीच्य / Registrar लामिया निल्लिया इस्तामिया / Jamia Milia Islamin केन्द्रिय शिव्यविद्यालय / Central University

नई विल्ली / New Delhi - 110025

Mr. A. P. Siddiqui, The Registrar, Jamia Millia Islamia,

Place: New Delhi

Date: .



Section-C

BRIEF SUMMARY OF THE RESEARCH PROPOSAL

[Adequate information must be furnished in a brief but self-contained manner to enable the Ministry to assess the project

1. Title of the Research Project: Insight into the effect of extracts from Boswellia serrata on transferrin and ferritin: A possible therapeutics for Alzheimer's therapy.

2. Objectives

Boswellia serrata is one of the ancient and most valued herbs in Ayurveda & Unani system of medicines. Extracts from Boswellia serrata, which is also called Boswellia, can be exploited to cure Alzheimer's disease if the mechanism of interaction of Boswellia with proteins is delineated. We hypothesize that Boswellia affects structure and conformation of transferrin and ferritin in a way such as to improve their functionality; both these key players of iron homeostasis (ferritin and transferrin) works more efficiently in presence of Boswellia. To address this hypothesis, this study has been planned which will cover the following objectives:

- > In vitro study of ferritin and transferrin with Boswellia employing various biophysical techniques like Isothermal Titration Calorimetry (ITC) and Fluorescence.
- > In silico study of ferritin and transferrin with Boswellia will also be performed by molecular docking and MD simulation studies, using High-End Servers available with the research group of the PI.

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- > To report the structural changes induced in ferritin and transferrin upon interaction with Boswellia using UV-vis, fluorescence and CD spectroscopy.
- To analyze the functional changes induced in ferritin and transferrin upon interaction with Boswellia using atomic absorption spectroscopy, CD spectropolarimeter, UV vis, Fluorescence and FTIR spectroscopy.
- > Targeting the development of new drugs with high curing potential and their comparison with existing drugs available in the Unani system of medicine.
- ▶ Based on structure based information, improvement of the efficacy of existing Unani medicines.
- 3. Methodology
- I. In vitro Approach: Studying the interaction of Boswellia with transferrin and ferritin using biophysical techniques and isothermal titration calorimetry (ITC).

Different spectroscopic techniques will be employed to analyze the interaction of Boswellia with transferrin and ferritin. Some of the techniques are discussed below.

- UV-visible spectroscopy: This technique is most commonly used to study protein interaction and environment of aromatic amino acids.
- Fluorescence Spectroscopy
- Circular Dichroism (CD) Measurements
- Fourier Transform Infrared (FTIR) Studies
- Estimation of Thermodynamic Parameters by Isothermal Titration Calorimetry
- ANS fluorescence assay
- Thioflavin T assay
- Congo red assay: CR is another dye that specifically binds to β -sheet and this upon binding with aggregates shows a red shift in wavelength.
- Advanced Glycation End-Products (AGEs) detection
- Microscopic analysis: Seeing is believing. Scanning electron microscopy (SEM) and Transmission electron microscopy (TEM) along with confocal microscopy will be done.



- II. In silico Approach: Studying the interaction of Boswellia with transferrin and ferritin using molecular docking and MD simulation studies
 - Molecular docking: Docking studies of transferrin and ferritin with active components of Boswellia serrata will be performed using Auto-Dock Vina. Different binding conformations and binding energies will be reported.
 - MD Simulation: Simulation studies will be also be performed. Gromacs or Amber MD will be used to perform the simulation studies in different conditions.

III. Functional analysis:

Iron carrying capacity of transferrin will be evaluated in native form and in presence of Boswellia employing atomic absorption spectroscopy.

4. Anticipated Outcome

Over the past decade, vigorous research pertaining to neurodegenerative disorders is being carried out with very little output in terms of Alzheimer's therapy. The most significant outcome of our study would be the development of connecting link between Unani medicine and Protein biochemistry. The expected output of our study is that we will be able to evaluate the effect of Boswellia extract on transferrin and ferritin. The most significant outcome of this study would be the establishment of connecting link between altered structure and function of ferritin and transferrin with the development of neurodegenerative disorders.

In case of possible achievement of our hypothesis, Boswellia serrata can be established as a possible therapeutic along with other drugs in use for Alzheimer's therapy. Thus, aspect of our study might be the use of Boswellia serrata drugs in one or other form in combination with cholinesterase inhibitors already in use for Alzheimer treatment.

5. Summary of the proposed research (up to 150 words) indicating overall aims of the research, importance of the objectives and their application in the context of the priority areas set out in application form.

We shall investigate the structure and function of transferrin and ferritin proteins in the presence of Boswellia extract. Alteration in the structure of these proteins shall enhance proteins' function to prevent Alzheimer' disease. We shall correlate the functional



enhancement with binding of the proteins with Boswellia using ITC, fluorescence and SPR. Altered proteins shall work more efficiently in maintaining iron homeostasis which is usually disrupted in neurodegenerative disorders. This study shall evaluate the protective effect of *Boswellia* in Alzheimer's disease in terms of functional enhancement of ferritin and transferrin which is pivotal in these disorders. This work shall contribute immensely to understand and cure one of the most important non-communicable disease (Alzheimer 's disease) which is going to affect everybody in the near future as life expectancy is increasing. The application of this project lies in connecting Unani system to the main stream of medicines in curing Alzheimer's using fundamentals of Protein Biochemistry; further, providing a progressive development in its therapy as lethal nature of this disorder and its high rate of progression, is dangerous to the intelligence of the country.

6. Relevance and usefulness of the study with particular reference to concerned AYUSH system.

One of the priority areas is Non-communicable disease and Alzheimer's disease is a one that top the chart being a lethal disorder widespread across the globe. Alzheimer's disease (AD) is a degenerative brain disease that is the leading cause of dementia among human population (Mahaman, Y. A. R., Huang, F., Kessete Afewerky, H., Maibouge, T. M. S., Ghose, B., & Wang, X. (2018). Involvement of calpain in the neuropathogenesis of Alzheimer's disease. Medicinal research reviews.). Dementia affects 50 million people worldwide - a number that will almost triple by 2050. More than half of all people with dementia live in low and middle income countries where as few as 10% of individuals receive a diagnosis. In 2018, dementia will become a trillion-dollar disease. There are over 9.9 million new cases of dementia each year worldwide, implying one new case every 3.2 seconds. Thus, need for advancements and insights into research targeting Alzheimer's therapy is a need of hour and our proposed project rightly falls into that domain. Our ancient system has documentation of cure of diseases related to old age, especially Alzheimer's. Boswellia is known to prevent Alzheimer's disease but the mechanism of its function is not known. This study shall delineate the mechanism of cure of Alzheimer by Boswellia which shall bring confidence in using this important Unani



product. Latest studies with sophisticated equipments shall help in documentation of ancient drugs. We got some exciting results to favour this project.

Some preliminary experiments were carried out to check the feasibility of our proposed work. We carried out *in silico* investigations to check the interaction of transferrin and boswellic acid (An important constituent of *Boswellia serrata*).

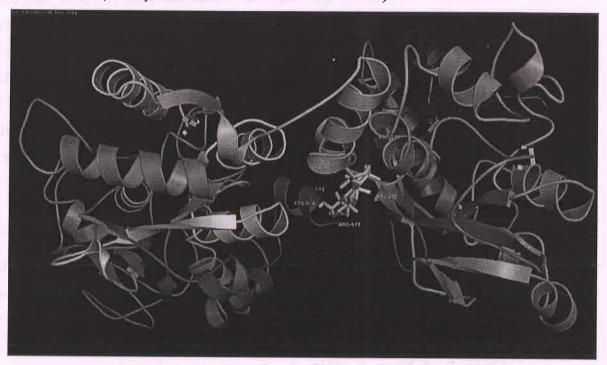


Figure 1: Boswellic acid in the vicinity of human transferrin. A high binding energy of -8.3 kcal/mol was obtained for this interaction.

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Z. 18017/187/Nur/KR-02/2018-19-NMPB Government of India Ministry of AYUSH National Medicinal Plants Board

1st Floor, Indian Red Cross Annexe Building, Indian Red Cross Society Complex Near Parliament House Red Cross Road, New Delhi - 110 001 E-mail: info-nmpb@nic.in

Dated: 10th Apr, 2019

NMPB/IFD/GIA/NR/PL/2019-20/

To,
The Pay & Accounts Officer (Sectt.),
Ministry of Health & Family Welfare
Nirman Bhawan,
New Delhi- 110011

Subject: Grant-in-aid for Central Sector Scheme for the year 2019-20, release of payment of ₹10,12,500/- in favor of National Institute of Unani Medicine, Bangalore, Karnataka.

Sir,

In exercise of powers delegated under DFPR rules 1978, I am directed to convey the sanction of the President to the payment of ₹10,12,500/- (Rupees Ten Lakh Twelve Thousand Five Hundred Only) as 1st & Final installment for the project entitled "Establishment and Maintenance of Small Nursery center at NIUM, Bangalore" in favour of National Institute of Unani Medicine, Bangalore, Karnataka for the year 2019-20.

This grant is of non-recurring nature and for one year from the date of releasing GIA in respect of 1st & final installment date of releasing of GIA.

S. No.	File No. and Project No.	Name of the Grantee/ Institution	Amount (₹)
1	Z. 18017/187/Nur/KR-02/2018- 19-NMPB (Project No. NUR/KR-02/2019- NMPB)	National Institute of Unani Medicine, Bangalore Karnataka	₹10,12,500/-

The grant is to be utilized during the year 2019-20 in accordance with approve costing of the project. Payment of grant will be made directly by Real Time Gross Settlement (RTGS) payable to the office bearer viz. National Institute of Unani Medicine, Bangalore, Karnataka authorized to operate upon it's State Bank of India account No.30095385134 and to bind it financially in accordance with rules & regulations.

The grant-in-aid will be subject to the conditions laid down in Rules-228 to 245 of the General Financial Rules 2017.

The accounts of the grantee institution/ organization shall be open to inspection by the sanctioning authority and audit both by the CAG of India under the provision of CAG (DPC) Act, 1971 and internal audit wing of the O/o CCA of the Ministry, whenever the institution or organization is called upon to do so.

The grant is debitable under Demand No. 5, Ministry of AYUSH, 2210-Medical & Public Health (Major Head), 02200-Other Systems (Minor Head), 13-National Medicinal Plants Board, 130031-Grant-in-Aid (General) for the year 2019-20 (Revenue).

No UC is pending against the grantee.

The Agency has been boarded in EAT Module.

The project is not violating Model code of conduct in force in connection with general Elections 2019.

"As the Research Project involves biological resources, the obligations under the Biological Diversity Act, 2002 as applicable shall be compiled with by the Project Investigator".

Certified that no unadjusted balance is lying with the grantee and no utilization certificate is pending against the grantee organization.

This issue with the approval of IFD vide Concurrence Dy. No C-16 dated 05.04.2019.

Yours faithfully

Finance & Administrative

Copy to:-

1. The Under Secretary (Budget), Ministry of AYUSH, New Delhi.

2. Prof. Mohd, Zulkifle, Director I/c, National Institute of Unani Medicine, Magadi Main Road, Kottigeplaya, Bangalore - 560 091, Karnataka kindly acknowledge the receipt of funds transferred through RTGS with the request that the following documents in original duly signed by the competent authority and certified as correct by Govt. Auditor or Chartered Accountant, as the case may be, shall also be sent to this Ministry within a period of twelve months by the grantee:-

Utilization certificate in the prescribed Performa in **GFR-12-C** format to the effect that the grant has been utilized for the purpose for which it was sanctioned duly signed by

competent authority and audited by Govt. Auditor or Chartered Accountant.

(ii) Audited accounts reflecting therein the grant-in-aid released and the item-by-item expenditure incurred there against duly signed by competent authority and audited by Govt. Auditor or Chartered Accountant.

- (iii) A Certificate stating that grantee/institution/organization has not received financial assistance for the same purpose from any other department of the Central or State Government or any other Government Agency.
- (iv) An achievement-cum-performance report explaining:-
 - (a) The purpose for which the grant was received.
 - (b) The manner in which it has been utilized.
 - (c) How the grant helped to improve the performance of the instt.

(ASHOK KUMA)

Finance & Administrative Officer

py also to:-

- The Director of Audit, Central Revenues, I.P. Estate, New Delhi.
- 2. Planning Commission (Health Division), Yojna Bhawan, New Delhi.
- 3. The Secretary (Health) of the concerned State Governments/U.Ts
- 4. Prof. Mohd, Zulkifle, Director I/c, National Institute of Unani Medicine, Magadi Main Road, Kottigeplaya, Bangalore 560 091, Karnataka.
- Dr. Shariq Shamsi, Lecturer & I/c of Herbal Garden, National Institute of Unani Medicine, Magadi Main Road, Kottigeplaya, Bangalore 560 091, Karnataka.
- 7. Regional Director, Kerala Forest Research Institute (KFRI), Peechi 680 653, Thrissur, Kerala.
- 7. Sh. Ashok Kumar, Finance and Administrative Officer (F&AO), NMPB.
- 8. Dr. Jeetendra Kumar Vaishya, Research Officer (MPs/Agro.), NMPB.
- 9. Cash (AYUSH) section with one spare copy with the request to transfer the funds through RTGS.
- 10. ISM (E.III) Section/P&E Cell/Fin. Desk II/Sanction Register.
- 11. Account Section, NMPB.
- 12. Computer Operator, NMPB, for uploading the sanction order on NMPB's website.
- 13. Concerned file/ Sanction folder.

Finance & Administrative Office