Annexure-VIII

UNIVERSITY GRANTS COMMISSION
BAHADUR SHAH ZAFAR MARG
NEW DELHI – 110 002

ANNUAL/FINAL REPORT OF THE WORK DONE ON THE MINOR RESEARCH PROJECT.

1. **Project report number:** Final
2. **UGC Reference No and Date:** F. No.-43-41/2014(SR) dated: 08/07/2015
3. **Period of report:** 10/02/2016 to 30/06/2018
4. **Title of the research project:** "Management of hypertension and associated risks by inhibiting pro-hypertensive enzymes using novel peptides"
5. **(a) Name of the Principal Investigator:** Dr. B. S. Vishwanath
   (b) Department: Department of Studies in Biochemistry
   (c) College where work has progressed: University of Mysore

6. **Effective date of starting of the project:** 10/02/2016

7. **Grant approved and expenditure incurred during the period of the report:**

a. **Total amount approved Rs:** 13,84,000.00

b. **Total amount released Rs:** 12,07,725.00

c. **Total expenditure Rs:** 11,11,275.00

d. **Report of the work done: (Please attach a separate sheet)**

i.	Objectives of the project	1. Management of hypertension by cumulative inhibition of three enzymes - angiotensin converting enzyme (ACE), neutral endopeptidase (NEP) and aminopeptidase N (APN) which regulate ACE dependent and ACE independent pathways. 2. To design, screen and synthesize peptide inhibitor(s) that can inhibit all these three enzymes. 3. Evaluation of the inhibitory potential of the potential peptide(s) on ACE, NEP and APN in vitro and in vivo. 4. Assessment of the adverse effects by acute and chronic toxicity studies.

ii.	Work done so far	1. Peptide designing and screening. 2. Peptide synthesis. 3. Isolation and purification of ACE, NEP and APN. 4. ACE, NEP and APN inhibition studies. 5. Circular dichroism study of inhibitor with ACE, NEP and APN enzymes. 6. Standardization of dexamethasone, nitro-L-arginine methyl ester and angiotenin II -induced hypertensive rat models. 7. Inhibition of hypertensive models and AT-1R receptors using novel peptides. 8. Inhibition of ACE using tetraethyl thiuram disulfide (TTD) by zinc chelation.
	Publications, if any, resulting from the work	1. Jalahalli M. Siddesha, Nataraju Angaswamy and **Bannikuppe S. Vishwanath.** Phytochemical screening and evaluation of *in vitro* angiotensin-converting enzyme inhibitory activity of *Artocarpus altilis* leaf. **Natural Product Research.** https://doi.org/10.1080/14786419.2010.497962 2. Mysuru Natarajan Savitha, Jalahalli Mariswamy Siddesha, Kanve Nagaraj Suvilesh, Manjunath Yariswamy, Hamse Kameshwar Vivek, Cletus J.M. D'Souza, Muddegowda Umashankar, **Bannikuppe Sannanaik Vishwanath**. Active-site directed peptide l-Phe-d-His-l-Leu inhibits angiotensin converting enzyme activity and dexamethasone-induced hypertension in rats. **Peptides.** https://doi.org/10.1016/j.peptides.2018.11.002 3. Mysuru Natarajan Savitha, Supriya Sarkar, Kanve Nagaraj Suvilesh, Shravan Kumar S L, **Bannikuppe Sannanaik Vishwanath**. Blood pressure lowering and anti-fibrotic effect of zinc-specific chelator-tetraethyl thiuram disulfide in the rat model of L-NAME-induced hypertension. **Progress in Biology.** https://doi.org/10.15419/pb.v3i1.398 4. Mysuru Natarajan Savitha, Kanve Nagaraj Suvilesh, Jalahalli Mariswamy Siddesha, M.D. Milan Gowda, Manisha Choudhury, Devadasan Velmurugan, Muddegowda Umashankar, **Bannikuppe Sannanaik**

		Vishwanath. Combinatorial inhibition of Angiotensin converting enzyme, Neutral endopeptidase and Aminopeptidase N by N-methylated peptides alleviates blood pressure and fibrosis in rat model of dexamethasone-induced hypertension. **Peptides.** https://doi.org/10.1016/j.peptides.2019.170180
iii.	Has the progress been according to original plan of work and towards achieving the objective. if not, state reasons	Yes.
iv.	Please indicate the difficulties if any, experienced in implementing the project	Second instalment of the grant was not released on time.
v	If project has not been completed, please indicate the approximate time by which it is likely to be completed.	Project has been completed.
vi	If project has been completed, please enclose a summary of the findings of the study. One bound copy of the final report of work done may also be sent to the concerned Regional Office of the UGC.	Enclosed.
vii	Any other information which would help in evaluation of the work done on the project. At completion of the project, the first report should be indicate the output, such as (a) Manpower trained (b) PhD awarded (c) publication of the results (d) other impact.	1. Manpower trained: 8 M. Sc students were carried out their project work on the topic related to this project and were trained in the project. 2. PhD: One candidate completed the PhD. 3. Publications: 4 research papers were published and 2 manuscripts being prepared.

B.S. Vishwanath

SIGNATURE OF PRINCIPAL INVESTIGATOR

Prof. B. S. Vishwanath, M.Sc., Ph.D
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REGISTRAR

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Annexure- IX

UNIVERSITY GRANTS COMMISSION
BAHADUR SHAH ZAFAR MARG
NEW DELHI – 110 002

PROFORMA FOR SUBMISSION OF INFORMATION AT THE TIME OF SENDING THE FINAL REPORT OF THE WORK DONE ON THE PROJECT

1. **Title of the project:** Management of hypertension and associated risks by inhibiting pro-hypertensive enzymes using novel peptides.
2. **Name and address of the principal investigator:** Dr. B. S. Vishwanath
3. **Name and address of the institution:** Department of Studies in Biochemistry, University of Mysore, Mysuru, India.
4. **UGC approval letter no. And date:** F. No.-43-41/2014(SR) dated: 08/07/2015
5. **Date of implementation:** 10/02/2016
6. **Tenure of the project:** 3 years. July 2015 to June 2018.
7. **Total grant allocated:** 13,84,000.00
8. **Total grant received:** 12,07,725.00
9. **Total grant released:** 12,07,725.00
10. **Final expenditure:** 11,11,275.00
11. **Total amount to be released:**
12. **Title of the project:** Management of hypertension and associated risks by inhibiting pro-hypertensive enzymes using novel peptides.
13. **Objectives of the project:**
    1. Management of hypertension by cumulative inhibition of three enzymes - angiotensin converting enzyme (ACE), neutral endopeptidase (NEP) and aminopeptidase N (APN) which regulate ACE dependent and ACE independent pathways.
    2. To design, screen and synthesize peptide inhibitor(s) that can inhibit all these three enzymes.
    3. Evaluation of the inhibitory potential of the potential peptide(s) on ACE, NEP and APN in vitro and in vivo.
    4. Assessment of the adverse effects by acute and chronic toxicity studies.
14. **Whether objectives were achieved: Yes.**
15. **Achievements from the project:**
    1. Peptide designing and screening.

2. Peptide synthesis.
3. Isolation and purification of ACE, NEP and APN.
4. ACE, NEP and APN inhibition studies.
5. Circular dichroism study of inhibitor with ACE, NEP and APN enzymes.
6. Standardization of dexamethasone, nitro-L-arginine methyl ester and angiotenin II - induced hypertensive rat models.
7. Inhibition of hypertensive models and AT-1R receptors using novel peptides.
8. Inhibition of ACE using tetraethyl thiuram disulfide (TTD) by zinc chelation.

16. SUMMARY OF THE FINDING:

Hypertension is a global public health burden leading to cardio-renal and cerebro-vascular complications and is directly attributed to poorly controlled blood pressure (BP). Various natural and synthetic peptides are being used as potent anti-hypertensive agents, which target renin-angiotensin system (RAS) – the master regulator of hypertension with angiotensin converting enzyme (ACE) as the chief effector in generation of vasopressor Angiotensin (Ang) II. Despite the availability of potent anti-hypertensive drugs, still there is scope for development of new ACE inhibitors due to associated side effects. Custom designed drugs containing either D-amino acids or N-methyl amino acids where the peptide bond replaces N-H with N-CH3 groups. Peptide bonds due to D - amino acids or with CH3 groups instead of N-H are not susceptible for proteolytic cleavage. To substantiate the in vitro inhibitory activity of hypertensive enzymes an in vivo hypertension animal model is necessary

17. CONTRIBUTION TO THE SOCIETY

- Screening of novel anti-hypertensive peptides.
- Established dexamethasone, nitro-L-arginine methyl ester and angiotenin II - induced hypertensive rat models.
- Inhibition of hypertensive enzyme through zinc ion chelation by TTD.
- 8 M. Sc students were carried out their project work on the topic related to this project and were trained in the project.
- One candidate completed the PhD.

18. WHETHER ANY PH.D. ENROLLED/PRODUCED OUT OF THE PROJECT:

Yes. Mr. Milan Gowda M D, project fellow working as full time research scholoar registered for PhD.

19. NUMBER OF PUBLICATIONS OUT OF THE PROJECT:

4 research papers were published and 2 manuscripts being prepared.

B. S. Vishwanath

PRINCIPAL INVESTIGATOR

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