SUBMISSION OF

ANNUAL PROJECT REPORT

ENTITLED

"Synthesis and biological evaluation of novel Nitrogen,Oxygen and Sulfur containing heterocycles as antimicrobial agents"

TO

UNIVERSITY GRANTS COMMISSION

By
Mrs.R.G.Gajjar
(B.Sc., M.Sc.)
Department of Chemistry
Smt. S. M. Panchal Science College,
Talod -383 215 (Gujarat-India)

To,
Dr. G. Srinivas,
Deputy Secretary
Ganeshkind, Poona University Campus
Poona - 411 007 (MAHARASHTRA)

SUB: Annual progress report of the research project titled "Synthesis and biological evaluation of novel Nitrogen,Oxygen and Sulfur containing heterocycles as antimicrobial agents" (Sanction letter No.47-2039/11(WRO))

Dear Sir,
Kindly find a copy of Annual progress report of the research project entitled "Synthesis and biological evaluation of novel Nitrogen,Oxygen and Sulfur containing heterocycles as antimicrobial agents" (Sanction letter No. 47-2039/11(WRO)) for the period of 22/02/2012 to 14/09/2015, funded by your office to Mrs.R.G.Gajjar, working as Associate professor at Chemistry Department , Smt.S.M.Panchal Science College,Talod.

She has completed all practical work and biological results are awaited. She will submit his detail report within two to three months.

Kindly acknowledge the same, do needful and oblige.

Thanking You,
Yours Sincerely,

(Mrs.R.G.Gajjar) (Dr.S.C.Parikh)
Principal Investigator **Principal**

Enclo:

1. Annual Progress Report.
2. Utilization certificate.
3. Audited statement expenditure with recurring items.
4. Statement of expenditure on field work.
5. Assets Certificate.
6. Accession Certificate.
7. Acceptance Certificate.
8. Certificate of unspent balance.

Annual Progress Report of the work done on the Minor Research Project.

1. **Project report No**. : First

2. **UGC Reference No**. : F- 47/2039 /11 (WRO)

3. **Period of report** : From 22/02/2012 to 14/09/2015

4. **Title of research project** : "Synthesis and biological evaluation of novel Nitrogen,Oxygen and Sulfur containing heterocycles as antimicrobial agents"

5. (a) **Name of the Principal Investigator** **:** Mrs.R.G.Gajjar

   (b) **College where work has progressed** : Chemistry Department, Smt.S.M.Panchal Science college, Talod-383215. (Gujarat)

6. **Effective date of starting of the project** **:** 23/03/2012

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

   (a) **Total amount approved Rs** : 1,35,000.00
   (b) **Total expenditure Rs**. : 1,33,087.00
   (c) **Report of the work done** **:** Please see Annexure

INVESTIGATOR **SIGNATURE OF THE PRINCIPAL**

Annexure

❖ Report of the work done:

1. Brief objective of the project :

The chemistry of the heterocyclic compounds is as logical as that of aliphatic or aromatic compounds. This study is of great interest both from the theoretical as well as practical stand point. A heterocyclic compound is one which possesses acyclic structure with at least two different kinds of atoms in the ring. The most common type, contain largely carbon atom, nitrogen, oxygen and sulphur are the most common heteroatoms,but many other elements, including even bromine, chlorine can also serve. The heterocyclic compounds containing the less common atoms have been subject to much investigation in recent years.

The variety of heterocyclic compounds is enormous, their chemistry is complex and synthesizing them requires great skill. Among large number of heterocycles found in nature nitrogen heterocycles are most abundant than those containing oxygen of sulphur owing to their wide distribution in nucleic acid instance and involvement in almost every physiological process of plants and animals.

Benzimidazole and benzothiazepines is a heterocyclic aromatic organic compound. This bicyclic compound consists of the fusion of benzene and imidazole. The most prominent benzimidazole compound in nature is *N*-ribosyl-dimethylbenzimidazole, which serves as an axial ligand for cobalt in vitamin B12.

Benzimidazole and its derivatives are used in organic synthesis and vermicides or fungicides as they inhibit the action of certain microorganisms. Examples of benzimidazole class fungicides include benomyl, carbendazim, chlorfenazole, cypendazole, debacarb, fuberidazole, furophanate, mecarbinzid, rabenzazole, thiabendazole, thiophanate. Benzimidazole structure is the nucleus in some drugs such as proton pump inhibitors and anthelmintic agents.

Detailed Report of Research Work done :

Research in the field of pharmaceutical has its most important task in the development of new and better drugs and their successful introduction into clinical practice. Central to these efforts, accordingly stand the search for pharmaceutical substances and preparation which are new and original.

In addition to these objectives the searching for drug which exhibit a clear advantage over a drug already known. Such advantages may be qualitative or quantitative improvement in activity, the absence of undesirable side effect, a lower toxicity, improved stability of decreased cost. It is important at the outset to note that drug discovery is not an unambiguous term in the pharmaceutical R & D world.

In light of the affinity they display towards a variety of enzymes and protein receptors, medicinal chemists would certainly classify them as privileged ‘sub-structures’ for drug dosing. The incorporation of the nucleus is an important synthetic strategy in studies of antimicrobial drug discovery. In the past few decades, benzimidazole , benzothiazepines and its derivatives have received much attention due to their chemotherapeutic values.

As per the proposed work plan I have synthesized verity benzimidazole and benzodiazepines derivatives. All the synthesized compounds were crystallized and purified by column chromatography. Compounds were obtained in good yield. They are off white to light brown coloured compounds freely soluble in ethanol, di chloro methane an acetic acid. Structural characterization of all the compounds was done by various spectroscopic method viz; IR,^{1}HNMR, ^{13} CNMR and Mass spectroscopy.

The minimal inhibitor concentration (MIC) of synthesized compound has been send for evaluation of their biological activity against two representatives Gram positive organisms viz. *S.aureus*(MTCC 96), *S.pyogenus* (MTCC 442) and two Gram-negative organisms viz. *E.coli*(MTCC 443) ,*P.aeruginosa* (MTCC 1688) by the broth dilution method recommended by National Committee for Clinical laboratory (NCCL) standards[19] All the newly synthesized compounds were also tested for their *in vitro* growth inhibitory activity against the yeast-like pathogenic fungus *C. albicans.* The strains used for the activity were procured from Institute of Microbial Technology, Chandigadh. DMSO was used as diluent/vehicle to get desired concentration of drugs to test upon standard strains. . Standard anti bacterial agents like Ampicillin and Chloramphenicol and anti fungal agent like K.Nystenin were screened under identical conditions for comparison.

Physical characteristics of Synthesized derivatives:

No.	Molecular Formula (M.W)	RF	% of Yield	% of C	% of H	% of N	% of X
				Calculated (Found.)			
R-1	$C_{14}H_{12}N_2O_2$ (240)	0.65	67	69.99	5.03	11.66	-
				69.97	5.06	11.61	-
R-2	$C_{15}H_{14}N_2O_2$ (254)	0.59	75	70.85	5.55	11.02	-
				70.83	5.54	11.04	-
R-3	$C_{21}H_{17}BrN_2O_2$ (426)	0.71	80	62.13	4.98	6.59	18.79
				62.12	4.96	6.60	18.82
R-4	$C_{15}H_{14}N_2O_3$ (270)	0.63	69	66.66	5.22	10.36	-
				66.64	5.21	10.33	-
R-5	$C_{15}H_{13}BrN_2O_2$ (333)	0.77	70	54.07	3.93	8.41	23.98
				54.09	3.95	8.42	23.94
R-6	$C_{14}H_{11}N_3O_4$ (285)	0.57	64	58.95	3.89	14.73	-
				58.96	3.85	14.72	-
R-7	$C_{14}H_{11}BrN_2O_2$ (320)	0.64	74	52.69	3.47	8.78	25.04
				52.70	3.46	8.75	25.06
R-8	$C_{16}H_{16}N_2O_2$ (268)	0.68	89	71.62	6.01	10.44	-
				71.61	6.03	10.45	-
R-9	$C_{16}H_{16}N_2O_2$ (268)	0.73	73	71.62	6.01	10.44	-
				71.60	6.04	10.42	-
R-10	$C_{17}H_{18}N_2O_2$ (282)	0.59	66	72.32	6.43	9.92	-
				72.30	6.41	9.90	-
R-11	$C_{21}H_{18}N_2O_2$ (330)	0.61	60	76.34	5.49	8.48	-
				76.31	5.52	8.53	-

R-12	$C_{13}H_9N_3O_4$ (271)	0.76	70	57.57	3.34	15.49	-
				57.55	3.32	15.50	-
R-13	$C_{15}H_{13}BrN_2O_2$ (333)	0.65	68	54.07	3.93	8.41	23.98
				54.11	3.91	8.44	23.96
R-14	$C_{15}H_{13}BrN_2O_2$ (333)	0.58	72	54.07	3.93	8.41	-
				54.06	3.95	8.40	-
R-15	$C_{22}H_{20}N_2O_2$ (344)	0.69	60	76.72	5.85	8.13	-
				76.71	5.83	8.11	-
R-16	$C_{20}H_{16}N_2O$ (300)	0.72	72	79.98	5.37	9.33	-
				79.94	5.33	9.31	-
R-17	$C_{13}H_8Cl_2N_2$ (263)	0.67	68	59.34	3.06	10.65	26.95
				59.30	3.03	10.61	26.96
R-18	$C_{16}H_{15}ClN_2O_2$ (303)	0.66	77	63.47	4.99	9.25	11.71
				63.45	4.98	9.23	11.73
R-19	$C_{15}H_{13}ClN_2O_2$ (289)	0.73	65	62.40	4.54	9.70	12.28
				62.44	4.53	9.75	12.28
R-20	$C_{18}H_{14}N_2O$ (274)	0.65	59	78.81	5.14	10.21	-
				78.83	5.15	10.25	-
R-21	$C_{14}H_{11}BrN_2O_2$ (319)	0.59	68	52.69	3.47	8.78	25.04
				52.72	3.49	8.79	25.07
R-22	$C_{13}H_9ClN_2O$ (245)	0.72	70	63.81	3.71	11.45	14.49
				63.84	3.75	11.43	14.55

- **TLC Solvent System**: - n-Hexane : Ethyl acetate (2:1 V/V)
- Some of compounds were characterized by IR, ^{1}HNMR**,** ^{13} CNMR and LCMS.
- Synthesized compounds are already sent for biological evaluation. Results are awaited.
- Structure of the compounds has been kept confidential as possible lead molecule will be patented after completion of the project.
- Further 16 compounds are already synthesized and are under characterization.

CERTIFICATE OF STARTING AND COMPLITION OF PROJECT

It is certified that Mrs. R.G.Gajjar has started her project work on 23/03/2012 and completed on **15/09/2015** funded by the university Grants Commission vide its sanctioned letter F. No. 47-2039/11 (WRO) dated 22nd Feb. 2012

Investigator Principal

CERTIFICATE OF UNSPENT BALANCE

It is certified that **Mrs.R.G.Gajjar** received MRP funded by the University Grants Commission vide its sanctioned letter F. 47-2039/2011 (WRO) dated 22nd Feb. 2012. She has utilized Rs. 1,33,087.00 from her all sanction amount and there is Rs. 1,345.00 unspent balance with her.

Investigator Principal

Annexure – VI

UNIVERSITY GRANTS COMMISSION
BAHADUR SHAH ZAFAR MARG

NEW DELHI-110 002
STATEMENT OF EXPENDITURE INCURRED ON FIELD WORK/TRAVELLING

Name of the principal investigator: Mrs.R.G.Gajjar

Name of the place visited	Duration of the visit		Mode of journey	Expenditure Incurred (Rs.)
	From	To		

Certified that the above expenditure is in accordance with the UGC norms for minor research project

SIGNATURE OF PRINCIPAL INVESTIGATOR **PRINCIPAL**

Name of the Scheme : Financial assistance to college for undertaking Minor Research Projects

PROJECT COMPLETION REPORT (PCR)

It is certify that the **Minor Research Project (Science)** in **Chemistry** subject sanctioned by **University Grants Commission** vide their letter File No. **47-2039/11(WRO)** dated **22/02/2012** towards **Mrs.R.G.Gajjar**, Smt. S. M. Panchal Science College, Talod-383 215 entitled **"Synthesis and biological evalution of Novel Nitrogen,oxygen and Sulphur containing heterocycles as antjmicrobial Agents"** was started on **23/03/2012** and completed on

SIGNATURE OF PRINCIPAL INVESTIGATOR

PRINCIPAL

Annexure-VI

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

STATEMENT OF EXPENDITURE INCURRED ON FIELD WORK

Name of the Principal investigator : Mrs.R.G.Gajjar

Name of the place visited	Duration of the Visit		Mode of journey	Expenditure Incurred(Rs.)
	From	To		
Inflibnet Centre (Ahmedabad) 23/05/2012	Gandhinagar	Ahmedabad	Hire Car	750.00 Rs.
Inflibnet Centre (Ahmedabad) 01/05/2013	Gandhinagar	Ahmedabad	Hire Car	750.00 Rs.
HNGU (Patan) 02/06/2014	Gandhinagar	Patan	Hire Car	1410.00 Rs.
HNGU (Patan) 24/06/2014	Gandhinagar	Patan	Hire Car	1410.00 Rs.

Certified that the above expenditure is in accordance with the UGC norms for Major Research Projects

SIGNATURE OF PRINCIPAL INVESTIGATOR **PRINCIPAL**