**UNIVERSITY GRANTS COMMISSION**
**WESTERN REGIONAL OFFICE**
**GANESHKHIND, PUNE – 411 007.**

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

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| 1 | Name and Address of the Principal Investigator | **Dr. E. M. Khan**<br>Allana Staff Quarters,<br>Allana College of Pharmacy Buiding,<br>Azam Campus, New Modikhana,<br>Camp, Pune – 411001 |
| 2 | Name and Address of the Institution | **Abeda Inamdar Sr. College of Arts, Science and Commerce, Pune.**<br>2390-B, K. B. Hidayatullah Road,<br>Azam Campus, New Modikhana,<br>Camp, Pune – 411001 |
| 3 | UGC Approval No. and Date | F. 47-1134/14 (General/92/WRO) dated 24/03/2017 |
| 4 | Date of Implementation | 24-03-2017 |
| 5 | Tenure of the Project | 2 Years |
| 6 | Total Grant Allocated | Rs. 4,20,000/- |
| 7 | Total Grant Received | Rs. **2,92,500/-** |
| 8 | Final Expenditure | Rs. **3,01,714/-** |
| 9 | Title of the Project | Design and Synthesis of Novel Quinone-Coumarin hybrids as Anticancer Agents Against Pancreatic Cancer |
| 10 | Objectives of the Project | i) Design of hybrids of Quinone-Coumarin through computational tools.<br>ii) Synthesis of best candidate molecules with determination of inhibitory potential.<br>iii) *In vitro* testing against pancreatic cancer cell lines and further lead optimization. |
| 11 | Whether Objectives Were Achieved (Give Details) | The hybrids of Quinone-Coumarin were synthesized, characterised and evaluated for their anticancer potential against different cancer cell lines. Their binding affinities were checked using molecular docking tool. These hybrids were further evaluated for their drug-likeliness and found to exhibit promising ADMERT and drug-likeness properties. |
| 12 | Achievements From the Project | The synthesis of novel Quinone-Coumarin hybrids was synthesized and the structures were confirmed by spectral characterization. The hybrids were further evaluated for *in vitro* anticancer activity and their mode of action was studied using molecular docking. All the synthesized hybrids exhibited good anticancer potential. The computational tools were used for the identification of the target proteins implicated in cancer progression and generation of drug resistance to chemotherapeutic treatment. |
| 13 | Summary of the Findings (In 500 Words) | New Quinone-Coumarin hybrids were synthesized from 3-acetylcoumarin and 2,6-ditertiarybutyl-1,4-benzoquinone and tested for *in vitro* anticancer activities against five |

different cancer cell lines viz. MCF-7, MDA-MB-231, COLO-205, HT-29, A-549 and MIA-Pa-Ca-2. The cytotoxicity of the synthesized hybrids was tested on human peripheral mononuclear cells (PBMCs) and they were found to non-cytotoxic to the normal cells. From the calculated GI50 values of the analogs, it is observed that the hybrids DTBSB and DTBSN exhibited good anti-proliferative potential against all types of tested cancer cell lines. The compound DTBSB was found more active against MCF-7, HT-29 and MIA-Pa-Ca-2 cell lines with remarkable GI50 values while DTBSN exhibited its best potential against MDA-MB-231, COLO-205 and A-549 cancer cell lines. The GI50 values of both these analogs are in the range of 24 to 40 μg/ml making them the choice of interest for further lead development. The *in vitro* results appear to be in agreement with the observations in molecular docking study. The predicted absorption, distribution, metabolism, excretion and toxicity (ADMET), pharmacokinetic properties and drug likeness via *in silico* methods are in desirable range which shows that these compounds are pharmacokinetically compatible and hence could be the appropriate lead structures for the design of new chemotherapeutics. The pharmacokinetics and drug likeness evaluation showed a high level of GI absorption upto 94% and with all these analogs and the molecules have a great solubility potential in water. The VDss, BBB membrane permeability (logBB) and CNS permeability were used to characterize the distribution of compounds and all these analogs showed a good distribution in the body. All the synthesized analogs were unable to inhibit CYP2D6 and but they were found to be good CYP3A4 inhibitors depicting the ability of these analogs to metabolize the xenobiotics in the body. The predictions also showed non-toxic nature of these analogs, which is reflected through high values of the total clearance, non-hepatotoxic nature and no skin sensitization. These results of ADMET studies revealed that the compounds have got good ADMET and pharmacokinetic properties. Furthermore, the drug likeness study revealed that most of the compounds fulfilled all the requirements of Lipinski, Ghose and Veber but the hybrid DTBSN exhibited one violation in Egan filter due to larger TPSA value. All the analogs showed Muegge's filter violations which corresponds to XLOGP3 >5. All molecules resist Brenk's rule due to coumarin, quinone and imine fragments. All analogs contains

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| | | quinone moiety, which is responsible for one alert in PAINS. These preliminary results with few exceptions may provide the lead for the design of more potent and selective anticancer drugs. Further in vitro and in vivo studies would be needed for confirmation of the chemoinformatics investigation. |
| 14 | Contribution to the Society (Give Details) | At this time, these studies and predictions about the pharmacological effects of the developed quinone-coumarin may not immediately benefit society. However, future research and development could lead to the development of drug-like compounds with improved target selectivity and safety profiles. |
| 15 | Whether Any Ph. D. Enrolled/ Produced out of the Project | No |
| 16 | No. of Publications out of the Project (Please Attach Re-Prints) | No |

**(PRINCIPAL INVESTIGATOR)**

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**(REGISTRAR/PRINCIPAL SIGNATURE & SEAL)**

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