Project Title: Quantum Computational research on medicinal drug development

Abstract: The project's objective is to investigate how Density Functional Theory (DFT) can be used to treat chronic diseases using specific biomolecules turned into nanoparticles with specific composites. The novelty in CADD techniques are introduced via Drug Solubility, Permeability, Force Field, Molecular Docking / Drug Design, 3D QSAR Approach, Pharmacophore Modelling, and Target-based Drug Design. To identify the new drug for protein-ligand complexes, pharmacokinetics and pharmacodynamics require correct ligand apprehension; however, a qualitative and quantitative evaluation of experiences further supports drug development.

Keywords:

Health; Molecular Dynamics; DFT: Target prediction; Quantum Mechanics; Computer Aided Drug Design

Faculty Details:

Note: It is mandatory that the project guide shall be the PI of the Project under Faculty Project Program.

1.1. Name: Dr.A. Suvitha

1.2. Department: Physics

1.3. Designation: Associate Professor

1.4. Institution Name: CMR Institute of Technology

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1.7. Gender: Female

1.8. List of projects applied and sanctioned

S. No	Title	Cost in Lakh	Project Title	Role as PI/Co- PI	Agency/Date	Status
1.	Young Researcher Award**-**	**2500000**	Quantum computational drug design of selected nanoparticles for immune enhancement	Principal Investigator	**LTMT-2022**	**Applied**
2	Swarna Jeyanthi	2500000	Ligand creativity to counter COVID 19 by Quantum computational aided drug design	Principal Investigator	DST (2020-21)	Selected for Final round.
3	VGST(RGS/F)	500000	Spectroscopic and CADD study of compounds used for treating Ebola virus	Principal Investigator	Research Grants for Scientists	Applied

					/Faculty (RGS/F) (2018-19	
4	S. Ramachandran-national bioscience award for career development 2019	965548	Re purposing of Neurological Drugs using CADD Technique	Principal Investigator	S.R-National Bioscience Award 2019	Applied
5	DST-Swarna Jayanti Fellowships 2017-18	38,00001	Molecular studies on neurological drugs using quantum computational techniques	Principal Investigator	DST, March 2018	Applied
6	Scheme for Early career Research Award	21,00000	Spectroscopic and Quantum computational study of compounds used for treating Ebola virus	Principal Investigator	DBT, Aug 2017	Applied
7	TATA INNOVATION FELLOWSHIP 2016-17	15,00000	Molecular structure activity on pharmaceutical applications of certain Bio molecules using spectroscopic investigation	Principal Investigator	DBT, Nov 2016	Applied
8	Scheme for Funding Industry Relevant R&D	50,00000	Molecular reports on neurological drugs using quantum computational techniques	Principal Investigator	DST-SERB, Nov 2016	Applied
9	Jawaharlal Nehru memorial fund	1,00000	Quantum Computational studies of certain Bio molecules in pharmaceutical field using spectroscopic investigation	Principal Investigator	Jawaharlal Nehru memorial, Dec 2016	Applied
10	Women's Scientist award A scheme	5,30000	Molecular structure activity on pharmaceutical applications of certain molecules using spectroscopic investigation	Principal Investigator	June 6th 2013	Selected

Section B: Technical Details

1. Background:

1.1. Description of the problem:

A healthy lifestyle, as recently highlighted by the World Health Organization, improves all bodily functions, including immunity. A healthy diet that promotes immunity is an important part of living a healthy lifestyle because it promotes a healthy immune system that protects against infection and other diseases. The availability of such an immune-boosting drug that is easily accessible and affordable to the average person is thus a top priority.

Over the last 40 years, the complexity of drug development has increased dramatically, necessitating preclinical testing, investigational new drug (IND) applications, and completed clinical testing before receiving FDA marketing approval. Computer-aided drug design (CADD) encompasses a variety of theoretical and computational approaches used in advanced drug discovery. In addition, implementation on representative trends in current drug discovery that are shaping the development of novel methods, such as computer-aided drug repurposing, is underway.

1.2. Review of work already done:

In the report published recently in WHO, "Neurological disorders, and Public health challenges" cerebrovascular has rapidly became one of the deadliest diseases since its discovery [1]. In all over world more than one billion people are affected by this disease in that 6.8 million people are dying annually [1]. The survey reveals that the Neurological disorder, particularly cerebrovascular is the most common age-related disorder. In India, nearly 77 million people were affected by this disease in 2001, which will rapidly increase to around 177 million by the year 2025[2]. In one of the most populated and polluted city like Bengaluru, around 6260/100000 for both Urban and Rural people were affected by Parkinson's disease in 2004 [3]. In Bengaluru, due to stress approximately 50-60 patients of strokes are admitted to hospitals every month [4]. Nowadays 20-30% younger than 45 years old people are more affected by cerebrovascular disease in south India as compared to west India [5]. The following papers were published in reputed Journals based on subset of structures of bio medical compounds with properties and reactions observed by computational experimental methods.

1. A. Suvitha ,S. Periandy ,S. Boomadevi , M. Govindarajan "Vibrational frequency analysis, FT-IR, FT- Raman, ab initio, HF and DFT studies, NBO, HOMO–LUMO and electronic structure calculations on pycolinaldehyde oxime" Spectrochimica Acta Part A: 117 (2014) 216–224. Impact factor.3.23. (Q2 Journal)

2. M. Govindarajana, M. Karabacak, A. Suvitha, S. Periandy "FT-IR, FT-Raman, ab initio, HF and DFT studies, NBO, HOMO–LUMO and electronic structure calculations on 4-chloro-3-nitrotoluene" Spectrochimica Acta Part A 89 (2012)137– 148. Impact factor.3.23 (Q2 Journal)

3. A.Suvitha, S. Periandy, M. Govindarajan and S.Ramanlingam "Vibrational frequency analysis, HF and DFT(B3LYP and B3PW91) studies,HOMO–LUMO and electronic structure calculations on 2-chloro-5- nitropyridine" Asian Journal of physics 23, no 6, (2014) 1069-1078. Impact factor.1.166

4. A.Suvitha, S. Periandy, and M. Govindarajan "Vibrational spectroscopic studies, HOMO–LUMO, NBO, UV and NMR analysis of 4-acetylpyridine" Asian Journal of physics 23, no 6(2014)1053-1062. Impact factor.1.166

5. A.Suvitha, S. Periandy, M. Govindarajan and P.Gayathri "FT-IR, FT-Raman spectra and HF-DFT methods and NBO, HOMO-LUMO and electronic transition studies on 2, 2, 4 trimethyl Pentane"

Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 138 (2015)900– 912. Impact factor.3.23. (Q2 Journal)

6. Umadevi M, Suvitha A, Latha K, Rajkumar BJ, Ramakrishnan .v "Spectral investigations of preferential solvation and solute-solvent interactions of 1,4-dimethylamino anthraquinone in CH2Cl2/C2H5OH mixtures". Spectrochim Acta A Mol Biomol Spectroscopy 67(2007)910-915. Impact factor 3.23. (Q2 Journal)

7. A.Suvitha, S. Periandy, and P.Gayathri "NBO, HOMO–LUMO, UV, NLO, NMR and vibrational analysis of veratrole using FT-IR, FT-Raman, FT-NMR spectra and HF–DFT computational methods" Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 138 (2015) 357–369. Impact factor.3.23. (Q2 Journal)

8. Sudhir M. Hiremath, A. Suvitha, Ninganagouda R. Patilc , Chidanandayya S. Hiremathd, , , Seema S. Khemalapured,Subrat K. Pattanayake, Veerabhadrayya S. Negalurmath, Kotresh Obelannavar, Molecular structure, vibrational spectra, NMR, UV, NBO, NLO, HOMO-LUMO and molecular docking of 2-(4, 6-dimethyl-1-benzofuran-3-yl) acetic acid (2DBAA): Experimental and theoretical approach, Journal of Molecular Structure, 1171 (2018) 362-374 May 2018. Impact factor.2.02 (Q2 Journal)

9. Sudhir M. Hiremath, A. Suvitha, Ninganagouda R. Patil, Chidanandayya S. Hiremath, Seema S. Khemalapure, Subrat K.Pattanayak, Veerabhadrayya S. Negalurmath, Kotresh Obelannavar, Sanja J. Armaković, Stevan, ArmakovićSynthesis of 5-(5-methyl-benzofuran-3-ylmethyl)-3H-[1, 3, 4] oxadiazole-2-thione and investigation of its spectroscopic, reactivity, optoelectronic and drug likeness properties by combined computational and experimental approach. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 205 (2018) 95–110, July 2018. Impact factor.3.23. (Q2 Journal)

10. Suvitha A, Spectral investigations, NLO, NBO, HOMO-LUMO, MEP, ADME parameters of 2-methyl- benzoquinoneUsing quantum computations and CADD technique, AIP Conference Proceedings 2162, 020037 Impact factor.1.2 (2019).

11. A. Suvitha, Insights of structure-based pharmacophore studies and inhibitor design against Gal3 receptor through molecular dynamics simulations, Taylor & Francis / Journal of Biomolecular Structure and Dynamics, IF: 3.22 (2020). (Q2 Journal).

12. A.Suvitha, Quantitative experimental and theoretical research using the DFT technique on the structural, UV, electronic, and FMO properties of Gammaxene 11, 6, 2021, 14240 - 14250 Biointerface Research in Applied Chemistry, Scopus (Elsevier) (Q4) Journal.

13. A.Suvitha, Nonlinear Optical Crystalline Nature Bis (2, 6-Diaminopyridine) Hydrogen Phthalate Nitrate Monohydrate (APPN) : Development and its Phase Matching Nature, Results in Optics 3 (2021) 100075.

14. A.Suvitha, The adsorption of 1-Chloro-1,2,2,2-tetrafluoroethane onto the pristine, Al-, and Ga-doped boron nitride nanosheet", has been accepted for publication in Iranian Journal of Science and Technology, Transactions A: Science(2021).

15. A.Suvitha, Quantum Chemical Studies on Structural, Spectroscopic, Thermochemistry, Photo-physical and Bioactivity Properties of m-Cresol Purple Dye(2021) has been accepted for publication in Biointerface Research in Applied Chemistry, Scopus (Elsevier) (Q4) Journal.

16. A.Suvitha, Boosted electronic, optical, and NLO responses of homo P-nanoclusters via conducting polymeric substituents, Computational and Theoretical Chemistry,2021 (Elsevier) (Q3) Journal. 113343

17. A.Suvitha, Exploring crystal electronic op□cal and NLO properties of ethyl 4-(3,4 dimethoxy Phenyl 6 methyl 2 thioxo 1,2,3,4 tetrahydro Pyrimidine 5 carboxalate (MTTHPC), published on 22nd July 2021 in Optical and Quantum electronics(Q2)

18. A.Suvitha, Boosted electronic, optical and NLO responses of Homo P nanoclusters via conducting polymeric substituents, Published on 21st June 2021 in Computational and theoretical chemistry(Q3)

19 A.Suvitha, Molecular structure, FT Raman, IR, NLO, NBO, HOMO-LUMO analysis, physicochemical descriptors, ADME parameters, pharmacokinetic Bioactivity report on 2, 3, 5, 6 –Tetra Chloro-P- Benzoquinone, published on April 2021 in Journal of Structural Chemistry/ Journal(Q3)

20. A.Suvitha, Experimental and theoretical validation studies of ASnO3 (A=Ba, Ca, Sr) nanofibers for bioactivity applications, accepted on 5th May 2021 on International Journal of Nanotechnology/ Journal(Q4).

20. A.Suvitha, Optimizing pharmacokinetics via ADMET, Bioactivity of Zr substituted Samarium-Doped Ceria Nanomaterials, accepted on 4th June 2021 on International Journal of Nanotechnology/ Journal(Q4)

21. A.Suvitha, Experimental and theoretical analysis for the structural, FT-IR, NLO, NBO and RDG properties of Lindane using DFT Technique, accepted on 25th and 26th August 2021 in AIP conference proceedings.

22. A.Suvitha, Exploring the electronic and optical absorption properties for homo and hetero pyrrole-graphene quantum dots, accepted on Aug 30, 2021 in Journal of Computational Electronics (Q2)

23. A.Suvitha, Experimental, Computational analysis of Butein and Lanceoletin for Natural Dye Sensitized Solar cells and stabilizing efficiency by IoT published on September 14th 2021 in Environment, Development and Sustainability (Q2)

24. Optical limiting behavior, Nonlinear optical studies geometrical descripters, chemical properties and Topology analysis on Tetraethylammonium L-tartarate dihydrate Single Crystal, Journal of Molecular Crystals and Liquid Crystals (Q3), accepted on 25th November 2021

25. Boosted electronic, NLO and absorption characteristics for quercetin and taxifolin; comparative experimental and DFT studies, Journal of Bio interface Research in Applied Chemistry (Q3), 7th November 2021.

26. Organic hexamine p-nitrophenol crystal: growth, optical, electrical, and mechanical density functional theoretical studies for nonlinear optical applications ,optical materials (Q1), 26th march 2022.

27. exploring the crystal, ft-IR, optical, and NLO properties of 3,4-dichloro-6-ehtyl-6h-pyrano[3,2- c]quinoline-2,5-dione (dcpq),jan 2022 28 Diamond Morphology CuO Nanomaterial's Elastic properties, ADMET, Optical, Structural Studies, Electrical Conductivity and antibacterial Activities Analysis, Inorganic and Nano-Metal Chemistry (Q3), Accepted on 17th Jan 2022

1.3. Enhancement / modification done with respect to previous work:

DFT is the most successful and also important approach to computing the electronic structure of molecules. The DFT calculations in quantum computation with the hybrid exchange-correlation functional method B3LYP [6-8], which are significant in systems with various calculations, are found to be very effective in the above parameters. These enormous unlimited potential and applications are the key to this work and the evaluation of the key experimental and theoretical parameters and their analysis of such biologically important molecules which are widely used in the treatment of neurological disorder. All CADD techniques, Drug solubility, permeability, Force field, Molecular Docking/ Drug designing, 3D QSAR approach, Pharmacophore modelling, Target based drug design Pharmacokinetics/ Pharmoco dynamics approaches are required accurate apprehension of the ligand to distinguish the new drug for protein-ligand complexes; Further over, a qualitative and quantitative appraisal of interactions further justifies the efforts in drug development.

- The following data is the theoretical data with a subset of structures, properties and reactions on the observed experimentally. The calculations are based on Schrodinger's equation which includes:

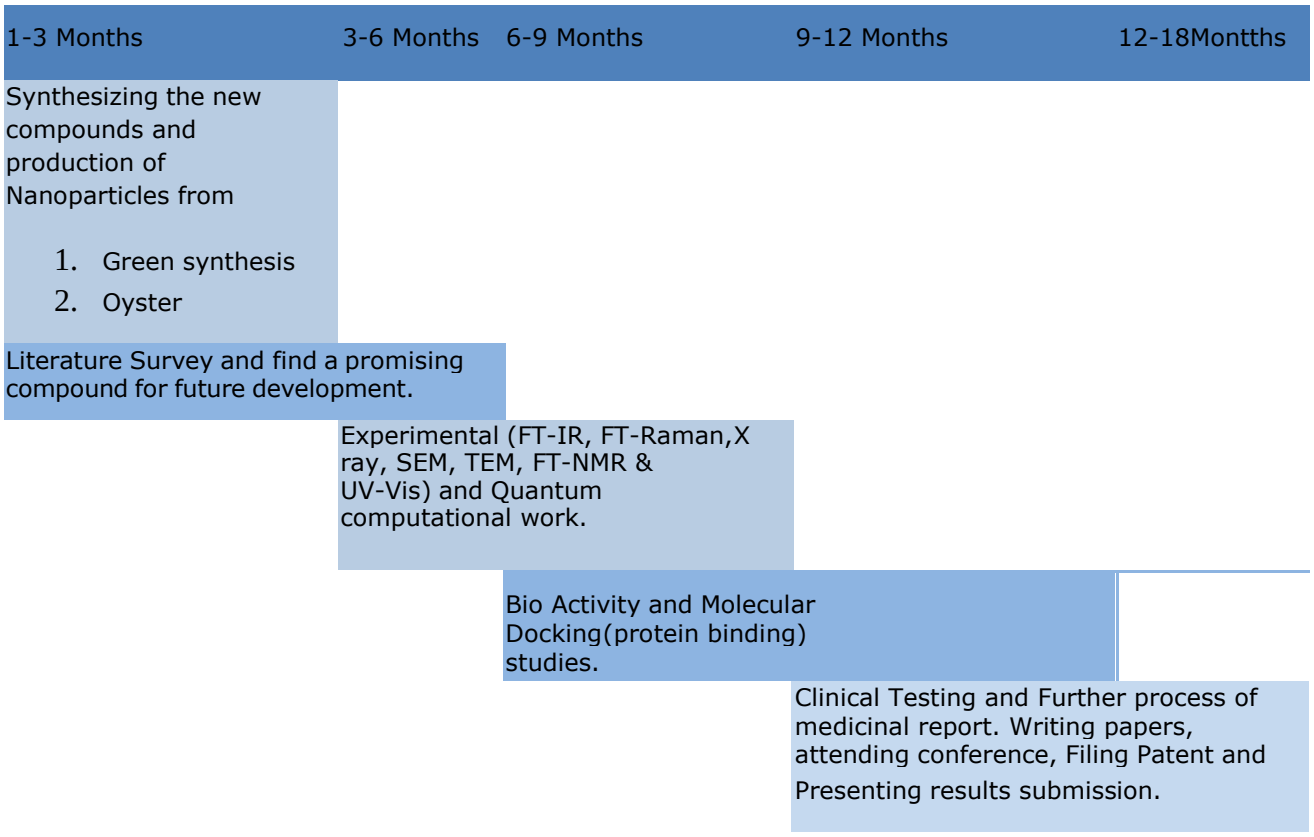
- Molecular Geometry optimizations
- FTIR, FT Raman Frequency mode of vibrations
- Transition structures
- Natural and mulliken charge calculations
- Molecular electrostatic potentials
- HOMO-LUMO energy distribution
- CADD approach using all the methods:
- Drug solubility/ permeability
- Chemical shift calculation by NMR technique

- Potential energy distribution (PED)
- Natural bond orbital analysis(NBO)
- QR/ MR / Force field
- Molecular Docking/ Drug designing
- 3D QSAR approach
- Pharmacophore modelling
- Target based drug design
- Pharmacokinetics/ Pharmoco dynamics
- Thermodynamic calculations– reactions of heat and activation of energy. They are also useful for:

    - Determination of properties that are inaccessible experimentally.
    - Experimental Interpretation of Experimental Data.

All the techniques in CADD have been carried out in parallel using certain standard methods and molecular docking. These enormous unlimited potential and applications are the key to this work and the evaluation of the key experimental and theoretical parameters and their analysis of such biologically important molecules which are widely used in the treatment of chronic disease.

1.4. Rationale for taking up the project:



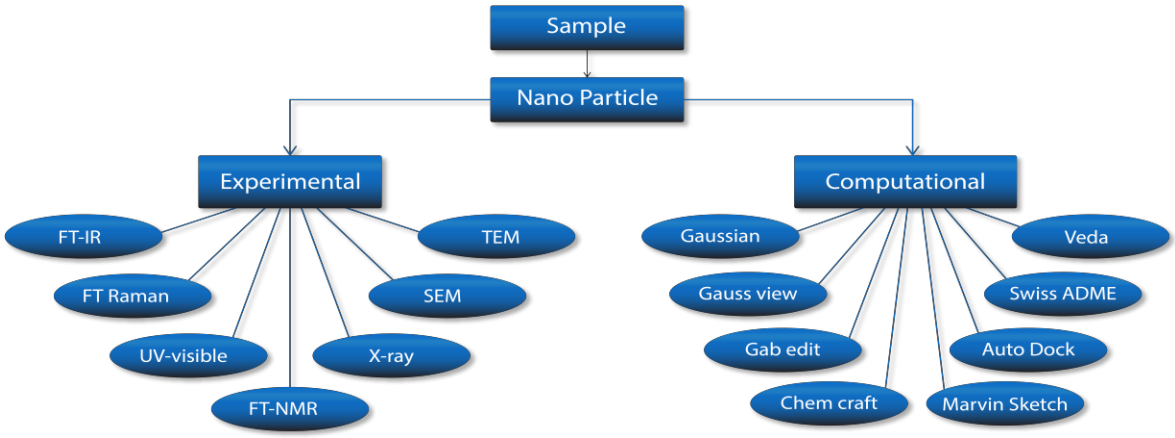
2. Description of the proposal:

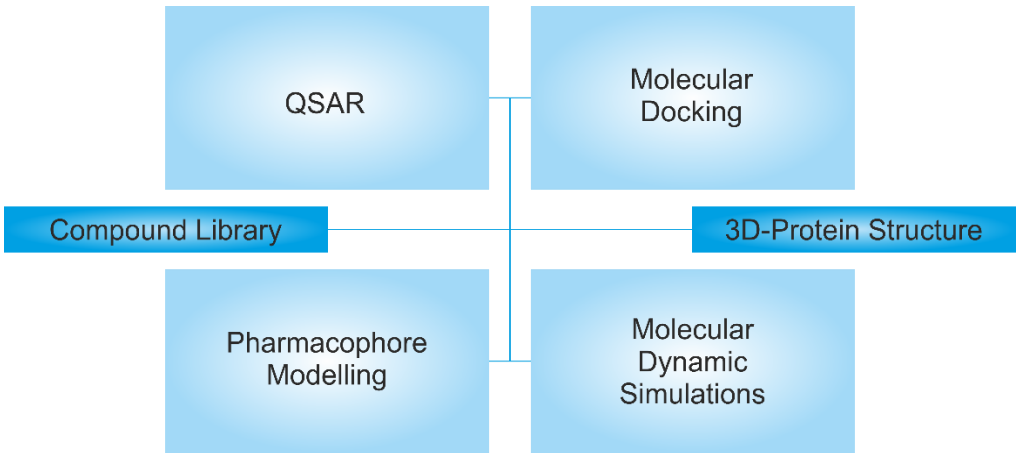
2.1. Objectives of the project:

- The project's objective is to investigate the drug design based on computational methods (CADD & Density Functional Theory (DFT)) which can be used to treat chronic diseases using specific biomolecules turned into nanoparticles with specific composites.
- The novelty in CADD techniques are introduced via Drug Solubility, Permeability, Force Field, Molecular Docking / Drug Design, 3D QSAR Approach, Pharmacophore Modelling, and Target-based Drug Design.
- To identify the new drug for protein-ligand complexes, pharmacokinetics and pharmacodynamics require correct ligand apprehension; however, a qualitative and quantitative evaluation of experiences further supports the healthy drug development.

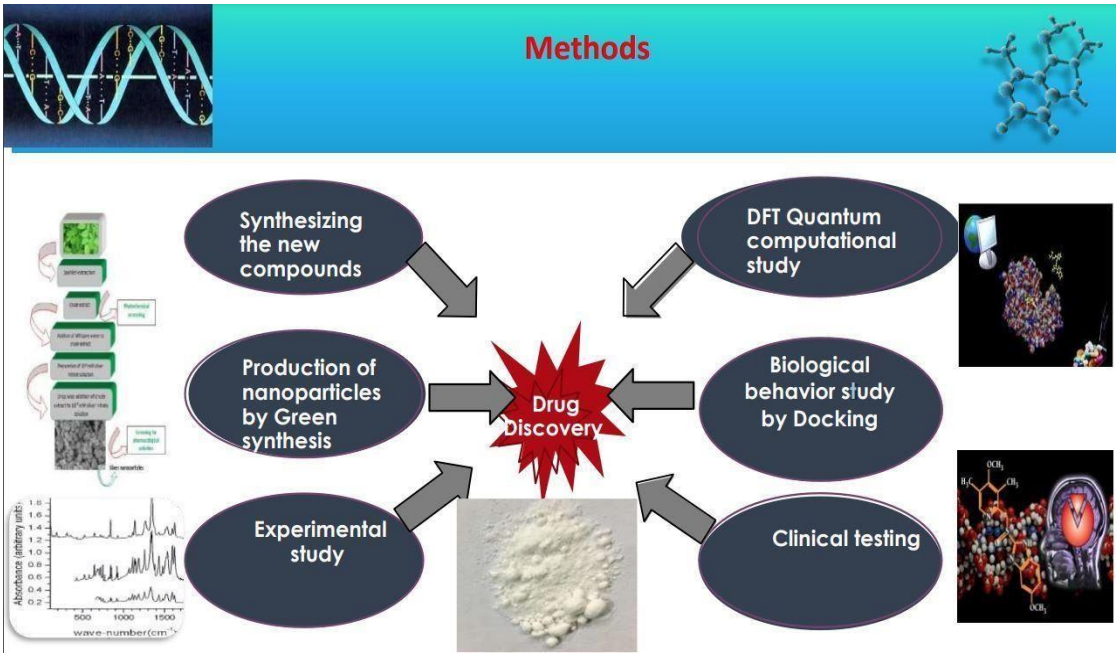
2.2. Methodology of the project:

- Generating nanoparticles by synthesizing highly biologically and pharmaceutically activeunknown compounds from selected sample materials.
- FT-IR, FT Raman, UV visible, FT-NMR, X-ray, SEM and TEM (Experimental approach)Various Scaled Quantum Mechanical approach by DFT (Computational Approach) and Nano science.
- Analyzing Biological activity by Molecular Docking and Computer aided drug design(CADD) Studies.
- Clinical testing From Hospitals & Filing a Patent.
- Approaching Pharma Companies for further Process of Production of Drugs.




QSAR
Molecular Docking
Compound Library
3D-Protein Structure
Pharmacophore Modelling
Molecular Dynamic Simulations

2.3. Diagrams/Designs/Flow charts:



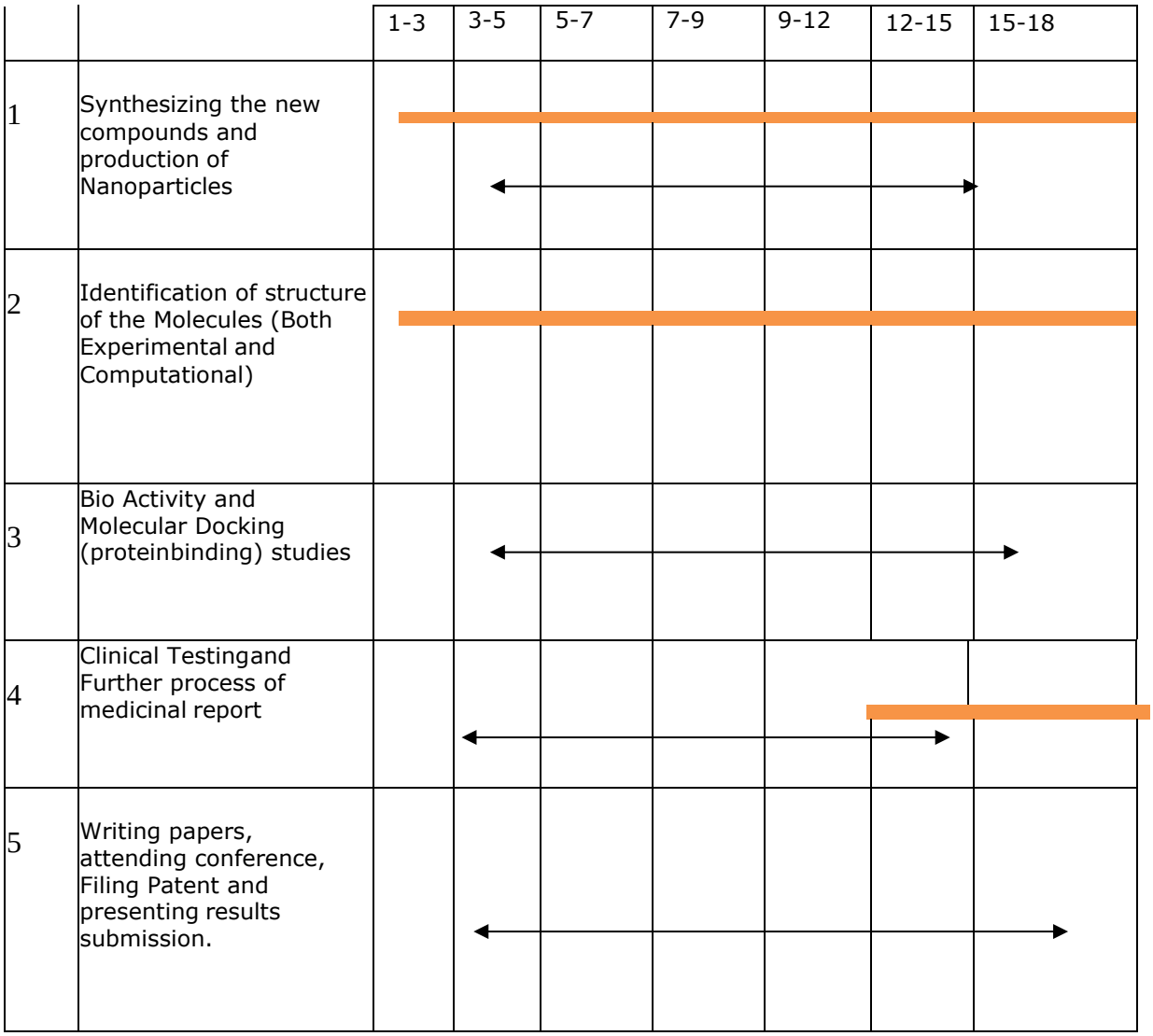
3. Expected output of the project:

- ✓ The availability of such a drug that is easily accessible and affordable to the average person is therefore of primary concern. As a result, this is critical in moving forward with some very important virus control compounds that are also cost-effective immunity boosters.
- ✓ Publication of findings in peer-reviewed international journals, and, if necessary, patent application. Articles will be presented at regional and international conferences, as well as workshops on process design and special computing devices.
- ✓ This same technology incubation will collaborate with a pharmaceutical company for drug development/start-up creation and process demonstrations.

4. Work plan:

	Work	Year -I	Year- I & II	Year-II
		(Months)	(months)	(months

		1-3	3-5	5-7	7-9	9-12	12-15	15-18
1	Synthesizing the new compounds and production of Nanoparticles							
2	Identification of structure of the Molecules (Both Experimental and Computational)							
3	Bio Activity and Molecular Docking (proteinbinding) studies							
4	Clinical Testingand Further process of medicinal report							
5	Writing papers, attending conference, Filing Patent and presenting results submission.							



5. Likely impact: (Please attempt to quantify)

5.1. Social Benefits:

Innovative solutions, particularly those that reduce poverty and benefit a wide number of people, are desperately needed. Given India's size and limited resources, low-cost, high-impact solutions are necessary. These advancements are linked to computing power, macromolecule structural information, and biochemical understanding of epigenetic control processes. These three components are expected to grow in importance over time, implying that CADD will play a larger role in medicinal chemistry in the development of high-selective, low-toxic, and more potent bioactive

molecules for the treatment of diseases involving lipid metabolism such as cancer, psychiatric disorders, and cardiac illness.

5.2. Economic Benefits:

Bioprocessing is paving the path for the research and manufacture of new medicines. Pharmaceutical firms face scaling challenges. The development stage is simulated and the exact required for pharmaceutical input to make a certain drug is developed using advanced analytics, quantum calculations, and CADD approaches.

6. Suggested post project activities:

The pharmaceutical industry and the scientific community will benefit greatly from useful observations and conclusions based on synthesized nanoparticles. Throughout the programme, the study will be published in mainstream and reputable international publications on a regular basis. For drug development/start-up creation and process demonstrations, the proposed technology incubation will work with a pharmacy sector.

7. Implementation arrangements proposed for the project (linkages and management structure):

Publication of findings in peer-reviewed international journals, and, if necessary, patent application. Articles will be presented at regional and international conferences, as well as workshops on process design and special computing devices.

8. Suggestions for replicability of the product outcomes:

1. The project's goal is to investigate the use of selective immunity booster biomolecules converted into nanoparticles with selected composites to boost immunity using Density Functional Theory, experimental techniques, and computer aided drug design (CADD).

2. As a result, the availability of such a drug that is easily accessible and affordable to the average person is of primary concern. As a result, moving forward with some critical virus control compounds that are also cost-

effective immunity boosters is critical.

3. The reports will make a substantial contribution to the advancement of information regarding medications used in the immune system. I'm hoping it will encourage more collaboration and innovation, as well as a dedication to preventing these terrible conditions and providing the best possible treatment for those who are affected.

9. Risks:

Not Applicable

10. Suggested plan of action for utilization of expected outputs from the project (commercialization / entrepreneurship / patent etc.):

Innovative solutions, particularly those that reduce poverty and benefit a wide number of people, are desperately needed. Given India's size and limited resources, low-cost, high-impact solutions are necessary. These advancements are linked to computing power, macromolecule structural information, and biochemical understanding of epigenetic control processes. These three components are expected to grow in importance over time, implying that CADD will play a larger role in medicinal chemistry in the development of high-selective, low-toxic, and more potent bioactive molecules for the treatment of diseases involving lipid metabolism such as cancer, psychiatric disorders, and cardiac illness.

Bioprocessing is paving the path for the research and manufacture of new medicines. Pharmaceutical firms face scaling challenges. The development stage is simulated and the exact required for pharmaceutical input to make a certain drug is developed using advanced analytics, quantum calculations, and CADD approaches.

As a result, valuable observations and conclusions based on project reports will substantially help the scientific community. I mapped the material and technique to highlight the trends in current research and to identify opportunities for further research in response to the increasing number and range of innovation studies on the pharmaceutical industry.

11. Any other information required related to the proposed project:

During the years 2021- 2022, I filed 6 patents, in that 2 patents are in final stage(grant) and I've published totally 20 international innovative papers in

reputable journals connected to this study, as well as a book co-authored with international professors from the Functional Food Centre inc. USA, which is accessible on AMAZON.

Halgurd Nadhim Mohammed, Layth Jasim Mohammed, Isaac Karimi, A Suvitha "A Computational Effort to Deciphering Putative COVID-19 3C-like Protease Binders in the Selected Recipes of Kurdish Ethnomedicine: An Approach to Find an Antiviral Functional Tea", Functional Foods and Viral Diseases. BOOK, ISBN: 979-8675209637.

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