**Training Report**

**On**

**Various Laboratories Techniques *and Hospitality***

**At**

***BLDEA.S.S.M. College of Pharmacy and Research Centre***

***Abhay Kumar Thakur***

***2004120015***

***6TH Semester, B. Pharm, 22-23***


**K.R. Mangalam University**

***School of Medical and Allied*** Sciences

**Gurugram**

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BLDE Association's
**SHRI SANGANABASAVA MAHASWAMIJI COLLEGE OF PHARMACY AND RESEARCH CENTRE**
Formerly : BLDEA's College of Pharmacy, Bijapur (Vijayapura), since 1982
Accredited by NAAC with 'A++' Grade

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Ref. No. BLDEA`S/BPC/156/2023-24 Date : 28/07/23

## TO WHOM IT MAY CONCERN

Certified that Mr. Abhay Kumar Thakur S/o., Shivji Thakur has successfully completed hands-on-training on various laboratory analytical techniques in BLDEA's SSM College of Pharmacy and Research Centre, Vijayapura and clinical departments in BLDE Hospital and Research Centre, Vijayapura from 11-07-2023 till 26-07-2023.

During the training period, his character and conduct were good. We wish him a successful and good career.

28/7/23
PRINCIPAL
Principal,
BLDEA's S.S.M. College of
Pharmacy & Research Centre
VIJAYAPUR-586103

## CANDIDATE'S DECLARATION

I, Abhay Kumar Thakur, roll no. 2004120015, a student of Pharma 6th semester of School of Medical and Allied Science, K.R. Mangalam University hereby declare thatI own the full responsibility for the information, results etc. provided in this report. I have taken care in all respect to honor intellectual property rights and have acknowledged the contribution all in my training. I am thankful for allowing me to use the learning for academic purposes.

**Signature:**
**Name of student: ABHAY KUMAR THAKUR**
**Roll number: 2004120015**
**Place:**
**Date:**

## ACKNOWLEDGEMENT

It's a great pleasure to present this report of training in BLDEA. S.S.M. College of Pharmacy and Research Centre (name of organization/hospital). At the outset, I would like to express my immense gratitude to my training guide/incharge Dr. C. Mallikarjuna Setty (principle), Mr. Ajay Shahapur (assistant professor, Dept. of Pharmaceutics),S.C.Marapur (HOD of Pharmaceutics ) ,Dr. H.Shivkumar (HOD of Pharmacology), Dr. E.N.Gaviraj (HOD of pharmacognosy),Dr. Santosh Kumar Karajgi (HOD of Quality Assuarance),Dr. S.Z.Inamdar (HOD of Pharmacy Practice), for guiding me from the inception till the successful completion of the training. I would also like to thank my friends and all my group members for their help and cooperation throughout the training. I am thankful to all who have helped me during the training. In addition, I thank one and all who have been instrumental in helping me complete this training. I am extremely grateful and indebted to my family for being pillars of strength, for their unfailing moral support, and encouragement. I treasure their blessings and good wishes and dedicate this study to them.

**Signature of student**

**Name: Abhay Kumar Thakur**
**Roll no. : 2004120015**
**Place:**
**Date:**

## ABSTRACT

I am Abhay Kumar Thakur from B.Pharma 6th semester, I am glad that I got a chance to do something different in a different environment. This training was for 15 days, which lasted from 11-07-2023 to 26-07-2023, meanwhile we got a chance to learn a lot, got a chance to immerse ourselves in a new environment. During this training session we learned and explored many things like we got to know the actual meaning of pharmacy, what is the job of pharmacy? After that we explored various subjects like pharmaceutical chemistry, pharmaceutics, Pharmacognosy, quality assurance, pharmacology and pharmacy practices.

The main motive of the internship is what we learned in previous syllabus that observed practically, because pharmacy is not a theoretical subject it is all depends on practical knowledge as well. In "BLDEA S S M College and research center", we did some practical work in different laboratory. In pharmacology studied about dose calculation, animal handling. In chemistry we studied about synthesis and drug design we used some software then we checked molecule (some software are like Pyrex, CDS, chemdraw etc.). Adding some protein chain in special structure and removal of some ligand from molecule then we checked the physicochemical parameter. In pharmacy practice we studied about how we control drug-drug interaction. In pharmaceutics we studied about tablet punching, spray dryer and lyophilization, similarly we explore the entire department.

After the laboratory work, I also visited hospital. In hospital visit, collecting some patient information I learned that how to connect with patient, how to collect patient past history and there past medical history. I also learned about how to listen human heartbeat with the help of stethoscope.

Finally, I got a chance to learn a lot. There professor and senior management team very helpful, they told us about future scope of pharmacy gave chance to operate advanced technology equipment.

## INTRODUCTION

**BACKGROUND: -** Internship gives students exposure to the working environment. The internship program is designed to provide students engaged in a field experience with an opportunity to share their insights, to explore the links between students' academic preparation and their field work, and to assist participants in developing and carrying out the major research project which will serve to culminate their internship experience. Internships are individualized and tailored to the needs and interests of each student in the program. As part of the internship experience, students are expected to take an active role in finding an appropriate internship for themselves.

**PURPOSE: -** An internship is an introductory position and is often a way into a particular career path. following are some purposes of an internship for students:

1. **Includes research experience: -** In scientific fields, for instance, an internship might consist of assisting with research in a laboratory. You can test the research skills you learned in your college courses in a practical setting and meaningfully contribute to the important research the laboratory does.
2. **Provides access to a variety of tasks and departments: -** Some internships may assign you specific tasks every day. Others might expose you to the duties and responsibilities of different departments. You might help senior management, attend meetings, complete small tasks for projects or observe the daily functions of the office.
3. **Creates a professional network: -** Internships are a practical way to expand your professional network. Meeting others and making friends in your field can be beneficial to your future career, as they could potentially recommend you for open positions. The professionals you meet during your internship could be valuable connections for your future job prospects, so showing enthusiasm, curiosity and commitment can help professional contacts see your potential.

**SCOPE: -** Internship experience plays a vital role for every student to implement their theoretical knowledge and get practical knowledge from any organization. A student can implement this internship experience in his future work are.

During this internship we learned through is below timetable: -

In chemistry department, I spent about 2 days in which firstly I learned about the different instrumental handling then next day performed synthesis. In instrumental handling practices, we handled ice flakes, Melting Point apparatus, Rotary Evaporator, Parallel synthesizer, Hot Air Oven and HPLC.

On 2nd day, I synthesized p-bromo acetanilide from acetanilide.

- Pharmaceutics, I already learned in the syllabus about Tablet, capsule, cosmetics and different formulation studies. During training period, I performed tablet punching, in its firstly took raw material then made granules and punched the tablet.

  Spray dryer, it is used for two purposes one is for making nanoparticle and another is as a dryer.
- Pharmacology, in this subject we studied many things like animal handling, digital cell counter, dose calculation etc...

  It is one of my favorite subjects. I think it is the subject where we could learn many things.

In this subject, we already learned since three semesters so I performed some practical during this internship and gain some practical knowledge and if we do master degree in pharmacology specialization then it will help me.

- Pharmacognosy, it is the subject in which we study about herbs and crude drugs. In this subject we performed extraction, phytochemical screening, Ash value of crude drug and percentage LOD (loss on drying).
- Microbiology, the subject which deal with micro and nano particle. In which we prepare agar media and nutrition media. Also work in Laminar flow to determine the bacterial growth in our sample.
- Quality assurance, the subject that came in our 6th semester in which we studied about the quality and quantity of compound. So, in theory I learned some test for primary, secondary and tertiary for packing. During internship we perform all the test related packing.
- Pharmacy practices, one of the best subjects that help to know about patient information and that monitor and management of the patient • this is most interesting subject in which we learned how to control drug-drug interaction with the help of micrometer software.

***BLDEA Shri. Sanganabasava Mahaswamiji College of Pharmacy and ResearchCentre***
***Vijayapura, Karnataka***

BLDEA (Bijapur Lingayat Education Association) is a leading education organization in the North Karnataka region. It has a legacy of more than 100 years and 75 education institutions under its banner, which comprise professional institutes, colleges of humanities and social sciences, public schools and research institutes.

BLDEA's goal is to use education as a tool to bring about social and economic transformation in the North Karnataka region, empower women and the oppressed, reduce social inequality in educational opportunity and contribute to national development.BLDEA has laid considerable emphasis on imparting quality education, cutting across professional and general institutions and create new standards in research and allied activities. All its institutions have a reputation for their unwavering commitment to excellence and expanding the horizons of knowledge.

BLDE Association's SSM College of Pharmacy and Research Centre was founded in 1982 and since then it has earned great respect and reputation across the state of Karnataka for imparting quality pharmaceutical education. The college is affiliated to Rajiv Gandhi University of Health Sciences, Bangalore, and recognized and approved by Pharmacy Council of India, New Delhi, and All India Council for Technical Education, New Delhi. It is also accredited by the National Assessment and Accreditation Council with A++ grade.

**Dr.M.B.Patil**
**President**

**Dr.C.Mallikarjuna Setty**
**Principal & Professor**

The College offers PG Courses in six departments, namely, Pharmaceutical Chemistry, Pharmaceutics, Pharmacognosy, Pharmacology, Pharmacy Practice and Pharmaceutical Quality Assurance. Integrated PG, B.Pharm and D.Pharm are the other courses offered. Values Added Courses offered include Certificate Course in Clinical Research, Certificate Course in Chemical and Biochemical Analysis.

The college has excellent infrastructure consisting of classrooms with modern information and communication technology facilities and laboratories comprising state-of-the-art equipment. The college has given top priority to research activities. Over the last five years, it has published over 350 research papers.


***S S M College of Pharmacy and*** **Research Centre**


***Shri B.M.Patil Medical College Hospital*** **and Research Centre**

## PRACTICAL TRAINING

During internship we had 15 days to do hands on hand training with complete discipline. In which we follow time table that given by the organization.

TIMETABLE: -

| **DATE** | **SUBJECT** |
|---|---|
| 11-07-23 and 12-07-23 | Pharmaceutical Chemistry |
| 13-07-23 and 14-07-23 | Pharmaceutics |
| 15-07-23 and 17-07-23 | Pharmacognosy and Microbiology |
| 18-07-23 and 19-07-23 | Pharmacology |
| 20-07-23 and 21-07-23 | Quality Assurance |
| 22-07-23 to 25-07-23 | Pharmacy Practice |
| 26-07-23 | Site seen |

**Day 1st: -**

In the first day a small orientation class was conducted by the organization. In which they give some overview about their college. Then they told us about the scope of pharmacy.

After that orientation we went in chemistry lab and learned basic information of instrument.

Following are some instrument –

1. **Hot Air Oven: -**

   A hot air oven is a type of dry heat sterilization. Dry heat sterilization is used on equipment that cannot be wet and on material that will not melt, catch fire, or change form when exposed to high temperatures. Moist

heat sterilization uses water to boil items or steam them to sterilize and doesn't take as long as dry heat sterilization. Examples of items that aren't sterilized in a hot air oven are surgical dressings, rubber items, or plastic material. The commonly-used temperatures and time that hot air ovens need to sterilize materials is 170 degrees Celsius for 30 minutes, 160 degrees Celsius for 60 minutes, and 150 degrees Celsius for 150 minutes.


2. **UV Cabinet: -**

   UV-Cabinets works by treating the surface of the item with a high dosage rate of UV-C light at the prescribed wavelength of 253.7 nanometers. Inside the CABINET is equipped with a number of opposing high power Ultraviolet Germicidal Irradiating lamps along highly polished reflective internal surfaces.


3. **HPLC:-**

HPLC can be used to separate the constituents of a compound, tell you how much of each compound is found within the mixture and helps to identify what each compound is HPLC is the technique of choice when analyzing materials for a wide range of organic compounds.

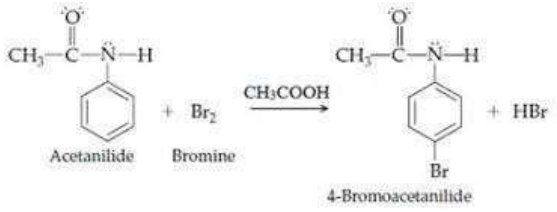
**2nd Day: -**

On 2nd day we synthesized of two compounds

1. P-bromo acetanilide from acetanilide
2. 1, 4-Dihydropyrimidine derivatives using microwave assisted synthesis.

- **Aim: -** Synthesis of p-bromo acetanilide from acetanilide
  **Chemical required-** acetanilide,potassium bromide,ceric ammonium sulphate,ethanol,water,etc

**Reaction: -**




**PROCEDURE: -**

1. Dissolve 1.35gm acetanilide in 15ml alcohol in conical flask.
2. Simultaneously prepare a solution of 1.19gm potassium bromide and10gm ceric ammonium sulphate using 15ml water and transfer in burette.
3. Drop the solution from burette into conical flask with constant stirring.
4. After completion of adding continue to stir at room temperature foranother 10min and add crushed ice to precipitate out the product.
5. Filter and dry the product.

| | |
|---|---|
| Theoretical yield (acetanilide) is found to be | 1.74gm |
| Practical yield (acetanilide) given | 1.35gm |

Percentage yield= $\frac{practical\ yiels}{Theoretica\ \ yield}$ X100

Percentage yield is found to be =77.5%

**P-bromo acetanilide**

**DRUG DESIGN**

Making novel drug designs utilizing applications like CADD, PDB, DSB, PUBchem and pyrx was another experiment I conducted CADD- IT stands for Computer-Aided Drug Design. It is a computational approach used in the field of drug discovery to design and optimize potential drug candidates using computer-based tools and techniques. CADD plays a crucial role in the early stages of drug development by assisting in the identification of potential lead compounds and optimizing their binding interactions with specific target proteins or biomolecules.

The CADD process typically involves the following steps:

1. Target Identification: Identify a specific biological target, such as a protein or enzyme that is associated with a disease or condition.

2. Virtual Screening: Use computational tools to screen large chemical databases for potential drug candidates that could interact with the target.

3. Molecular Docking: Employ molecular docking simulations to predict how the drug candidates bind to the target and evaluate their bindingaffinity.

4. Lead Optimization: Modify and optimize the drug candidates based on the docking results to improve their potency, selectivity, and drug-like properties.

5. ADMET Prediction: Predict the Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) profiles of the optimized drug candidates to assess their pharmacokinetic and safety properties.

6. Molecular Dynamics Simulations: Conduct molecular dynamics simulations to study the dynamic behavior of the drug-target complex over time.

7. Predicted Activity and Prioritization: Evaluate the predicted activity and properties of the drug candidates to prioritize the most promising compounds for further experimental validation.

PROTEIN DATA BANK

The Protein Data Bank (PDB) is a public database that provides access to experimentally determined three-dimensional structures of biological macromolecules, including proteins, nucleic acids, and complex assemblies

STEPS-

1. Visit the PDB Website: Go to the official PDB website (https://www.rcsb.org/) using a web browser.

2. Search for a Protein: Use the search bar to enter the name, PDB ID, or keywords related to the protein of interest.

3. Select the Entry: Review the search results and select the desired protein entry by clicking on its PDB ID or title.

4. Explore the Structure: Once on the protein's page, you can explore its structure in various ways, including 3D visualization, 2D representations, and structural analysis tools.

5. Download the Structure: If you want to download the protein structure, click on the "Download" button and select the desired file format (PDB, CIF, etc.).

6. Access Additional Information: You can access additional information related to the protein, such as experimental methods, ligands, associated publications, and related structures.

SWISSDOCK

SwissDock is an online protein-ligand docking service provided by the Swiss Institute of Bioinformatics (SIB). It is a web-based platform that allows researchers to perform docking simulations to predict the interactions between a protein and a small molecule ligand.

STEPS-

1. Access Swiss Dock: Go to the Swiss Dock website (https://www.swissdock.ch/) using a web browser.

2. Upload Protein and Ligand: Upload the 3D structure file of your protein (in PDB format) and the ligand (in SDF or MOL2 format) to the Swiss Dock server.

3. Set Docking Parameters: Choose the docking parameters, such as the binding site on the protein, the type of docking algorithm, and other settings.

4. Submit the Job: Once you have selected the protein, ligand, and docking parameters, submit the job to the Swiss Dock server for docking calculations.

5. Wait for Results: The docking calculations may take some time to complete, depending on the complexity of the docking simulation and the server's workload. Wait for the results to be generated.

6. Wait for Results: The docking calculations may take some time to complete, depending on the complexity of the docking simulation and the server's workload. Wait for the results to be generated.

7. Review the Docking Results: Once the docking calculations are done, you will receive the results in the form of predicted ligand-protein binding poses and interaction scores.

8. Analyze and Visualize Results: Analyze the docking results to understand the binding interactions between the ligand and the protein. You can visualize the docking poses using the tools provided by Swiss Dock.

**3rd Day and 4th Day: -**

**Pharmaceutics*: -*** In pharmaceutics we mainly learned about nanoparticle formulation, spray dryer and tablet.

1. **Nanoparticles*: -*** *In wh*ich we used lyophillizer and Freeze Dryer


Freeze-drying or lyophilization is the most commonly used approach to preparing stable injectable nano formulations. A detailed understanding of the freezing stress on nanoparticles is essential to the successful preservationof original particle attributes and to the development of reliable lyophilization processes.

2. **Spray Dryer: -** Nano spray drying process produces powder with submicron particles from a solution, nanoemulsion, or nanosuspension. The major advantages of nano spray drying over conventional spray drying includes use of small liquid sample for drying, production of fine particles (0.3–5 μm) and higher yields.

3. **Tablet: -** the solid unit dosage form of medication with suitable excipients. It comprises a mixture of active substances and excipients,

-During this tablet punching we also know about the various part of this instrument.

**PARTS: -**

Hopper: -The area that holds the powder mixture prior to compression.

Die Cavity: -The area where compression occurs. Its shape determines the tablet's size and diameter.

Punches: -Components which compress the powder mixture.

Dosing plow: - Pushes a small, precise amount of product into the die cavity.

Ejection Cam: -Pushes the bottom punches upwards, ejecting the finished tablet from the die cavity.

PUNCHING OF TABLET: -

We take some granules and then fill in die after filling we start the punching machine then the punches enter into the compression stage, the top and bottom punches move between two large wheels called compression rolls. These compression rolls push the punches to words the die to formthe product.

**4th Day: -**

On the 4th day we work in pharmacognosy lab in which we used Soxhlet Apparatus. We learned that how to extract the particular compound from the entire plant.

- We extracted vasaka leaves.
- The Soxhlet apparatus is a standard laboratory tool used for solvent extraction of solid materials, including plant materials like Vasaka leaves.

STEPS; -

- Preparation of Vasaka Leaves: The Vasaka leaves are first dried and ground into a finepowder to increase the surface area for better extraction.

- Packing the Soxhlet Apparatus: A specific amount of the powdered Vasaka leaves is packedinto a thimble made of filter paper or a porous material.

- Solvent Selection: A suitable solvent, such as ethanol or methanol, is chosen based on the desired compounds to be extracted. The solvent should have a boiling point lower than that of the target compounds.

- Extraction Process: The packed thimble is placed inside the Soxhlet extraction chamber. Thesolvent is then heated in a round-bottom flask at the bottom of the apparatus until it reaches its boiling point.

- Recycling Process: As the solvent vapor rises, it condenses on the condenser and drips back down into the sample thimble. This continuous cycle of vaporization and condensation allows for efficient extraction by repeatedly washing the solid material with fresh solvent.

- Extraction Time: The extraction process continues for several hours, allowing the solvent toextract the desired compounds from the Vasaka leaves.

- Concentration: After the extraction, the solvent is evaporated using a rotary evaporator or bygentle heating, leaving behind a concentrated extract containing the extracted compounds.

- Filtration: The concentrated extract is then filtered to remove any remaining solid particles or impurities. Drying: The final extract is often dried under reduced pressure or by using a freeze-drying process to obtain a dry powder for further analysis or use.


**5th day: -**

On the 4th day we go in the microbiology lab and do "ANTIMICROBIAL" activity on DRUGS.

- I used the cup-and-plate method measure the antimicrobial activity of a medication.


- The cup-plate method is a commonly used technique in microbiology to determine the antimicrobial activity of various substances, such as antibiotics, plant extracts, or synthetic compounds.

STEPS; -

- Preparation of Agar Medium: A suitable agar medium, such as Mueller-Hinton agar for bacteria or Sabouraud agar for fungi, is prepared and poured into a sterile petri dish to form a uniform layer.
- Inoculation: A standardized suspension of the target microorganism is evenly spread on the surface of the solidified agar using a sterile cotton swab.

- Placement of Wells (Cups): Small wells or depressions (cups) are made on the agar surface using a sterile cork borer or a pipette tip.

- Loading the Substance: The tested substance, often in the form of a liquid or a sterile paper disc impregnated with the substance, is placed into each well.
- Incubation: The petri dishes are incubated at an appropriate temperature for the specific microorganism, allowing it to grow.
- Measurement of Inhibition Zones: After incubation, the plates are examined for zones of inhibition, where the microorganism's growth is restricted around the wells. The diameter of the clear zone around each cup indicates the antimicrobial activity of the tested substance.
- Control Samples: Positive control discs with known antimicrobial activity (e.g., standard antibiotics) and negative control discs (e.g., sterile water) are included in the experiment to validate the results.


**6th and 7th Day: -**

On the 6th and 7th day we work in the pharmacology lab.

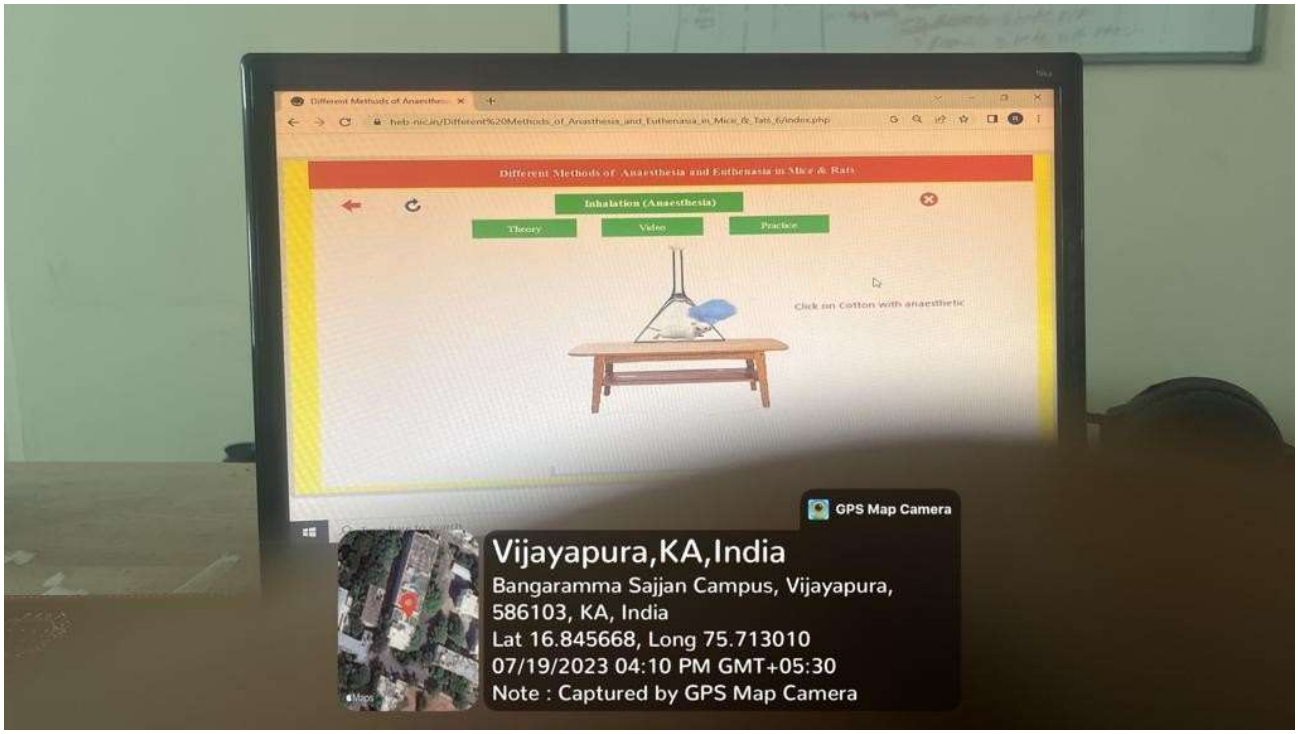
In this department I personally feel that this subject is most interesting, if in future I got any chance to do master's degree then we select Specialization in pharmacology.

1. Animal Handling
2. Experiment on Software
3. Rat and Mice Dose Calculation

- **Animal Handling: -**

  Animals should be approached in a calm and confident manner, avoiding exaggerated or sudden movements, such as waving of the hands and arms. Using soft tones and a quiet voice when talking to animals may help alert them to a non-threatening approach and reinforce a caring attitude in the handler**.**

- **Experiment on Software: -** We used “Ex Pharm” online Software to do experiment in which we perform the anesthesia and Euthanasia in rat and mice.




- **Rat and Mice Dose Calculation: -**This can be calculated simply using the conversion factor.
- In rat 1/5$^{th}$ concentration of dose to be given in animal. The volumeof stock solution of drug to be given not exceeding 1ml/rat.
- In Rat the ideal body weight is 150-200g.
- In mice 1/10$^{th}$ concentration of dose to be given. The volume ofstock solution of drug to be given not exceeding 0.5ml/Mice.
- In Mice the ideal body weight is 18-30g.

**FOR RAT:-**

| Sr.no. | Body weight in mg | Dose of drug 20mg/kg | 1/5th conc. S.S. from 0.5ml/100kg |
|---|---|---|---|
| 1 | 150 | 3mg | 0.75ml |
| 2 | 180 | 3.6mg | 0.9ml |
| 3 | 200 | 4mg | 1ml |
| 4 | 190 | 3.8mg | 0.95ml |
| 5 | 160 | 3.2mg | 0.8ml |

**Calculation: -**

1000g.....20mg

150g.....?

150x20/1000 =3mg

Now,0.5ml/100g

20mg

3x0.5/20=0.75

- **8th and 9th Day: -**

On the 8th and 9th day we worked in Quality Assurance laboratory to perform some qualitative test for secondary packing.

1. Powder Glass Test
2. Leakage Test

- **Powder Glass Test: -**

It is done to estimate the amount of alkali leached from the powdered glass which usually happens at the elevated temperatures.

Procedure: -

Step-1: Preparation of glass specimen: Few containers are rinsed thoroughly with purified water and dried with stream of clean air. Grind the containers in a mortar to a fine powder and pass through sieve no.20 and 50.

Step-2: Washing the specimen: 10gm of the above specimen is taken into 250 ml conical flask and wash it with 30 ml acetone. Repeat the washing, decant the acetone and dried after which it is used within 48hr.

10gm sample is added with 50ml of high purity water in a 250ml flask. Place it in an autoclave at 121ºC±2ºC for 30min.Cool it under running water.Decant the solution into another flask, wash again with 15ml high purity water and again decant. Titrate immediately with 0.02N sulphuric acid usingmethyl red as an indicator and record the volume.

- **Leakage Test: -**

  Fill 10 containers with water, fit with intended closures and keep them inverted at room temperature for 24hr.The test is said to be passed if there are no signs of leakage from any container.

**-10$^{th}$, 11th, and 12$^{th}$ Day: -**

After completing the entire department, I got chance to visit hospital. So, on the 10$^{th}$, 11th and 12$^{th}$ day we visit hospital and learned about pharmacy practice.

1. SOAP Analysis of patient
2. Micromedex

- **SOAP Analysis: -**

  The SOAP note plays one of the central roles in the pharmacists' PCP (PPCP) to achieve the utmost patient care within the integrated health care team. The PPCP approach represents a framework for consistent, quality, and uninterrupted delivery of pharmaceutical services via 5 steps: collect, assess, plan, implement, and follow-up, where the SOAP note may get integrated. These help in clinical reasoning andmedication therapy management to improve patient care initiatives promoting continuity of care focusing on safety concerns.

- Some variants of SOAP notes have also been trialed. For example, Donnelly suggested that SOAP note be modified to HOAP (history, observations, assessment, and plan) note to ensure comprehensive history taking at the early stage of the PCP. Similarly, the "systems SOAP" note (SSOAP or S-SOAP) was developed in a structurallysimilar format as a typical SOAP note format.

- **Micromedex: -**

This is the mainly software where we see the drug –drug interaction their management and all.


**Drug Interaction**

- METRONIDAZOLE
- CEFTRIAXONE SODIUM
- OCTREOTIDE ACETATE

| **CEFTRIAXONE SODIUM** | **METRONIDAZOLE** | **CEFTRIAXONESODIUM** |
|---|---|---|
| **USES: -** Used to treat the bacterial infection (like UTI) | Used to treat severe diarrhea and other symptoms that occur with certain intestinal tumor. | Used to treat serious bacterial infections in different areas of the body. |

diabetes, mellitus, hypertension, coronary artery disease, and QT prolongation with moxifloxacin. She received diuretics, ACE inhibitors, omeprazole, and bronchodilators and developed nosocomial pneumonia. Two days after initiation of metronidazole, QTc was 559 msec and T waves were inverted. Metronidazole was discontinued and ECG returned to normal within 48 hours (Altin et al, 2011). A 90-year-old woman with no known history of structural heart disease developed QT prolongation after metronidazole treatment for aspiration pneumonia. QTc was 324 msec on admission and 703 msec the next day, after initiation of ceftriaxone 1 g/day IV and metronidazole 500 mg 3 times daily. Metronidazole wasdiscontinued and QTc gradually returned to initial value without significant arrhythmias. The patient was advised to avoid medications known to cause QT prolongation (Cohen et al, 2008). A 71-year-old woman with antibiotic-induced pseudomembranous colitis developed ECG QTc interval prolongation andtorsades de pointes with concurrent amiodarone 450 mg bolus followed by 900 mg/day IV and metronidazole 1500 mg/day oral administration. Baseline QTc interval was 440 msec. Amiodarone was added after atrial fibrillation developed with 3 days of amiodarone therapy. Conversion to sinus rhythm occurred 2 days later; however, the follow-up ECG revealed a QTc interval of 625 msec. Symptoms progressed to sustained torsades de pointes-variant ventricular tachycardia that required emergent cardioversion/defibrillation to restore normal sinus rhythm. Amiodarone and metronidazole were immediately withdrawn, and the QTc interval slowly returned to baseline values without further clinicallysignificant arrhythmia events (Kounas et al, 2005).


**13th, 14th and 15th Day: -**

When we successfully got knowledge with good experience in alldepartments then they made program of site scene for 2 days and we got to know about BLDE association**.** So, in the end we got exposure to the moderninstrument there and got to learn a lot about environment management there and got a chance to learn a lot in 15 days under a right guidance.

## LEARNING OUTCOMES

1. We gained Expert knowledge of instrument
2. We learned that Mathematics and statistics needed for the application of these sciences to drug therapy and human health.
3. We learned some future scope in Pharma field that may be come in future.
4. We did some Document patient care related activities.
5. We learned how to apply legal, ethical, and professional standards within a medication use system.
6. Know about how to do team work.
7. We did Evaluation of personal, social, economic, and environmental conditions to maximize health and wellness.
8. Understand principles, instrumentation and application of various chromatographic techniques employed for the analysis of APIs and formulations.
9. To study the basic of instrumentation of various analytical instruments and their calibration.
10. To understand History and general aspects of the design & development of drugs.
11. To Synthesize, recrystallize and understand reaction mechanisms involved in synthesis of medicinally important organic compound. Synthesize medicinally important organic compounds using microwave assisted organic synthesis
12. Learned about mass spectroscopy detailing its principle, instrumentation and applications.

## CONCLUSION

In the end I am glad to tell you that training in BLDEA S S M College and Research Centre was an excellent and fabulous experience. During the training I actually learned about the laboratory and above it working the theoretical knowledge is worth for getting a degree, and it is accessible in the book.

We can only imagine about the thing we read, but practical life is always different and excellent one. During my training period, I had seen the various instruments and apparatus in the laboratory. The highly sophisticated instruments that work precisely must be operated with intense care for optimum use. We could acquire a lot of information regarding the latest instruments and their working procedures.

Similarly, from practical point of view a laboratory and hospital is very difficult to run. During the training session I tried to my level best to gain practical knowledge as much as I can. I improved my basic classified doubts and also understood the importance of maintaining the laboratory system and hospital ward in any college and hospital. I was successfully able to complete my shortventure of training. lastly, I hope that my training reports fulfill the intended requirements.

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# NANO HERBAL FORMULATION: AN IMPACTFUL APPROACH FOR ALZHEIMER DISEASE

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**Abstract**

Alzheimer's disease (AD) is a neurobiological disorder that impairs motor and cognitive function. Currently available drugs like acetylcholinesterase inhibitors fail to prove their efficacy due to poor brain permeability, lower solubility, and slow bioavailability. Blood brain barrier and enzymatic degradation are major challenges for the treatment of AD. Herbal drugs and phytoconstituents have proven their efficacy in the treatment of this disease. Phytoconstituents also have poor availability across BBB as well as less systemic bioavailability which are major obstacles for their use but since this approach reduces systemic toxicity thus these medicines are more researched and promoted for treatment of neurological diseases like AD.

Nanotechnology improves BBB permeability and bioavailability of drug. This technology can be used to improve bioavailability as well as BBB penetrability of phytoconstituents used for the treatment of AD. Nanocarriers have variable and interesting features that can be used with plant based medicines for the treatment of AD.This review summarizes the impact of nanotechnology on the development and improvement of efficacy of phytoconstituents for effective treatment of AD.

**Keywords:** Alzheimer disease, Phytoconstituents, Nanotechnology, Blood-brain barrier, drug permeability, acetylcholinesterase inhibitors.

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## 1. INTRODUCTION

Neurodegenerative disease is characterized by the gradual loss of neural function. It refers to a group of conditions that involve extrapyramidal movement, as well as cognitive and behavioural difficulties. Which appear for no apparent reason and continue to progress. Proteotoxic stress and its attendant anomalies in the ubiquitin –proteasomal and autophagosomal/lysosomal systems, oxidative stress, programmed cell death, and neuroinflammation are all associated with increased neuronal impairment and mortality in neurodegenerative disorders [1]. Age is a major risk factor for neurodegeneration[2]. Alzheimer's disease (AD) and Parkinson's disease (PD) are major neurodegenerative illnesses that primarily affect the elderly, and the risk of developing the disease increases with age[3].

The most prevalent cause of dementia is Alzheimer's disease (AD). Age, family history, head trauma, hyperlipidemia, depression, diabetes mellitus, and vascular variables are all substantial risk factors [4]. The early signs of dementia are frequent memory loss and poor judgement. The patient's symptoms, as well as those of those who care for him, become more severe as the condition develops. The patient is entirely degenerative at this point and requires continuous monitoring[5]. Intracellular neurofibrillary tangles (NFTs) and extracellular amyloid beta plaques are linked to Alzheimer's disease [6]. According to the "2021 Alzheimer's disease facts and figures" report, the mortality rate owing to Alzheimer's disease has climbed to 145.2 percent in the United States between 2000 and 2019. They also supplied data on predicted risk in males of 10.5 percent at 45 years old, 11.6 percent at 65 years old, and females of 19.5 percent at 45 years old, 21.1 percent at 65 years old [7].

Only cholinesterase inhibitors, such as donepezil, galantamine, and rivastigmine, and NMDA receptor antagonists, such as Memantine, have been approved by the US Food and Drug Administration (FDA) for symptomatic treatment of AD.[8] Acetylcholinesterase (AChE) appears to be a highly effective therapy target for the onset of symptoms in Alzheimer's disease (AD) caused by cholinergic depletion, a consistent and early finding in AD [9] [10]. The amount of acetylcholine (ACh) in the cholinergic synapse is directly increased by cholinesterase inhibitors. There has been some improvement in cognitive performance in Alzheimer's patients [11]. Memantine has been found to inhibit neuronal death caused by excitotoxicity [12]. In randomised clinical trials of these medicines, however, substantial dropout rates and severe adverse events have been documented. As a result, safety concerns about cholinesterase inhibitors and memantine have been raised [13]. High-dose requirements, inadequate bioavailability, quick first-pass metabolism, and poor pharmacokinetics are some of the drawbacks of drug delivery tablets, capsules, and liquids [14].

Herbal methods for Alzheimer's disease have gained popularity due to the side effects, inefficiency, and contraindications of conventional drugs. Ayurvedic treatments tend to increase ACh levels or decrease AChE levels in the brain, which can aid in the treatment of Alzheimer's disease. Salvia officinalis, which inhibits cholinesterase, and Panax notoginseng, which is claimed to improve memory and learning ability [15], are two examples of therapeutic plants. Other medications have been examined, such as selegiline, oestrogen, Vitamin E, and anti-inflammatory pharmaceuticals, although their usage is still contentious [16]. Herbal techniques, on the other hand, have drawbacks. They are unable to pass the blood-brain barrier (BBB). The development of medicinal medicines from natural products faces significant hurdles, including obtaining large quantities of active compounds[17]. These medications are commonly linked to negative side effects and do not treat the disease by altering its pathophysiology [6].

Nanoparticles can circumvent these obstacles by increasing permeability across the blood-brain barrier and delivering optimum efficacy at a lower dose. These systems can be utilised to distribute medications to specific cells or tissues, increase bioavailability, maintain drug release, or solubilize pharmaceuticals for systemic distribution [18]. When a drug is loaded into an appropriately constructed nanocarrier and crosses the BBB and accumulates in the relevant neuronal cell, it can boost drug concentrations in brain cells compared to the drug alone [19]. Organic (liposomes, polymers, solid-lipid NPs, emulsions, and dendrimers) and inorganic (silica, carbon, and gold) nanodelivery systems can be generally categorised based on the nature of the carrier material [14]. In this review, we looked at Alzheimer's risk factors, treatment obstacles, and nanotechnology techniques using phytoconstituents to solve such challenges.

### Risk Factors

#### Age

Aging is the most prevalent cause of Alzheimer's disease. It has been discovered that at the age of 65, there are more incidences of disease onset that progresses. Younger people are more likely to develop the disease [20]. There is an age-related

decline in brain weight and volume, enlargement of ventricles, and loss of synapses and dendrites in specific areas accompanied by SP and NFT in a cognitively intact brain [21]. Changes in cortical neurotransmitters are difficult to understand, just as they are in normal ageing [22]. Early pathological changes in AD patients are difficult to identify from those in a healthy elderly person [23].

**Diet**

Several micronutrients, such as antioxidants, lipids, vitamins, and carbs, can help to lower the risk of Alzheimer's disease. Although the effects of these nutrients on AD are unclear, they are thought to play a role in the progression of AD by reducing oxidative stress and amyloid beta-peptide (A) formation. Vitamin A and -carotene are nutrients that inhibit the development of A oligomers and fibrils [24]. However, some saturated fatty acids and a high-calorie diet have been linked to an increased risk of Alzheimer's disease[25]. Malnutrition is considered a risk factor for Alzheimer's disease. Folate, vitamin B12, and vitamin D deficiency have all been linked to a decline in cognitive function[26]. Patients with Alzheimer's disease also have issues with eating and swallowing, which might raise the risk of malnutrition[27].

**Medical factors**

**Cardiovascular disease:** Hypertension is considered as a major risk for stroke. There has been reliable clinical data on the prevalence of poststroke dementia, increasing the risk of AD in elderly [28]. It has been seen that stroke could promote the production of Aβ, interfere with Aβ clearance, and/or aggravate synaptic and neuronal loss already triggered by Aβ and tau pathology[29] Heart failure may cause cerebral hypoperfusion and changes including white matter hyperintensity (WMH). A study suggests that reduced cerebral perfusion is related to greater Wmh, which causes cognitive impairment [30].

Atherosclerosis can also be considered as a risk factor for AD. Cholesterol is consistently associated with AD. High levels of cholesterol can be linked to increased levels of Aβ and greater cognitive impairment leading to progression in AD. Cholesterol seemed to have impaired Aβ degradation and promoted its production [31]

**Obesity:** Chronic inflammation, oxidative stress, as well as mitochondrial dysfunction are all factors that contribute to neurodegenerative diseases[32]. Increases in BMI in middle age are connected with an increased chance of developing Alzheimer's disease (AD).[21]

**Type-2-diabetes:** according to the study, there are several factors that link diabetes to AD, including oxidative stress, formation of advanced glycation end-products (AGEs), and overt immune system activation. These factors represent common targets for both the diseases[33].

**Smoking**

In a study conducted, it was found that smoking was associated with faster declines in verbal memory and with slower speeds of visual search[34]. Another study reported smoking increased the severity of some abnormalities typical of AD, which includes amyloidogenesis, neuroinflammation, and tau phosphorylation. This suggests that cigarette smoking may increase the onset and exacerbate the features of AD [35].

## 2. Challenges of brain drug delivery

Drugs that affect the Central Nervous System (CNS) must be delivered to the brain (CNS). Most medications cannot cross the blood-brain barrier (BBB) and enter the brain. As a result, most medication molecules are too big to penetrate the blood-brain barrier (BBB). Despite the fact that tiny pharmacological molecules are considered capable of crossing the BBB, nearly 98 percent of the compounds tested did not[36]. Tight connections between endothelial cells impede paracellular mobility. Lipophilic medicine with a molecular weight of less than 600 da, on the other hand, can pass through endothelial cells [37]. The combination of high lipophilicity and low molecular weight is required for efficient drug penetration. Due to its 800 Da molecular weight, Vincristine has a high lipid solubility, however its ability to traverse the BBB is limited (Grieg et al., 1990). Even though small-molecule peptide-mimetic drugs have been found to be effective, their dicarboxylic moiety prevents them from crossing the BBB (Ohlstein et al., 1994). As a result, to demonstrate its pharmacological activity, this medication may require conjugation to a BBB drug targeting system for penetration.

Its not just a physical barrier that stands in the way of these medications' development. Drugs and other exogenous compounds may be prevented from entering the brain by the presence of a number of enzymes found in the blood-brain barrier that are known to break down these substances in the liver. [38]. The biotransformation (functionalization/conjugation) of the drug is carried out by multigene families of isoenzymes. Numerous neurotransmitter-metabolizing enzymes are expressed in the BBB, including monoamine oxidases (MAO), catechol O-methyl transferase (COMT), cholinesterase, GABA

transaminase, aminopeptidases, and endopeptidases [39] [40]. Phase 1 and phase 2 enzymes are responsible for different parts of the drug metabolism process. cytochrome P450, UDP-glucuronyltransferases (UDPs), glutathione S-transferases (GSTs), sulphotransferases (SULTs), and N-acetyltransferases (NATs), particularly NAT2 in phase 2 according to the percentage of drug metabolised by them. Some analgesics, such as diclofenac and phenacetin, are metabolised by CYP46A1[41]. CYP2E1 metabolises anaesthetics and ethanol [42]. In addition to antidepressants and antipsychotics, CYP2D6 metabolises a number of other CNS medications. Reactive epoxide is inactivated by membrane-bound epoxide hydrolase, which is found in isolated microvessels[38]. Figure 1 depicts various methods of delivering drugs to the brain over the BBB, as shown in the figure.

## 3. Role of herbal nanoherbal formulation

Nanomedicine is a new concept developed by the convergence of nanotechnology and medicine. They are more safer, effective and have lower healthcare cost [43]. Recently, the attention has shifted towards a novel drug delivery system using herbal drugs [44]. Due to the side effects of current therapies, the attention has laid over the herbal approaches for the treatment of AD and other diseases [45]. They are preferred over the synthetic due to their negligible harmful and deleterious effects [46]. Various plants and their constituents enhance cognitive function, have a neuroprotective, anti-inflammatory, and antioxidant mechanisms ,along with acetylcholinesterase inhibition, and are known to alleviate other symptoms of AD, including depression, memory loss, and poor cognition [47] [48] . Some of the biologically active ingredients of herbal extracts are tannins, terpenoids, alkaloids and flavonoids. Along with this, the vital focus towards nanotechnology has helped in improving treatments. It was seen that the treatment options for AD are limited mainly due to the inability of the drugs to cross the blood–brain barrier(BBB) [49] [50]. Nanocarriers like synthetic biodegradable polymers are useful to form nano dosage forms which have enhanced solubility and bioavailability, reduced toxicity, and increase the pharmacological activity of the active drug [51]. These nanocarriers may help in increasing the biological activity of the herbal drug and their constituents. Coupled together, they improve solubility, enhance the retention rate of the drug, and with that, the ability to permeate through the blood brain barrier [52].

Curcumin encapsulated PLGA nanoparticles(NPs) were prepared by emulsion solvent evaporation method in a study [53]. The NPs potentially induced neuronal stem cell (NSC) proliferation and neuronal differentiation in vitro and in the hippocampus and subventricular zone of adult rats, in comparison with uncoated bulk curcumin. These nanoparticles were seen to reverse learning and memory impairments in an amyloid beta-induced rat model of AD-like phenotypes, by inducing neurogenesis through activation of the canonical Wnt/β-catenin pathway. Hence, it may offer a therapeutic approach for the treatment of Alzheimer's disease.

In another study, a quercetin (Qu) modified polysorbate 80 (P-80)-coated gold palladium (AuPd) core-shell structure was synthesized. The study conducted was to check the the activation of autophagy which eliminates the intracellular amyloid-β (Aβ) and slows down the neurotoxicity induced by Aβ [54]. The results of the study indicated that concave cubic Qu-P-80-AuPd activated the autophagy of SH-SY5Y cells, accelerated the clearance of Aβ, and protected SH-SY5Y cells from Aβ-induced cytotoxicity damage. Piperine (PIP) is a natural alkaloid with memory enhancement abilities. In a study [55], Tween-modified monoolein cubosomes (T-cubs) were used as nanocarriers for PIP. The results revealed T-cubs had the potential to significantly enhance PIP cognitive effects and even restore cognitive function to normal levels. T-cubs showed potential anti-inflammatory and anti-apoptotic activity of loaded PIP, indicating the potential to stop the progression of AD. Hear in Table 1 we listed 50 phytoconstituents with their biological sources along with the nano herbal formulation.

## CONCLUSION

Alzheimer's is the 3rd leading cause of death, whereas treatment of AD is a major challenge due to the presence of BBB. Cholinesterase inhibitors are used for the treatment of AD, which cannot completely cure the disease. Numerous evidence suggests that phytoconstituents show neuroprotective effects for the treatment of AD. However, poor permeability and low bioavailability minimise their potential. To overcome these limitations, researchers worked with nanotechnology, and research suggested that nanoparticles improved drug permeability and bioavailability. Currently, researchers are showing more interest in phytoconstituents and their nano-herbal formulations for the effective treatment of AD. Nanoparticles have proven their potency. However, further study is required to make them more essential. Additionally, the clinical efficacy

of nanoparticles for AD needs long-term assessments for the design of nano formulations with more specificity.

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