IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

USE OF ARTIFICIAL INTELLIGENCE IN NOVEL DISSOLUTION ENHANCEMENT TECHNIQUES

[1]Akshay B. Jadhav, [2]Indrajeet D. Gonjari, [3]Pranita K. More, [4]Divya B. Jagdale, [5]Shreevidya M. Yamatkar

[1]Research scholar, [2]Assistant professor, [3]Research scholar, [4]Research scholar, [5]Research scholar
Department of Pharmaceutics,
Government College of Pharmacy, Vidyanagar, Karad, Dist. Satara,
Pin code: 415124, Maharashtra, India.

Mr. Akshay Baban Jadhav
Government College of Pharmacy, Vidyanagar, Karad, Dist. Satara,
Pin code: 415124, Maharashtra, India.

Abstract:
Intelligent modelling, which aids in knowledge conception, problem solving, and decision making, is the aim of artificial intelligence (AI). The first studies of what is now called artificial intelligence (AI) were carried out in 1943 by Walter Pits and Warren McCulloch. It used to be believed that artificial intelligence (AI) was only used in engineering. However, artificial intelligence (AI) is now widely applied in the pharmacy sector across a wide range of areas, including hospital pharmacy, drug discovery, formulation development for drug delivery, marketing, management, and marketing. Artificial neural network (ANN) techniques are widely used in pharmaceutical research for data filtering and experimental outcome prediction. Regression analysis and a backpropagation network were used in this work to model a new dissolution outcome prediction and screen system. Drug research and the development of drug delivery formulations involve a large number of Artificial Neural Networks (ANNs), including Deep Neural Networks (DNNs) and Recurrent Neural Networks (RNNs). The technology's promise in quantitative structure-property relationship (QSPR) or quantitative structure-activity relationship (QSAR) has been validated, and several drug discovery implementations have been studied. De novo design also promotes the creation of pharmacological compounds with significantly novel properties in terms of intended or ideal attributes. Robots are used by doctors nowadays for a range of medical procedures since they are more dependable than people, have more sophisticated work features, and can finish any task swiftly and effectively. We draw the conclusion that artificial intelligence (AI) is the burgeoning subject that is affecting every business, including pharmacy, and that more work must be done in this area in order to advance the state of the art and carry out fresh investigations. Because of the way the input data was prepared, the relevant data could still be used to train the ANN model even after the formulation composition was changed. This system uses the reference line regression methodology (RLRM) and the effective data regression method (EDRM) to predict dissolution results with a high accuracy rate. Nevertheless, compared to the orthogonal experiment, it requires a smaller database. Additionally, this system implements a decision tree-based data screen function. The drug prediction system created by this artificial neural network (ANN) model is distinct.

Keywords: Artificial Intelligence, Artificial Neural Networks (ANNs), Dissolution Techniques, Theories of Dissolution, Long Short-Term Memory Networks (LSTMs), EDRM, RLRM

1. INTRODUCTION-

The term "drug dissolution" describes the process of dissolving a solid drug substance, usually in a liquid media. This is a crucial stage in the delivery of drugs since it controls the rate at which the medication is released and eventually absorbed by the body. For a medicine to be absorbed by the body after ingestion, it must be dissolved or solubilized. This is true because only liquid-state materials can interact with and be absorbed by cells and tissues. When the medication material comes into touch with digestive juices in the small intestine, the breakdown process starts in the stomach and continues there.

The physical and chemical qualities of the medicine, the formulation (such as tablet or capsule), and the circumstances inside the gastrointestinal tract are some of the factors that affect how well a drug dissolves. The rate and degree of drug dissolution can be influenced by variables such particle size, crystal shape, solubility, and the presence of excipients. Dissolution testing is a procedure used by pharmaceutical firms to assess and verify the efficacy of new drugs. This test simulates the physiological environment by measuring the amount of medication released from a dose form over time under particular conditions. The price and volume of drug dissolution can influence the drug's bioavailability, that's the percentage of the administered drug that reaches systemic circulation. Poorly soluble pills can also have constrained dissolution, main to decrease bioavailability and probably reduced therapeutic effects. By expertise the dissolution characteristics of a drug, researchers and formulators could make modifications to the method or explore exclusive methods to enhance dissolution and improve healing effects.

Theories of Dissolution - Various theories to explain drug dissolution

1. Diffusion layer model / film theory
2. Dankwert‘s version / penetration or floor renewal concept
3. Interfacial barrier version / double barrier or confined salvation theory

Solubility:- Solubility refers back to the potential of a substance, called the solute, to dissolve in a specific solvent. It is a chemical property that describes how an awful lot of a solute can dissolve in a given amount of solvent at a detailed temperature and pressure. The solubility of a substance is generally expressed as the maximum quantity of solute which could dissolve in a set amount of solvent, frequently measured in grams according to liter (g/L) or moles in step with liter (mol/L). This most quantity of solute that could dissolve in a given solvent, at a specific temperature and stress, is referred to as the solubility restriction.

Factors affecting solubility include temperature, pressure, and the nature of each the solute and the solvent. In general, as temperature increases, the solubility of maximum stable solutes in liquid solvents also will increase. However, this dating might not observe to all materials, as a few showcase a lower in solubility with growing temperature. The nature of the solute and solvent molecules also closely affects solubility. Like dissolves like, that means that materials with similar polarities and intermolecular forces tend to dissolve in one another. For example, polar solutes tend to dissolve in polar solvents, even as nonpolar solute-solvent combinations are much more likely to dissolve in each other.

Solubility is an crucial concept in diverse fields including chemistry, biochemistry, pharmaceuticals, and environmental sciences. It performs a crucial role in understanding and predicting the conduct of different substances, their interactions, and the formation of solutions.

By manipulating solubility situations, inclusive of adjusting temperature, stress, or introducing other solvents or solutes, it's far viable to manipulate the dissolution and precipitation strategies and affect various chemical reactions.

2. REQUIREMENT OF SOLUBILITY ENHANCEMENT: - Drug absorption from the gastrointestinal tract may be restricted with the aid of a range of factors, most enormous members being poor aqueous solubility and poor membrane permeability of the drug molecule. When handing over an active agent orally it need to first dissolve in gastric and/or intestinal fluids earlier than it may permeate the membranes of the GI tract to attain systemic stream. Hence, two areas of pharmaceutical research that focus on improving the oral bioavailability of active marketers include; improving solubility and dissolution price of poorly water-soluble drugs and enhancing permeability of poorly water soluble tablets.[1]

3. LIST OF DISSOLUTION APPARATUS FOR SOLID DOSAGE FORM (TABLET & CAPSULE)

- I.P. & E.P.
  Apparatus I – paddle apparatus
  Apparatus II – basket apparatus
- B.P. & U.S.P.
  Apparatus I – basket apparatus
  Apparatus II – paddle apparatus
- B.P. & E.P.
  Apparatus III – flow through cell apparatus

➢ Conditions (for all)
Temp. - 37±0.5^{0}C
PH - ±0.05 unit in specified monograph
Capacity – 1000 ml
Distance between inside bottom of vessel and paddle/basket is maintained at 25±2 mm.

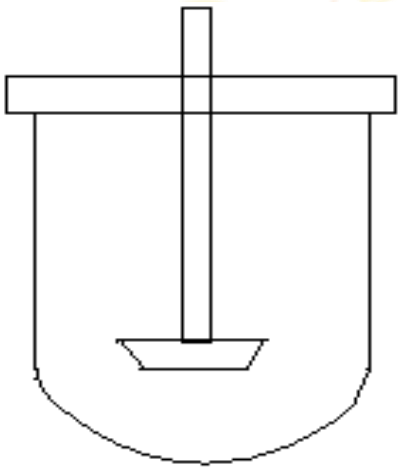

figure 1 – paddle apparatus

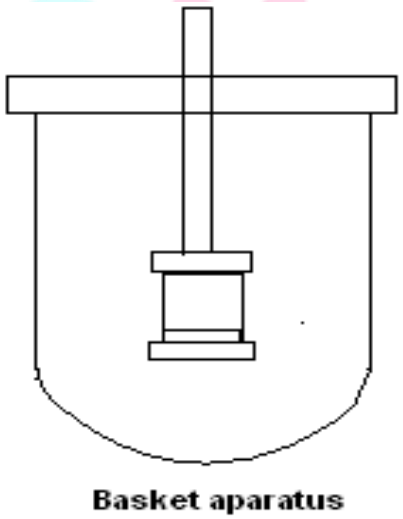

figure 2 - basket apparatus

- **Apparatus III – Reciprocating cylinder**
  - Consist of a cylindrical**,** that bottom vessel that accommodate a glass reciprocating cylinder whose end are close with a polypropylene mesh screen.
  - The dosage unit placed in reciprocating cylinder & the release of drug into solvent within the cylinder measured.
  - **Apparatus IV – flow through cell**
  - Used flow though cell with a filter system, through which the dissolution medium is pumped.

Temp. for both apparatus III & IV at **37±0.5^{0}C**.

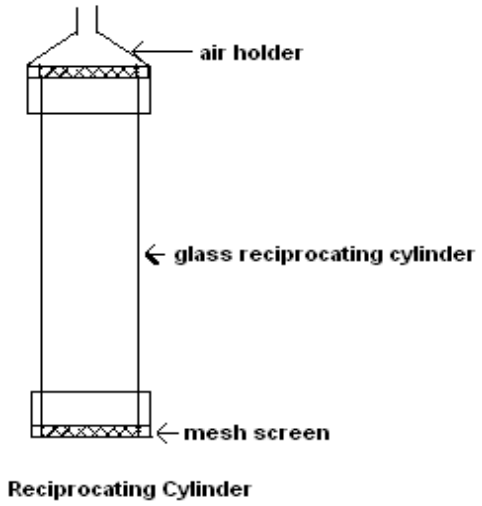

figure 3 – reciprocating cylinder

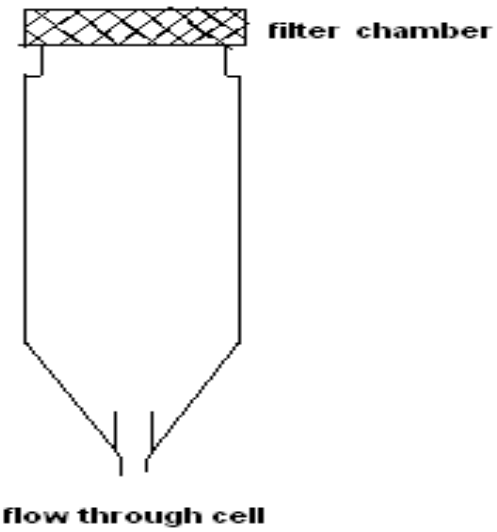

figure 4 – flow through cell

- **Apparatus V – Paddle over disk**.
  - The disk assembly design to minimize to any dead volume.
  - The disk assembly is located at 25±2 mm from the bottom the paddle.
- **Apparatus VI – cylinder**
  - Used basket apparatus except that the basket and shaft are replaced with a stainless steel cylinder stirring element.
- **Apparatus VII – (reciprocating holder)**
  - Use solution container in which a specifically designed disk sample holder may be made to reciprocating.
- **For apparatus V, VI&VII**
  - Procedure carried out at **32±0.5^0 C**. (because deliver system are used on the skin)

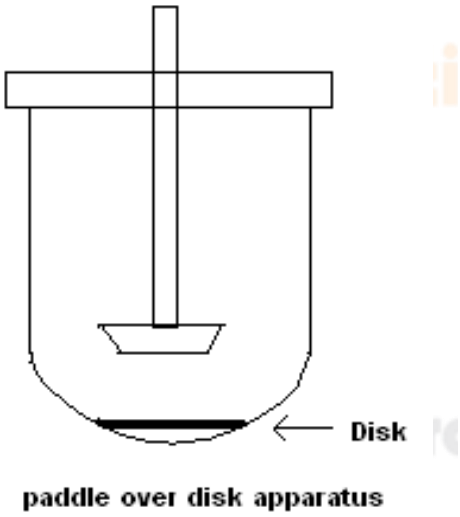

figure 5 – paddle over disc

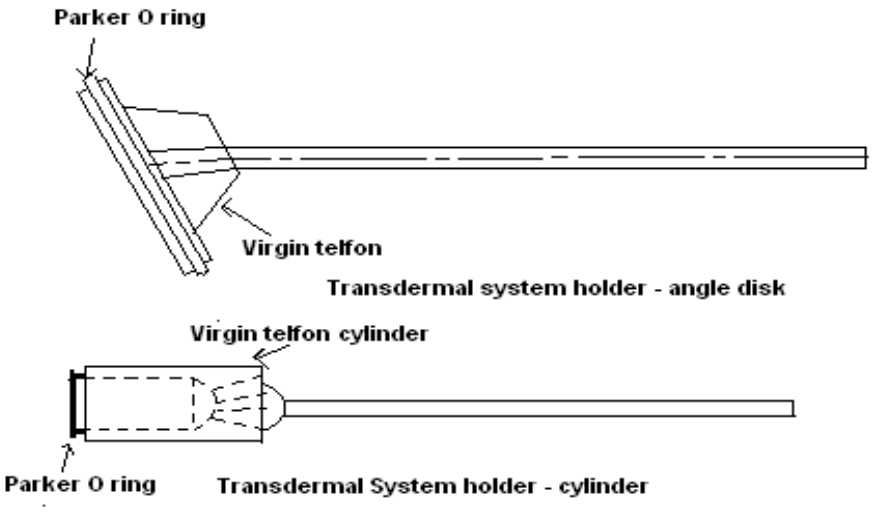

figure 6 – reciprocating holder apparatus

4. SOLUBILITY ENHANCEMENT TECHNIQUES

4.1 Particle Size Reduction:

The solubility of drug is often intrinsically related to drug particle length as a particle becomes smaller, the floor region to extent ratio increases. The large surface place lets in a more interplay with the solvent which purpose increase in solubility. Conventional techniques of particle size reduction, including comminution and spray drying, depend upon mechanical stress to disaggregate the active compound.[2]

4.2 Complexation:

a. Physical Mixture: Active drug with appropriate polymer in distinct ratios mixed in a mortar for about one hour with steady trituration. The combination is handed via sieve no. Eighty and stored in dessicator over fused calcium chloride.

b. Kneading method: Active drug with suitable polymer in unique ratios is delivered to the mortar and triturated with small amount of ethanol to put together a slurry. Slowly the drug is included into the slurry with constant trituration. The prepared slurry is then air dried at 25o C for 24hrs. The resultant product is pulverised and handed through sieve no. Eighty and saved in dessicator over fused calcium chloride.[3]

c. Co-precipitate method: Active drug is dissolved in ethanol at room temperature and suitable polymer is dissolved in distilled water. Different molar ratios of active drug and appropriate polymers are mixed respectively. The mixture is stirred at room temperature for one hour and the solvent is evaporated. The resultant mass is pulverized and surpassed through sieve no. Eighty and stored in a desiccators.[4]

4.3 Hydrotropy:

Hydrotropy is a solubilization phenomenon whereby addition of massive amount of a 2nd solute outcome in an growth inside the aqueous solubility of every other solute. Concentrated aqueous hydrotropic answers of sodium benzoate, sodium salicylate, urea, nicotinamide, sodium citrate and sodium acetate have been determined to enhance the aqueous solubilities of many poorly water soluble drugs.[5-6]

4.4 Solid dispersion Techniques:

The fusion (soften) technique Accurately weighed amounts of service(s) are positioned in an aluminum pan on a warm plate and melted, with steady stirring, at a temperature of approximately 60°C. An correctly weighed amount of energetic drug is included into the melted provider(s) with stirring to make sure homogeneity. The mixture is heated till a clean homogeneous melt is received. The pan is then eliminated from the new plate and allowed to cool at room temperature. The solvent technique Accurately weighed quantities of energetic drug and provider(s) are dissolved in minimal portions of chloroform in a round-backside flask. The solvent is removed using a rotary evaporator. The resultant stable dispersion is transferred to an aluminum pan and allowed to dry at room temperature.[14] Dropping approach A stable dispersion of a melted drug-provider mixture is pipetted after which dropped onto a plate, wherein it solidifies into spherical particles. The size and form of the particles may be influenced through factors such as the viscosity of the melt and the size of the pipette. Because viscosity is exceptionally temperature established, it's miles very critical to alter the temperature so that once the melt is dropped onto the plate it solidifies to a spherical shape.[5]

4.5 Spray drying techniques:

Preparation of microparticles via spray drying Spray dried debris consisted of active drug simplest and drug/suitable polymer in exceptional ratios are prepared by way of dissolving the drug or drug/polymer mixture in ethanol/water solution. The answer is spray dried the use of Mini Spray Dryer. The shaped microparticles are separated the usage of cyclone separator, gathered and stored in a desiccator at ambient temperature till equipped to be used. Preparation of microparticles by way of spray chilling Spray chilled debris are organized through melting the drug or drug/suitable polymer mixture in distinctive ratios at 90°C. The soften is stored at 90°C and atomised with a mainly built pneumatic nozzle into air kept at 20°C. The debris are accrued the usage of cyclone separator and stored in a desiccator.[6]

4.6 Supercritical Fluid Technologies:

a. Supercritical Antisolvent precipitation The SAS apparatus works in a continuous co-modern-day mode and it consists of a precipitator wherein the antisolvent and the liquid solution are one by one fed to the top of the chamber and are continuously discharged from the lowest. The liquid answer is pumped into the chamber through a high-pressure piston pump. The antisolvent is delivered with the aid of excessive pressure piston pump. The precipitator is a cylindrical vessel with an internal quantity of 500cm^3. The liquid solution is brought into the chamber thru a stainless-steel nozzle. The supercritical carbon dioxide is heated before getting into the precipitator in a tube section through an electric powered cable, that's related to a temperature controller. The precipitator is heated by using two electric skinny bands heater also connected to a temperature

controller. A clear out of sintered metal with enough porosity is located at the bottom of the vessel to gather the debris produced. The solvents are separated and recovered from a 2nd vessel.[7]

b. Gas Antisolvent Recrystallisation - It is possible to induce fast crystallisation with the aid of introducing the antisolvent gasoline into an answer containing dissolved solute. One of the requirements for this technique is that the provider solvent and the SF antisolvent should be at least in part miscible. Solution-improved Dispersion via Supercritical Fluids The drug solution and the SF are delivered simultaneously into the particle formation vessel the usage of a co-axial nozzle arrangement inflicting rapid dispersion, mixing and extraction of the drug answer solvent by means of SF leading to very excessive supersaturation ratios. The temperature and strain together with accurate metering of flow fees of drug solution and SF via a nozzle offer uniform conditions for particle formation. This allows to control the particle length of the product and by way of deciding on an appropriate liquid solvent, it's miles possible to govern the particle morphology.[8]

4.7 Methods for Nanosuspensions:

a. Media milling (Nanocrystal or Nanosystems) The nanosuspensions are prepared through using excessive-shear media generators. The milling chamber charged with milling media, water, drug and stabilizer is turned around at a totally excessive shear rate underneath controlled temperature for several days (as a minimum 2-7 days). The excessive electricity shear forces are generated as a result of the impaction of the milling media with the drug ensuing into breaking of microparticulate drug to nanosized debris.

b. Homogenization in water (Dissocubes) Homogenization includes the forcing of the suspension underneath stress through a valve having a narrow aperture. The instrument may be operated at strain various from 100 – 1500 bars (2800 –21300psi) and upto 2000 bars with volume capacity of 40ml.

c. Combined precipitation and homogenization (Nanoedege). In this technique, The caused suspension is homogenized leading to discount in particle size and keeping off crystal increase.

d. Nanojet technology Nanojet technology This technique called opposite stream or nanojet technology, uses a chamber where a stream of suspension is divided into two or more parts, which colloid with each other at high pressure. The high shear force produced during the process results in particle size reduction.

e. Emulsification-solvent evaporation technique This technique involves preparing a solution of drug followed by its emulsification in another liquid that is a non-solvent for the drug. Evaporation of the solvent leads to precipitation of the drug. Crystal growth and particle aggregation can be controlled by creating high shear forces using a high-speed stirrer.[9]

4.8 Preparation of nanocrystals:

The coaching procedure involves steps Preparation of drug solution in organic solvents: Different concentrations of drug solution is ready by way of getting ready solution of drug in natural solvent (based totally on solubility of drug especially solvent). Addition of drug answer in water: Nanocrystals are organized with the aid of adding the microliter quantity of drug strategy to milliliter quantity of water quickly with non-stop stirring on magnetic stirrer at a thousand rpm Solvent is eliminated through overnight stirring at 500 rpm. Then it's far centrifuged at 5000 rpm and the product is solidified.[10]

4.9 Nanopure XP technology:

PharmaSol uses in its Nanopure XP technology a pretreatment step with next homogenization to supply debris nicely below one hundred nm. Drug nanocrystals with a length of about 50 nm and under are fantastically smaller than the wavelength of the visible light, and so the nanosuspensions are translucent.[11]

4.10 Co-Solvent Evaporation Method:

The solvent evaporation of drug and polymer answer in specific ratio is finished with the aid of the use of a appropriate evaporator. The answers are prepared through dissolving drug in methanol and polymer in distilled water and blended each answers, which produces clean answer. The clean answer evaporated in evaporator.[12]

4.11 Spray Drying:

The solvent evaporation of drug and polymer solution in special ratio is achieved by the use of spray dryer. The answers are organized with the aid of dissolving drug in methanol and polymer in distilled water and mix

both solutions, which produces a clear solution. The solvent evaporated by way of the use of evaporator. The spray dried mixture of drug with polymer is acquired in 20–30 min.[13]

4.12 Formulation of Self microemulsifying drug delivery systems-

A collection of SMEDDS formulations are prepared the usage of Surfactant/cosurfactant mixture and oil. Accurately weighed active drug is located in a tumbler vial and oil, surfactant and cosurfactant are delivered. Then the components are combined via mild stirring and vortex mixing on a magnetic stirrer, till drug is flawlessly dissolved. The combination is stored at room temperature until further use.[14]

4.13 A chitosan-based solvent change approach-

A chitosan-based totally solvent change approach The composition of different crystal formulations are organized. Chitosan solution is prepared by way of soaking chitosan in 1% glacial acetic acid for three h. A weighed quantity of the drug is dispersed in chitosan answer via the use of high dispersion homogenizer. This dispersion is then added to distilled water or sodium citrate approach to precipitate chitosan on drug crystals. The precipitate received is filtered through Whatman No. 1 filter paper using vacuum filtration unit and dried. The dried product is then exceeded thru sieve No. 60 to attain a uniform size distribution.[15]

4.14 Preparation of dry elixir-

Dry elixir is ready by means of a twig drying technique. A laboratory scale spray drying is completed the usage of the spray dryer with a well-known nozzle. Different compositions of spraying answer are prepared. Drug is dissolved in ethanol, at the same time as dextrin and SLS are dissolved in distilled water. Each answer is pre-warmed to 55–60 °C and then mixed. SLS is employed to prevent spray- dried particles from attaching to the internal wall of spray-drying chamber, to provide loose-flowing powder, to address with clean and to growth the encapsulation of ethanol inside the dry elixir. The very last answer is added to spray dryer. The drug is amassed in cyclone separator and saved in a conical tube.[16]

4.15 Preparation of drug composite particles –

Active drug is dissolved in methanol and the answer is then clear out through a nylon membrane to dispose of any particulate impurities. Next, polymers are dissolved in deionized water, that is used as an anti-solvent. The drug solution is poured hastily into the anti-solvent with magnetic stirring at a charge of 2500 rpm. After stirring, a suspension containing drug nanoparticles are received. This suspension is then processed thru spray drying to generate drug composite debris. Spray drying is accomplished the use of a lab-oratory scale spray dryer.[17]

4.16 Preparation of dihydrochloride salt form-

Active drug is suspended in 800 ml of acetone and into the suspension heated below reflux, the anhydrous gas of hydrogen chloride is bubbled slowly. After approximately 30 min, the suspension became an answer and in every other five– 10min, the precipitate of the salt is formed. The skip of hydrogen chloride lasted for two h and the aggregate is permitted to stand in a single day at room temperature. The product is gathered with the aid of filtration, washed with acetone and dried at one zero five ◦C.[18]

5. HOW SOLUBILITY OF DRUG INFLUENCES THE PERMEABILITY TO PLASMA CONCENTRATION:

The solubility of a drug can affect its permeability and therefore its plasma concentration in several ways. Here are some key points should be consider:

5.1 Dissolution Rate:- The solubility of a drug determines how readily it dissolves in a biological fluid, such as gastrointestinal fluids or blood. Drugs with higher solubility will dissolve more quickly, leading to faster absorption and potentially higher plasma concentrations. Conversely, drugs with lower solubility may dissolve more slowly, resulting in slower absorption and potentially lower plasma concentrations.

5.2 Absorption Mechanism:- The solubility of a drug can influence the mechanism of its absorption. Lipophilic (or hydrophobic) drugs tend to dissolve better in fat-rich environments, such as cell membranes. This can facilitate passive diffusion across biological barriers, including the intestinal membrane or blood-brain barrier, leading to higher plasma concentrations. On the other hand, hydrophilic drugs may rely on active

transport mechanisms or specialized transporters, which could affect their permeability and plasma concentration.

5.3 Formulation and Delivery:- Drug solubility also affects the formulation and delivery system used. For example, poorly water-soluble drugs may require specific formulation techniques, such as using solubilizing agents or prodrug conversion, to enhance their solubility and absorption. The choice of delivery system, such as oral tablets, capsules, or intravenous formulations, can affect the dissolution rate and subsequent plasma concentration.

5.4 Pharmacokinetics:- Once in the bloodstream, drug solubility can impact its distribution, metabolism, and elimination kinetics. Highly soluble drugs may distribute more readily to various tissues, leading to lower plasma concentrations. Conversely, drugs with low solubility may have limited tissue distribution, resulting in higher plasma concentrations. Furthermore, solubility can influence drug metabolism and elimination rates, affecting the overall plasma concentration profile over time.

5.5 Bioavailability:- The solubility of a drug is closely linked to its bioavailability, which is the fraction of the administered dose that reaches systemic circulation unchanged. Drugs with higher solubility generally have better bioavailability since they can dissolve readily and be absorbed into the bloodstream. Conversely, drugs with low solubility may exhibit lower bioavailability due to incomplete dissolution and poor absorption.

5.6 pH Dependence:- The solubility of a drug can be pH-dependent, which can have implications for its permeability and plasma concentration. For instance, weakly acidic or basic drugs may exhibit changes in solubility depending on the pH of the surrounding environment. This can impact their absorption across different biological barriers, including the gastrointestinal tract or renal tubules, thereby influencing plasma concentration.

5.7 Solubility-limited Absorption:- In some cases, the solubility of a drug can be the rate-limiting step for its absorption. If a drug's solubility is very low, its dissolution and subsequent absorption may be slow or incomplete. This can result in lower plasma concentrations, reduced therapeutic efficacy, or the need for larger dosages to achieve the desired therapeutic effect.

5.8 Supersaturation and Precipitation:- Drugs with high solubility can undergo supersaturation, where they dissolve in a solvent beyond their thermodynamic limit. However, upon encountering a different environment, such as a change in temperature or pH, the drug may precipitate out of solution. This precipitation can reduce drug absorption, limit permeability, and impact plasma concentration.

5.9 Drug Interactions:- The solubility of a drug can also influence its interactions with other substances. For example, certain drugs may form complexes or interact with other molecules in a way that affects their solubility. These interactions can alter the drug's permeability, absorption, and subsequent plasma concentration.

Overall, the solubility of a drug plays a crucial role in its permeability and subsequent plasma concentration. It affects the dissolution rate, absorption mechanism, formulation, delivery, and pharmacokinetics, all of which can impact the drug's therapeutic effectiveness and safety. Understanding and optimizing drug solubility is an important aspect of pharmaceutical development and drug delivery systems.

It is important to note that the relationship between drug solubility, permeability, and plasma concentration is complex and can depend on various factors, including the specific drug, its chemical properties, formulation, and physiological factors. Understanding these relationships is crucial in drug development, formulation optimization, and predicting the pharmacokinetic profile of a drug.

6. ARTIFICIAL INTELLIGENCE (AI)

It has the potential to greatly enhance dissolution techniques, which involve the measurement of how quickly a solid drug substance dissolves in a solvent. Dissolution testing is essential in the pharmaceutical industry to assess the performance and quality of solid dosage forms such as tablets and capsules.

7. APPLICATIONS OF AI IN DISSOLUTION TECHNIQUES-

7.1 Predictive Modeling:- AI algorithms can be used to develop predictive models that estimate dissolution rates based on various parameters such as chemical properties, formulation characteristics, and experimental conditions. These models can help determine dissolution behavior in different scenarios without the need for extensive experimental testing.[19]

7.2 Optimal Formulation Design:- AI techniques like machine learning can analyze large datasets of formulation compositions, dissolution profiles, and other variables to identify optimal drug formulations. By considering various factors, including solubility, particle size, excipient selection, and processing techniques, AI algorithms can suggest formulations that enhance dissolution rates and improve drug release.[23]

7.3 Real-time Monitoring:- AI can enable real-time monitoring of dissolution processes by analyzing data from sensors and spectroscopic techniques. By continuously evaluating dissolution kinetics, AI algorithms can identify abnormalities or deviations from expected dissolution profiles, allowing for prompt troubleshooting and process optimization.[19]

7.4 Process Optimization:- AI algorithms can optimize dissolution methods by automatically adjusting process variables such as temperature, agitation rate, and sampling intervals. By analyzing data from previous dissolution runs and utilizing optimization algorithms, AI can help identify the most efficient and reproducible dissolution conditions.

7.5 Quality Control and Anomaly Detection:- AI-based systems can analyze dissolution data to identify outliers and detect any inconsistencies or abnormalities in dissolution profiles. By comparing new dissolution data with historical data, AI algorithms can recognize deviations and raise alerts, ensuring the quality and reliability of dissolution testing.[22]

7.6 R&D Support:- AI can support research and development efforts by providing insights into dissolution mechanisms and identifying key factors influencing dissolution behavior. By mining vast amounts of scientific literature and experimental data, AI algorithms can aid in the discovery of new dissolution methods and formulation strategies.

7.7 Adaptive Control Systems:- By combining AI with automated dissolution systems, adaptive control systems can be developed. These systems can continuously monitor dissolution parameters and make real-time adjustments to ensure optimal dissolution rates. AI algorithms can analyze feedback from sensors and control variables such as temperature, pH, and agitation speed, leading to dynamic control and precise dissolution performance.

7.8 Virtual Simulations and Modeling:- AI technologies enable the creation of virtual simulations and modeling platforms that can simulate and predict dissolution behavior. By inputting various parameters like drug properties, tablet morphology, and formulation characteristics, AI-powered simulations can provide valuable insights into dissolution performance. These virtual models can be used to test different scenarios, optimize dissolution conditions, and assess the impact of formulation changes, helping researchers save time and resources.

7.9 Drug Release Kinetics Analysis:- AI algorithms can analyze complex drug release kinetics data obtained from dissolution testing. By utilizing pattern recognition and sophisticated analysis techniques, AI can identify specific drug release profiles, classify them into relevant categories, and extract relevant information for further analysis. This enhanced understanding of drug release kinetics can aid in rationalizing formulation design and optimizing dosage forms.[21]

7.10 Data Integration and Visualization:- AI can help integrate and analyze large volumes of dissolution data from different sources, including historical data, experimental results, and literature databases. AI algorithms can extract meaningful information, identify trends, and visualize complex data patterns. This allows researchers and scientists to quickly access and interpret dissolution information, leading to better decision-making and more efficient development processes.

7.11 Quality Assurance and Compliance:- AI can improve the accuracy and reliability of quality assurance in dissolution testing. By automating data verification, anomaly detection, and compliance checks, AI systems can ensure adherence to regulatory standards and assist in the generation of comprehensive reports. This helps in maintaining data integrity, reducing human error, and increasing the overall reliability of dissolution testing processes.

7.12 Continuous Process Monitoring:- AI can be employed for continuous monitoring of dissolution processes in real-time, allowing the detection of subtle changes and variations. By analyzing data from multiple dissolution runs, AI algorithms can identify conditions that impact dissolution performance and highlight potential process improvements. This enables researchers to make informed decisions and implement changes to ensure consistent and robust dissolution outcomes.[20]

Overall, the integration of AI into dissolution techniques has the potential to transform the field by improving prediction accuracy, enhancing process efficiency, reducing costs, and enabling faster development of high-quality pharmaceutical products. It offers opportunities to optimize formulations, monitor processes, and support decision-making, leading to more effective and reliable dissolution testing in the pharmaceutical industry.

8. GENERALLY USED AL MODELS.

8.1 Long Short-Term Memory Networks (LSTMs) - LSTMs are a type of RNN that excel in modeling and predicting temporal dependencies. They had been utilized in pharmacokinetics and pharmacodynamics research to predict drug concentration-time profiles and examine drug efficacy.[25]

8.2 Artificial Neural Networks (ANNs) – It have been included as appropriate methods in pharmaceutical product improvement strategies in current years. ANNs successfully permit the estimation of nonlinear relationships between variables. They are broadly used in the pharmaceutical industry to interpret analytical results (pharmaceutical evaluation model in first-rate manipulate), design raw materials (QSAR and molecular modeling) and dosage paperwork (manufacturing system optimization), and convey biopharmaceuticals (pharmacokinetic and pharmacodynamic modeling, in vitro/in vivo correlation) The use of synthetic intelligence in drug technology has increased over time, and ANNs offer a higher understanding of the relationship between exceptional formulations and manner parameters even as saving money and time. ANNs are beneficial for information relationships among inputs (formulation parameters) and outputs (product traits). In this study, an ANN turned into used to estimate the change in solubility and dissolution profile in special areas of the gastrointestinal tract. Using this ANN, the dissolution profile of medicine within the different areas of the gastrointestinal tract and within the absorption place will be expected. Thus, a rational design can be accomplished at some point of pharmaceutical product development**.**[24]

9. TWO METHODS TO SOLVE THE PROBLEM OF UNSTABLE PREDICTION RESULT

9.1 Effective Data Regression Method (EDRM)

Since the version is trained thru a couple of sets of logical statistics, the predicted information are especially distributed close to the actual price so long as the model is valid. First, the opportunity and statistics technique obtain more than one prediction consequences of the same enter dataset via a couple of education and prediction. Then, the prediction end result received after every education is used as a choice tree. If it meets the necessities, it will be retained, and if it does now not meet the necessities, it will likely be deleted. According to statistical techniques, the model calculates the usual deviation of all predicted information and then calculates the common of all expected statistics. If the absolute value of the distinction among the expected price and the common fee is greater than the usual deviation, the information could be automatically deleted. In this way, the model can do away with the odd records generated whilst the predicted statistics converge to the highest quality local solution. However, in the end, we calculate the average of all the statistics to get an average curve. The stability of the prediction value is usually decided through the quantity of training and prediction time. Figure 7 suggests the flowchart of EDRM inside the software.

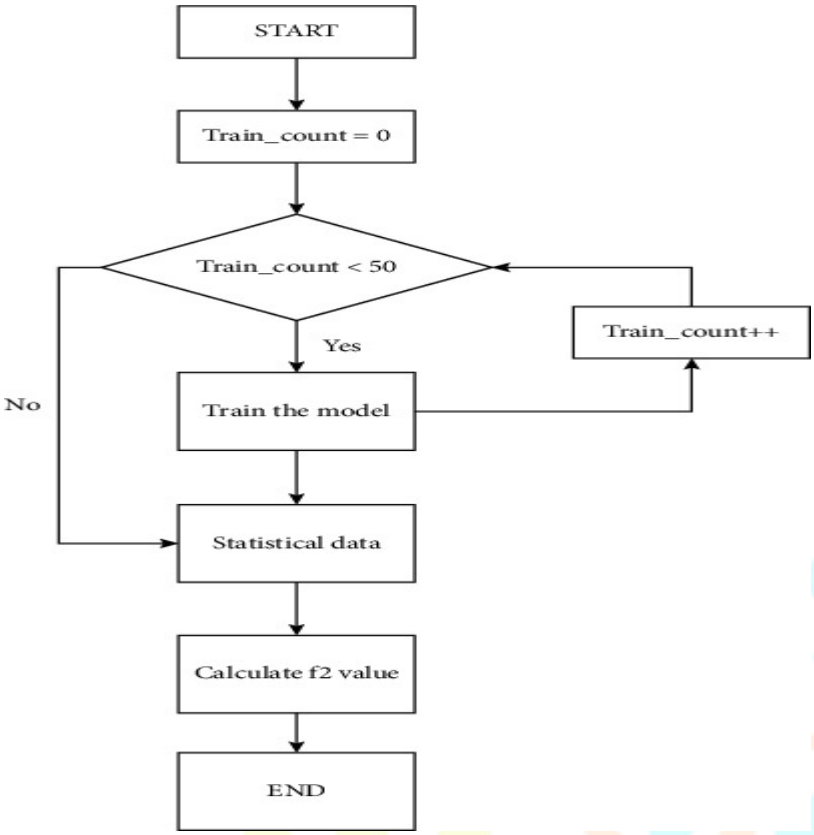

figure 7 – the flowchart of EDRM

9.2 Reference Line Regression Method (RLRM)

The 2D technique is based on the first approach and changes the screening approach for peculiar data generated when the anticipated records converge to the surest neighborhood solution. First, one or multiple units of experimental records from the training are set as reference information. In this check, depending at the wide variety of experimental records, handiest one set of statistics became selected for trying out. The reference data should also be tested through this system records display screen gadget (see the facts display screen version). After each version education, the version makes predictions on this dataset, compares the prediction consequences with the information, and calculates the F2 value. When F2 is less than the set fee (the initial F2 set cost of this version is 65, and this value may be custom designed according to the challenge), the version is considered to converge to the greatest nearby answer. The software robotically acknowledges it as an atypical model and deletes it. When the variety of fashions that meets the necessities reaches the set fee (the set fee is custom, and the initial set value of this version is 50), the filtered facts are averaged to get the regression line. Same as EDRM, while the wide variety of training predictions will increase, the cost of the curve tends to stabilize. The progress and the prediction result of formulation three of RLRM inside the software are shown in Figure 8.[26]

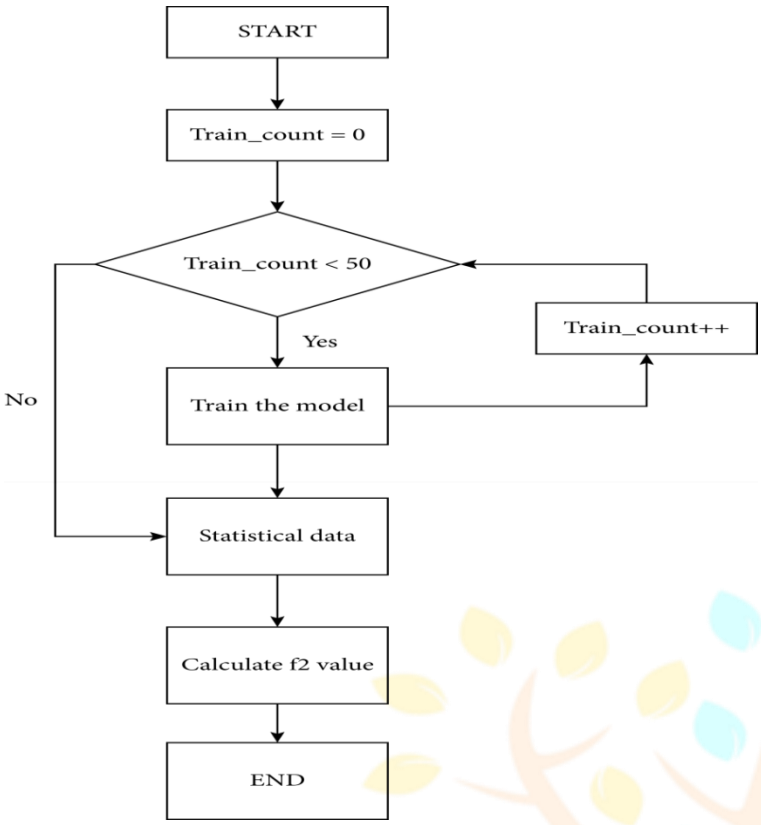

figure 8 – the flowchart of RLRM

10. CONCLUSION - Use of solubility characteristics in bioavailability, pharmaceutical moves and solubility enhancement of numerous poorly soluble compounds is a hard venture for researchers and pharmaceutical scientists. Dissolution enhancement of poorly water soluble drugs constitute an progressive approach, which triumph over the troubles of solubility and dissolution price proscribing step and provide a quick onset of motion.

AI continues to evolve, there'll likely be even more revolutionary packages in dissolution techniques. From optimizing formulations to manner control, great guarantee to records analysis, AI gives vast capability to revolutionize dissolution checking out within the pharmaceutical enterprise and boost up drug development approaches.

11. REFERENCES –

1) Ketan T. Savjani, Anuradha K. Gajjar, and Jignasa K. Savjani, Drug Solubility: Importance and Enhancement Techniques, International Scholarly Research Network, ISRN Pharmaceutics, Volume 2012, 1-10.
2) Atul Kumar Gupta and Susheel Kumar Sehrawat, Bioavailability Enhancement of Poorly Water Soluble Drugs: A Review, International Journal of Pharmacy & Life Sciences, Vol. 2, Issue 3: March: 2011, 640-650.
3) Das Saumya, Pattanayak Dharmajit, Sahu Nigam Prasad, Dissolution Enhacement of Nimesulide using HP-ßcd, Journal of Pharmacy Research 2012, 5(1), 508-510.
4) Samip S Shah, T. Y. Pasha, Atanu Kumar Behera and Anil Bhandari, Solubility Enhancement and Physicochemical Characterization Of Inclusion Complexes Of Itraconazole, Der Pharmacia Lettre, 2012, 4 (1):354-366.
5) Purwa Jain, Achhrish Goel, Shweta Sharma, Meghal Parmar, Solubility Enhancement Techniques With Special Emphasis on Hydrotrophy, Volume 1, Issue 1, July 2010, 34-45.
6) Tejas Patel, L. D Patel, Timir Patel, Sunil Makwana, Tushar Patel, Enhancement of Dissolution of Fenofibrate by Solid Dispersion Technique, Int. J. Res. Pharm. Sci., Vol-1, Issue-2, 2010, 127-132.
7) Amal A. Elkordy and Ebtessam A Essa, Dissolution of Ibuprofen From Spray Dried and Spray Chilled Particles, Pak. J. Pharm. Sci., Vol.23, No.3, July 2010, 284-290.

8) Ana Rita C. Duarte a, M. D. Gordillo, M. Margarida Cardoso, Ana Lu´ısa Simpl´ıcio, Catarina M. M. Duarte, Preparation Of Ethyl Cellulose/Methyl Cellulose Blends by Supercritical Antisolvent Precipitation, International Journal of Pharmaceutics xxx (2006) xxx–xxx, 1-5.
9) Vasu Kumar Kakumanu and Arvind K Bansal, Supercritical Fluid Technology in Pharmaceutical Research, Department of Pharmaceutical Technology (Formulations), National Institute of Pharmaceutical Education and Research, BUSINESS BRIEFING: LABTECH, 2004, 70-72.
10) Vishvajit A. Kamble, Deepali M. Jagdale and Vilasrao J. Kadam, Nanosuspension A Novel Drug Delivery System, International Journal of Pharma and Bio Sciences, Vol.1/Issue-4/Oct-Dec.2010, 352-360.
11) Basavaraj K. Nanjwade, Ganesh K. Derkar, Hiren M. Bechra, Veerendra K. Nanjwade and F.V. Manvi, Design and Characterization of Nanocrystals of Lovastatin for Solubility and Dissolution Enhancement, Nanomedicine & Nanotechnology, 2011, 2-7.
12) Suman Katteboinaa, VSR Chandrasekhar, Balaji. S., Drug nanocrystals: A Novel Formulation Approach for Poorly Soluble Drugs, International Journal of Pharmtech Research, Vol.1, No.3, July-Sept 2009, 682-694.
13) Venkat B.Yadav, Adhikrao V.Yadav, Enhancement of Solubility and Dissolution Rate of BCS Class II Pharmaceuticals By Nonaquious Granulation Technique, IJPRD/2010/PUB/ARTI/VOV-1/ISSUE12/FEB/008, 1-12.
14) Priyanka Pandya, Surendra Gattani, Pankaj Jain, Lokesh Khirwal and Sanjay urana, Co-solvent Evaporation Method for Enhancement of Solubility and Dissolution Rate of Poorly Aqueous Soluble Drug Simvastatin: In vitro–In vivo Evaluation, AAPS pharmscitech, Vol. 9, No. 4, December 2008, 1247-1252.
15) Divyakumar Bora, Priyanka Borude, Kiran Bhise, Formulation and Evaluation of Self Microemulsifying Drug Delivery Systems Of Low Solubility Drug For Enhanced Solubility And Dissolution, International Journal of Pharmaceutical Innovation, 2-19.
16) Srinivas Mutalik, Parambil Anju A, Krishnan Manoja, Achutha Nayak Usha, Enhancement of Dissolution Rate and Bioavailability of Aceclofenac: A Chitosan-Based Solvent Change Approach, International Journal of Pharmaceutics, 350, (2008), 279–290.
17) Seo-Ryung Kima, Jin-Ki Kima, Jeong-Sook Parkb,c, Chong-Kook Kimd, Dry Elixir Formulations Of Dexibuprofen For Controlled Release And Enhanced Oral Bioavailability, International Journal of Pharmaceutics 404 (2011) 301–307.
18) Zhiliang Zhanga, Yuan Lea, Jiexin Wanga, Hong Zhaoa, Jianfeng Chena,b, Irbesartan Drug Formulated As Nanocomposite Particles For The Enhancement of The Dissolution Rate.
19) Precision medicine: from science to value. Ginsburg GS, Phillips KA. *Health Aff (Millwood)* 2018;37:694–701.
20) Wearables and the medical revolution. Dunn J, Runge R, Snyder M. *Per Med.* 2018;15:429–448.
21) Machine learning directed drug formulation development. Bannigan P, Aldeghi M, Bao Z, Häse F, Aspuru-Guzik A, Allen C. *Adv Drug Deliv Rev.* 2021;175:113806.
22) Meyer-Berg, A.; Egert, R.; Böck, L.; Mühlhäuser, M. IoT Dataset Generation Framework for Evaluating Anomaly Detection Mechanisms. In Proceedings of the 15th International Conference on Availability, Reliability and Security (ARES'20), Virtual, 25–28 August 2020; Association for Computing Machinery: New York, NY, USA, 2020.
23) Dara S., Dhamercherla S., Jadav S.S., Babu C.M., Ahsan M.J. Machine Learning in Drug Discovery: A Review. *Artif. Intell. Rev.* 2022;55:1947–1999.
24) Leane, Michael M., Iain Cumming, and Owen I. Corrigan. "The use of artificial neural networks for the selection of the most appropriate formulation and processing variables in order to predict the in vitro dissolution of sustained release minitablets." *Aaps Pharmscitech* 4 (2003): 129-140.

25) Liu X., Liu C., Huang R., Zhu H., Liu Q., Mitra S., Wang Y. Long Short-Term Memory Recurrent Neural Network for Pharmacokinetic-Pharmacodynamic Modeling. *Int. J. Clin. Pharmacol. Ther*. 2021;59:138–146.

26) Wang, Haoyu, et al. "A Novel Artificial Intelligence System in Formulation Dissolution Prediction." Computational Intelligence and Neuroscience 2022 (2022).