ANALYSIS OF MASS AND ENERGY BALANCE OF A-1

Internship Report

Submitted for the partial fulfillment of the degree of

Bachelor of Technology

In

Chemical Engineering

Submitted By

Deepesh Sonowane

0901CM201014

UNDER THE SUPERVISION AND GUIDANCE OF

Prof. Anish P. Jacob

Assistant Professor & Department Coordinator

Department of Chemical Engineering

माधव प्रौद्योगिकी एवं विज्ञान संस्थान, ग्वालियर (म.प्र.), भारत

MADHAV INSTITUTE OF TECHNOLOGY & SCIENCE, GWALIOR (M.P.), INDIA

Deemed to be University

(Declared under Distinct Category by Ministry of Education, Government of India)

NAAC ACCREDITED WITH A++ GRADE

Jan – May 2024

DECLARATION BY THE CANDIDATE

I hereby declare that the work entitled "Analysis of Mass & Energy Balance of A-1"is my work, conducted under the supervision of**Prof. Anish P. Jacob (Assistant Professor & Department Coordinator)**,during the session Jan-May 2024. The report submitted by me is a record of bonafide work carried out by me.

Deepesh

Deepesh Sonowane

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Date: 26/03/24
Place: Gwalior

This is to certify that the above statement made by the candidates is correct to the best of my knowledge and belief.

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teva | api

Ref - TEVA/HR/ MLR/ TRG.CER/05/24 Date: 18th May 2024

To whom so ever it may concern

This is to certify that **Mr. Deepesh Sonowane** a student of Madhav Institute of Technology & Science, Gwalior (M.P.) has undergone a Training with us, on **"Mass and Energy Balance"** from **18.01.2024 to 18.05.2024.**

During the tenure of his training, he was found to be sincere and hard working.

We wish him all the best for his future endeavors.

For Teva API India Pvt. Ltd

18/05/24

(Sachin Jain)
HR Generalist II - HR

PLAGIARISM CHECK CERTIFICATE

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ACKNOWLEDGEMENT

The full semester internship has proved to be pivotal to my carrer. I am thankful to my institute, **Madhav Institute of Technology and Science** to allow me to continue disciplinary/ interdisciplinary internship as a curriculum requirement, under the provisions of the Flexible Curriculum Scheme (based on the AICTE Model Curriculum 2018), approved by the Academic Council of the institute. I extend my gratitude to the Director of the institute, **Dr. R.K Pandit** and Dean Academics, **Mr. Manjaree Pandit** for this.

Guidance and co-operation valuable for fulfilling and furnishing any kind of work. Similarly, I am dearly thankful to the Management for giving me this prestigious opportunity to learn from the field knowledge based on the theortical aspects and also for guiding me during the ongoing training period.

I am sincerely thankful to my faculty mentors. I am grateful to the guidance of **Anish P. Jacob**, Assistant Professor and Department Coordinator, **Department of Chemical Engineering**, for his continued supportand close mentoring throughout the internship. I am also very thankful to the faculty and staff of the department. And I am thankful to **Mr. RohitbabuNalwala** as an industry mentor who helped me a lot to get familiar with the industry for guiding me throughout my internship.

Deepesh.

Deepesh Sonowane

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IV Year,

Chemical Engineering

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Acronyms

1. API:- Active Pharmaceutical Ingredients
2. ANFD:- Agitated Nutsche Filter Dryer
3. FBT: - Flat Blade Agitator
4. RPM: - Revolution per minute
5. AS:- Antisolvent
6. COBC:- continuous oscillatory baffled crystallizer
7. CSD:- Crystal size distribution
8. KRM:- Key Raw Material
9. MSGL:- Mild Steel Glass Lined

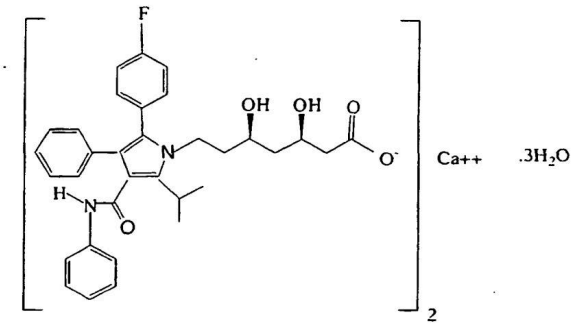
Nomenclature

1. Δp = Pressure drop
2. L = Length of Bed
3. μ = Fluid Viscosity
4. ϵ = Porosity
5. Dp = Diameter of Particle
6. v = Superficial Velocity
7. ρ = Density of Fluid
8. m = Mass
9. Cp = Specific heat capacity of substance
10. Q = Heat Added or Removed from the system
11. Δt = Temperature difference

LIST OF FIGURES

Chpter 1:- Introduction

4.1 About A-1: An medication that lowers blood cholesterol levels and guards against heart attacks, strokes, and angina (chest pain). It is also being researched for the treatment and prevention of several cancers and other illnesses. The API facilities owned by Teva comply with all applicable current Good Manufacturing Practices (cGMP) regulations as well as applicable quality standards from the United States, Europe, Japan, and elsewhere. Because TAPI uses banned chemicals in some of the goods that are sold in the United States, it must abide by the banned chemicals Act and any relevant laws that are overseen by the Drug Enforcement Administration. In aqueous solutions with a pH of four or higher, crystalline A-1 is an off-white to white solid that is insoluble.



Scheme 1

The increasing use of this class of drugs is largely attributed to the rise in cardiovascular diseases (CVD) (such as heart attack, atherosclerosis, angina, peripheral artery disease, and stroke) in many countries. An elevated cholesterol level (elevated low-density lipoprotein (LDL) levels in particular) is a significant risk factor for the development of CVD. Several landmark studies demonstrate that the use of A-1 is associated with both a reduction in LDL levels and CVD risk. A-1 were shown to reduce the incidences of all-cause mortality, including fatal and non-fatal CVD, as well as the need for surgical revascularization or angioplasty following a heart attack. Some evidence has shown that even for low-risk individuals (with <10% risk of a major vascular event occurring within five years) statin use leads to a 20%-22% relative reduction in the number of major cardiovascular events (heart attack, stroke, coronary

revascularization, and coronary death) for every 1 mmol/L reduction in LDL without any significant side effects or risks.

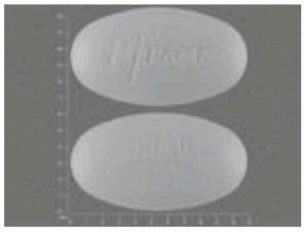


Fig:- Product Image

State Solid

PROPERTY	VALUE
melting point (°C)	176 °C
boiling point (°C)	722 ºC at 760 mmHg
water solubility	Practically insoluble

CHAPTER 2 :- LITERATURE SURVEY

On May 16, 2022, the National Library of Medicine conducted an earlier investigation on A-1. The development of A-1 biloaded capsules for oral administration of hypercholesterolemia was the title of this report. Creating A-1 biloaded, or instant release (IR) and sustained release (SR), capsules with a faster time to action and a superior dissolving profile on both the IR and SR fronts was the aim of this work.

In their article "Quality Assessment of different brands A-1 tablets in Riyadh, Saudi Arabia on September 19, 2022," BMC Pharmacology and Toxicology conducted another investigation. Evaluating the quality of various marketed brands of A-1 tablets that are accessible in Saudi Arabia was the primary goal of the study. The fact that A-1 was added to the Russian Federation's "Vital and Essential Drugs List" highlights the drug's significance for public healthcare systems. The National Library of Medicine is developing the industry-scale manufacturing of A-1 as part of a government-funded programme to support regional manufacture of the active pharmaceutical components for generic medications.

CHAPTER 3: COMPANY'S PROFILE

Teva now runs three cutting-edge Teva API manufacturing facilities in India: one in Gajraula, Uttar Pradesh; another in Malanpur, Madhya Pradesh; and the third in Ambernath, Maharashtra. These facilities produce a range of active pharmaceutical ingredients (APIs) and final intermediates. Every production facility follows the relevant Good production Practices (GMP) and is subject to audits by several ministries and regulatory bodies. Although Teva's primary focus in India is manufacturing, the company regularly makes use of the country's outstanding R&D capabilities by taking advantage of the availability of highly qualified technical personnel for its R&D. Largest synthetic R&D hub for Teva API is located in Greater Noida.

3.1 Goal:- Their goal is to improve patient lives worldwide by being a global leader in biopharmaceuticals and generics. Teva's medications have been used by medical professionals, patients, and carers for more than a century. Every year, Teva saves patients and healthcare systems billions of dollars by providing easily accessible generic substitutes for name-brand medications. Currently, Teva products are found in one out of every nine generic prescriptions written in the US, one out of every six generic prescription packs shipped to the UK, and one out of every eight prescriptions written in Germany.

3.2 Development & Research: - Over the course of more than seventeen years, Teva, the largest Israeli corporation in India, has operated under nine legal companies. Teva's operations support the development of pharmaceutical expertise and capacity in India while also being essential to the company's worldwide production and research and development initiatives. The company's presence in India shows the wide range of initiatives that aid in medication development as well as the notable calibre of professional personnel Teva has been able to draw to the country. India is a key component of the company's strategy because of its exceptional talent pool, enormous partnering possibilities, innovative, collaborative atmosphere, and scientific and clinical know-how.

3.3 History of Teva API India Ltd. :- Teva was founded in Jerusalem in 1901. Our international head office is situated in Israel. Our current portfolio includes over 3,500 medications, and we generate about 85 billion tablets and capsules annually. We operate more than 65 production sites in more than 30 nations. Mule trains and camel caravans were used by the fledgling enterprise, which was named after its chemist founders, Salomon, Levin and Elstein Ltd., to deliver imported medications around the region. The establishment of Assia, a business focused on the manufacturing of veterinary and pharmaceutical chemicals, in 1935 marked the beginning of Teva api's illustrious history. Teva Api has built and acquired prestigious production and research facilities all throughout the world over the years.

The company's expansion was fueled by the rising demand for regionally made medications during the ensuing decades. In 1976, the business changed its name to Teva Pharmaceutical Industries Ltd., which is the Hebrew word for "nature." Our people and culture, which have stayed true to our modest beginnings, have shaped our position as leaders. Our leadership has been characterised by perseverance, an entrepreneurial spirit, and a desire to make a positive difference in people's lives ever since Teva was founded. Teva expanded rapidly throughout the world as a result of multiple profitable acquisitions that combined and improved our knowledge of novel and generic pharmaceuticals, as well as new therapeutic areas and markets. Teva, a global leader in specialty and generic pharmaceuticals, is currently ranked among the top 15 pharmaceutical firms in the world.

3.3 Details of Products of Teva:- About 400 active pharmaceutical ingredients are produced by Teva Api, which covers a broad spectrum of goods such as respiratory, cardiovascular, anti-cholesterol, dermatological, hormonal, anti-inflammatory, oncology, immunosuppressants, and muscle relaxants. More than 1,200 granted patents and pending applications across the world are part of its API intellectual property portfolio.

Israel, Hungary, Italy, the United States, the Czech Republic, India, Mexico, Puerto Rico, Monaco, China, and Croatia are some of the fifteen countries where Teva produces its APIs. Chemical synthesis, semi-synthetic fermentation, enzymatic synthesis, high potency manufacturing, plant extract technology, synthetic peptides, vitamin D derivatives, and prostaglandins are only a few of the production methods in which TAPIs is skilled. Additionally, it can meet requirements for polymorphism, bulk density, specific surface area, particle size distribution (PSD), and other qualities thanks to its cutting-edge technology and solid-state particle ability. The API facilities of Teva satisfy all the current Good Manufacturing Practices (cGMP) requirements as implied by applicable quality standards in the United States, Japan, EuroP-1n, and other nations. In specific products that are sold in the US.

CHAPTER 4: PROBLEM FORMULATION

4.1 Basics of Material Balance The law of conservation of matter states that matter cannot be created or destroyed. This leads to the concept of mass, and the law may be stated in the form that the mass of the materials taking part in any process is constant. It is known now that the law is too restricted for matter moving at velocities near that of light or for substances undergoing nuclear reactions. Under these circumstances energy and mass are interconvertible, and the sum of the two is constant, rather than only one. In most engineering, however, this transformation is too small to be detected, and it is assumed that mass and energy are independent. Conservation of mass requires that the materials entering any process must either accumulate or leave the process. There can be neither loss nor gain. Most of the processes we are dealing with does not involve neither accumulation nor depletion, and the law of conservation of matter takes the simple form that input equals output. The law is often applied in the form of material balances. The process is debited with everything that enters it and is credited with everything that leaves it. The sum of the credits must equal the sum of the debits. Material balances must hold over the entire process or equipment and over any part of it. They must apply to all the material that enters and leaves the process and to any single material that passes through the process unchanged.

4.2 MANUFACTURING PROCESS:-

A procedure for creating amorphous A-1 includes the following steps:

a) **KRM Reaction:** 150 kg of KRM, 1938 L of M-1, 372 L, and 12.4 L of H-1 are added to a 6000 litre glass-lined reaction vessel and heated to 37°–43°C while being continuously stirred at 80–90 rpm.Subsequently, KRM is sampled; unreacted KRM should be less than 1%.

b) **DISTILLATION**: After that, 1008 litres of M-1are added and allowed to agitate for nine hours at a temperature of roughly 50°C.This technique distils off 95% of the M-1. Subsequently, KRM is sampled once again; unreacted KRM should be less than 0.1%.

c) **P-2 RMATION**: 19.375 kg of S-1are now added to produce an A-1 sodium salt at a temperature

d) **CRYSTALLISATION**: This sodium salt of A-1 is now charged into an SS-316L crystallizer together with 2635L of W-2, 13.18 kg of A-1 seeds, 13.4 kg of C-1, and 155 L of M-1. In this reactor, precipitate crystallisation takes place between 57°C and 63°C, forming A-1 crystals.

e) **FILTRATION**: A centrifugal filter is used to filter the crystals that have formed above. After extracting the mother liquor, the cake is cleaned with M-1and then W-2.

c) **DRYING**: To produce A-1, the product is dried in an ANFD at 60° to 70°C. After that, the dry product is put into barrels.

4.3 Mass and Energy Balance Equations:-

4.3.1 Mass balancing:- (All the amounts are in Kg)

i. For crystallizer:-

- $(W-2)_1$ + (seeding) + (C-1) + (Z) + $(W-2)_2$= M

2635 .59 + 13.375 + 2547.175 + 775 = 5977.14

ii. For centrifuge:-

- M + (w-2) – (mother liquor) = N

5977.14 + 1395 – 5600 = 377.14

iii. For ANFD:-

- N – (moisture) = (final product)

377.14 –(377.14)*(0.6) = 150.856

4.3.2 Energy Balancing:-

- In crystallization:-

- $Q_4 = (\sum F_i C_i)(\Delta T)$

Q_4 = (2547.175*0.5 + 2635*4.2 + 13.4*3.2 + 6.6*0.5 + 620*4.2 + 155*2.5)(75-60)

Q_4 = 230672.7 J/kg˚c

- In centrifuge:-

- $Q_5 = (\sum F_i C_i)(\Delta T) - (F_o C_o)(\Delta T)$

Q_5 = (5977.4*0.5)(25-20) – (5600*0.5)(25-20)

Q_5 = 943.5 J/kg˚c

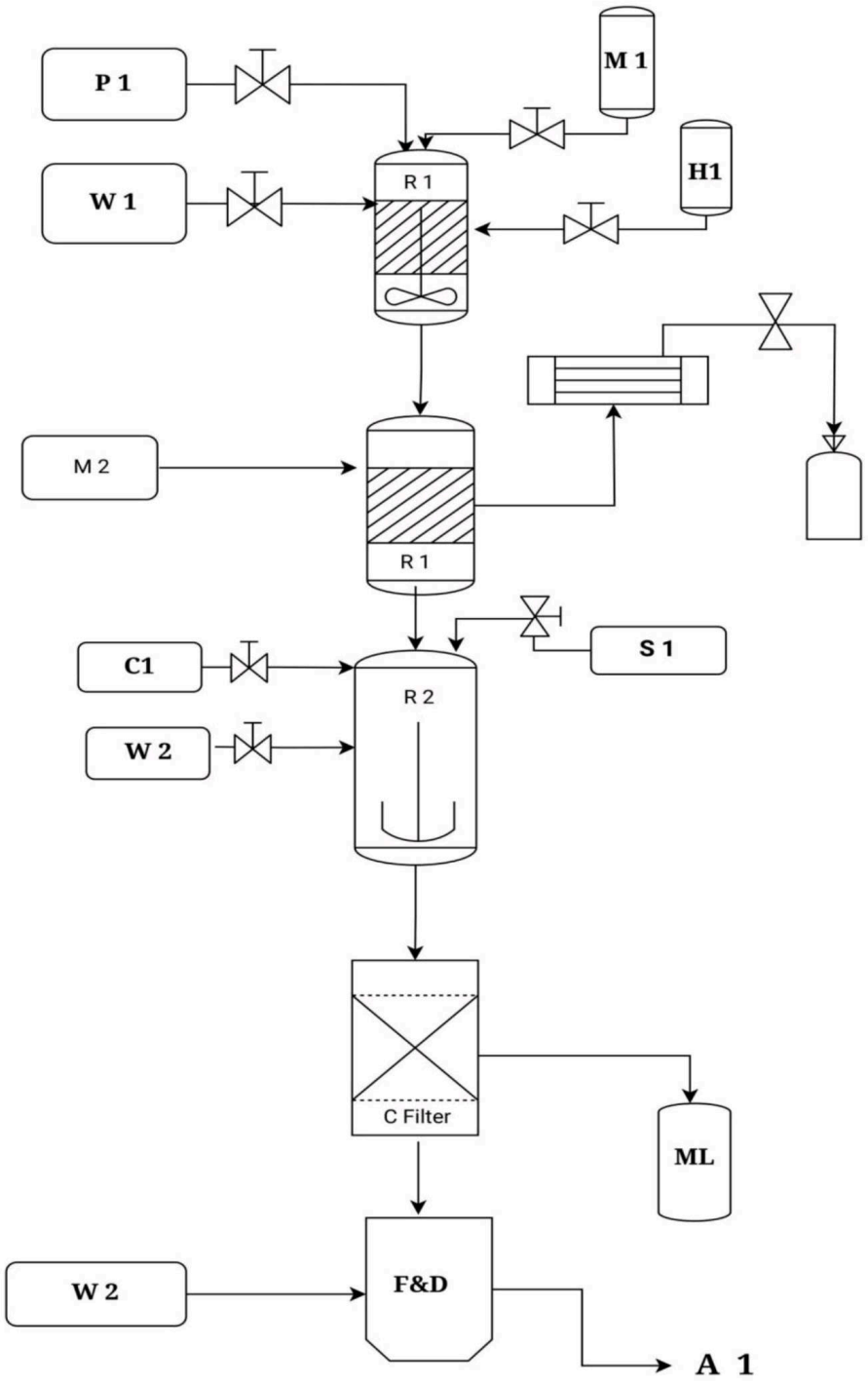
- In ANFD:-

- $Q_6 = (\sum F_i C_i)(\Delta T) - (F_o C_o)(\Delta T)$

Q_6 = (377.14*0.5)(70-60) – (226.284*0.5)(70-60)

Q_6 = 754.28 J/kg˚c

BLOCK FLOW DIAGRAM



Chapter 5:- Methodology

5.1 SS-316 Crystallizer: - 10% nickel, 2% molybdenum, and 16% chromium are present in SS 316. This 2% molybdenum aids in resistance to both general corrosion caused by reducing acids like sulfuric acid and localised corrosive attack by chlorides in an environment that promotes corrosion. It has an agitator of the Anchor + FBT type that rotates between 20 and 22 RPM.

Heat-sensitive medicinal compounds do not crystallise well using the conventional cooling-only method. Antisolvent is usually utilised for such systems in order to increase the product yield. Very high degrees of supersaturation are known to be produced by reactive crystallisation. Reactive crystallisation is the process of producing supersaturation of a crystallising molecule by a chemical reaction. Reaction times in reactive crystallisation can be extremely quick in comparison to the rates of mass transfer and crystal formation. High local supersaturations are the result. In order to attain the intended residence periods and final solvent composition, the API solution and the two AS solutions were fed into the COBC at different rates. The speeds at which the antisolvent and API solution flow were calculated as shown in equations (4) and (5).

$$TR=2V1/F1+2V1/(F1+F2)+3V1/(F1+2F2) \quad (4)$$

$$xIPA,f=xIPA,i\times F1/(F1+2F2) \quad (5)$$

where TR is the desired residence time, xIPA,i is the initial IPA solvent fraction, and xIPA,f is the final IPA solvent fraction. V1 is the volume of each section. F1 and F2 are the flowrates of the API solution and the antisolvent stream, respectively. The two antisolvent inlets' flowrates remained constant. By adding up the resident times for each section, Equation 4 determines the residence time in the COBC. Equation 5 determines the final solvent concentration by comparing the flowrates of the antisolvent and whole solution to the total IPA content in the API solution. Using the formula in equation 6, the productivity (P) of both batch and continuous crystallisation was determined.

$$P(gh\cdot L)=(m\Delta t\cdot Vtot) \quad (6)$$

Fig 1. SS-316 Reactor

Ref:- 1

5.2 Centrifuge:- A centrifuge is a device that uses a centrifugal force, which can be millions of times stronger than gravitational force, to replace the latter with force. To put it plainly, centrifugal filtering speeds up the process that happens naturally. A centrifugal filter extracts the particulate matter from the liquid by spinning the material at a high speed. A solid sludge cake is produced when the heavier solids are forced to the outside of the separator bowl by the centrifugal filter. The reaction mass is fine-filtered using a high flow bed after crystallisation, and it is then cleaned at a temperature of 20 to 25 degrees Celsius using M-1and W-2.

Because centrifugal force produces a strong filtering driving force that quickly separates solid and liquid phases, it is frequently utilised in industrial solid-liquid separation processes. The separation factor (Fr), which can be stated as follows, is the ratio of centrifugal acceleration to gravitational acceleration produced during centrifuge operation.Fr is equal to rw2/g (1), where g is the gravitational acceleration, ω is the rotation speed, and r is the radius of rotation. The centrifugal force acting on the particles increases with increasing separation factor (Fr), indicating a higher level of separation effectiveness.

Materials with a high solution viscosity and small particles require a centrifuge with a large separation factor. A particle in a fluid rotational system experiences two radial acting forces:

Stokes drag and centrifugal force, which cause the particle to travel outward. Consequently, when it comes to force equilibrium,

$$(\rho p-\rho f)4\pi/3(Dp/2)\text{^}3.\Omega\text{^}2.r=3\pi\mu Dp(Vp(r)-Vf(r)) \qquad (2)$$

where Dp is the particle size; $\boldsymbol{\lambda}p$ and ρf are the particle and fluid densities, respectively; and $Vp(r)$ and $Vf(r)$ are the particle and fluid radial velocities, respectively, in position r. Equation (2) makes the assumption that there is no turbulent flow pattern. Consequently,

$$Vp(ri) = [(\rho p-\rho f)D2p\Omega/18\mu]\ \Omega ri+Vf(ri) \qquad (3)$$

The radial velocity of the particles on the membrane surface (position ri) is represented by equation (3). The term enclosed in brackets is the particle Taylor number; the fluid viscosity is denoted by μ; the radius and rotational speed of the inner cylinder are represented by ri and Ω, respectively.

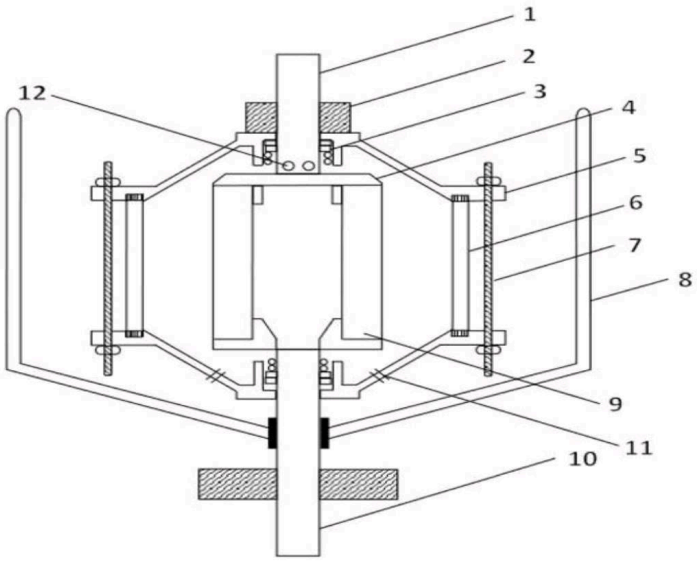


Fig2. Schematic diagram of the centrifugal filtration device. 1: fluid inlet pipe; 2: shaft seal pedestal; 3: shaft seal; 4: filter pedestal; 5: centrifugal chamber; 6: acrylic wall; 7: fixed screw; 8: receiving tank; 9: filter; 10: filtrate outlet; 11: centrifugate outlet; 12:fluid inlet pore

Ref:- https://separatorequipment.com/wha 1

5.2.1 Priciples of Filtration:- Filtration is a special example of flow through porous media. In filtration the flow resistances increase with time as the filter medium becomes clogged or a filter cake builds up. The chief quantities of interest are the flow rate through the filter and the

pressure drop across the unit. As time passes during filtration, either the flow rate diminishes or the pressure drop rises. In what is called constant-pressure filtration the pressure drop is held constant and the flow rate allowed to fall with time; less commonly, the pressure drop is progressively increased to give this is called constant-rate filtration. In cake filtration the liquid passes through two resistances in series: that of the cake and that of the filter medium. The filter-medium resistance, which is the only resistance in clarifying filters, is normally important only during the early stages of cake filtration. The cake resistance is zero at the start and increases with time as filtration proceeds. If the cake is washed after it is filtered, both resistances are constant during the washing period and that of the filter medium is usually negligible.

The overall pressure drop at any time is the sum of the pressure drops over medium and cake. If pa the inlet pressure, pb the outlet pressure, and p' the pressure at the boundary between cake and medium, $\Delta p = pa - pb = (pa - p') + (p' - pb) = \Delta pc + \Delta pm$ where Δp = overall pressure drop Δpc = pressure drop over cake Δpm = pressure drop over medium Pressure drop through filter cake: A general equation named Ergun equation employed to calculate the pressure drop across the packed bed for all flow conditions, The Ergun equation combines both the laminar and turbulent components of the pressure loss across a packed bed. Given as,

$$\frac{\Delta P}{L} = \frac{150\mu uL(1-\epsilon)^2}{(\emptyset Dp)^2 \epsilon^3}$$

5.3 ANFD:- An apparatus called an Agitated Nutsche Filter Dryer (ANFD) is used to dry wet materials and separate solids from liquids. The Agitated Nutsche Filter Dryer (ANFD) is a versatile apparatus utilised for the solid-liquid separation, cleaning, and drying of a wide range of chemicals, medications, and food items. The cylindrical jar used in the ANFD contains a stirrer inside and a perforated plate at the bottom. The following actions are necessary for ANFD to function:

1. Loading: Using the top manhole, the slurry or wet cake is loaded into the vessel.

2. Filtration: Next, the stirrer stirs the slurry and produces a vacuum beneath the filter medium. After passing through the filter media, the liquid is gathered in the vessel.

3. Washing: To get rid of any leftover product or contaminants, the solid cake is cleaned with a suitable liquid or solvent after filtering.

4. Drying: The solid cake is dried with a stirrer by using heat or a hoover after washing. A solid, dry cake is left behind as the solvent evaporates.

5. Discharging: The bottom discharge valve is used to remove the dry cake from the vessel when it has finished drying.

Compared to other filter types, the ANFD has a number of benefits, such as high filtration efficiency, little product loss, faster processing, and a closed system that removes the possibility of product contamination. The equipment is a popular option for a variety of industrial applications because it is also simple to maintain and clean.

Fig 3 ANFD Dryer

Ref: - https://www.google.com/imgres?q=a 1

5.4 Agitation Equipment:- Liquids are oftenly agitated in a tank without sharp edges having a round bottom. The top of the tank is mostly closed. The proportions of the tank may vary accordingly. The liquid depth is genrally equals to the diameter of tank. Tank has no bottom sharp edges so that liquid current would not penetrate into

the edges. An impeller is mounted on an overhung shaft, the shaft is connected to the motor, many times the shaft is connected to gearbox in order to alter the speed. Accesories such as inlet, outlet lines, coils, jackets, wells for thermometer or other temperature measuring device are usually included.

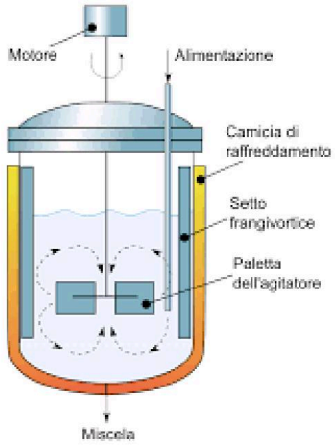


Fig.4 Agitation Process Vessel

Reference: Unit Operations of Chemical Engineering Mc Cabe and Smith

Agitators can handle various types of media, including liquids, gases, and solids (such as granules and powders). They are capable of working with slurries, suspensions, and highly viscous liquids. However, selecting the right agitator type, size, and design is critical, considering factors such as viscosity and sensitivity to shear stress. Agitators find widespread use in industries such as food and beverage, pharmaceutical, agricultural, biotechnology, paint, and water treatment. There are different types of agitators are used here are some examples:

a) Paddle Agitator - It consists of two flat paddle-shaped impeller blades extending to reach the tank walls. It is used if no extensive axial and radial flow is required. These impellers can produce a laminar low shear flow and are used for low viscosity liquid mixing, crystallization, dissolution, and heat transfer. It is typically operated at low speeds and dominantly gives a tangential flow pattern. Secondary blades can be installed on the paddle blades to enhance the mixing of more viscous materials.

b) Anchor Agitator - They have impellers having the shape of an anchor. They typically have a U-shape which matches the shape of the tank. They generate a dominant tangential flow

pattern. c) Propeller Agitator - An axial-flow, high-speed impeller for low-viscosity liquids is called a propeller. Propellers of different sizes rotate at different motor speeds: 1150 r/min for small propellers and 400–800 r/min for bigger propellers. The liquid flow currents exiting the impeller follow a certain path until they are redirected by the vessel's wall or floor. Static liquid is entrainted as it goes along by the extremely turbulent swirling column of liquid exiting the impeller, most likely much more than an identical column from a stationary nozzle would. The liquid is forcefully chopped or sheared by the propeller blades. Larger vessels might benefit from propeller agitators due to the continuous flow currents.

d) Pitched- Blade Agitator Pitched blade turbine agitators have flat angled blades. The most common type of pitched blade agitator is a four-blade turbine that makes a 45° angle with the vertical. It provides a combination of axial and radial flow, the axial flow is more dominant than the latter. It generates high shear and has good mixing efficiency. It is used in solid suspensions and gas dispersions.

Chapter 6:- Results and Discussion

6.1 Yield of the process:- Chemical reactions in the real world do not always go exactly as planned on paper. In the course of an experiment, many things will contribute to the formation of less product than would be predicted. Besides spills and other experimental errors, there are often losses due to an incomplete reaction, undesirable side reactions, etc. Chemists need a measurement that indicates how successful a reaction has been. This measurement is called the percent yield.

Percent Yield = Mass of Actual Yield / Mass of Theoretical Yield x 100 percent.

Composition of KRM in feed = 6.025%

Amount of KRM in Feed = 2457.175*(0.0625) = 153.57 kg

Amount of Product Formed = 150.856 kg

Percent Yield = 150.856/153.57 = 0.98 (with seeding)

Chapter 7: Conclusion

In conclusion, this internship's mass and energy balance study of A-1has shed important light on the steps involved in making this essential medication. I now have a thorough understanding of the inputs, outputs, and energy requirements associated with the manufacturing process thanks to my careful calculations and observations. The interdisciplinary character of pharmaceutical engineering has also been emphasised by this project, which emphasises the integration of pharmaceutical science and chemical engineering principles to ensure optimal process performance. As a practical way to control particle formation and enhance physicochemical properties in solid state, micro- and nanoparticle formation processes based on the use of supercritical fluids as solvents or antisolvents for poorly W-1 soluble active pharmaceutical ingredients (APIs) have been introduced recently. Furthermore, a strong association was observed between the solubility and the intrinsic dissolution rate. By increasing the intrinsic dissolution rate and decreasing the particle size, which raised the specific surface area, the dissolution rates of amorphous A-1nanoparticles were significantly higher than those of the medication in its unprocessed form.

Chapter 8

8.1 Outcomes

1. To obtain a better comprehension of the pharmaceutical industry's drug development and regulatory needs.

2. To increase my resume's relevance to the sector and become a more competitive applicant for jobs in the future.

3. To comprehend the phases of drug development, including preclinical research, clinical trials, regulatory approval, and commercialization, that go into getting a medication from discovery to market.

4. To gain experience in project management by working on certain projects inside the business, which include coordinating, scheduling, and carrying out tasks to satisfy deadlines and objectives.

8.2 Societal Relevance:- My research explores the energy needs of the process, including mixing, heating, cooling, and other unit operations. The study's conclusions not only advance knowledge of the A-1 production process but also provide insightful information that will benefit the larger pharmaceutical sector. Pharmaceutical manufacturers can increase resource efficiency, product quality, and waste generation by including mass and energy balance assessments into process design and optimisation efforts. This will help the sector move towards more sustainable practices.

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Appendices

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Appendix A:- Mass Balance

17		In Crystalizer	
18	RM	Quantity(kg)	Ratio
19	P-2	2547.175	16.4333871
20	W-2	2635	17
21	Seeding	6.59	0.042516129
22	C-1	13.375	0.086290323
23	W-2	620	4
24	M-1	155	1
25		5977.14	
26			
27			
28		In Centrifuge	
29			
30	RM	Quantity	Ratio
31	Material (fron	5977.14	38.56219355
32	ML	-5600	-36.1290323
33		377.14	
34			
35		In ANFD	
36			
37	RM	Quantity	Ratio
38	Wet A-1	377.14	2.43316129
39	Mioture remo	-226.284	-1.45989677
40	Total Dry Mat	150.856	

Appendix B:- Energy Balance

62	In Crystallization:-				
63	Componer	m	Cp	T	Energy(J/k
64	P-2	2547.175	0.5	15	19103.8125
65	W-2	2635	4.2	15	166005
66	Seeding	13.4	3.2	15	643.2
67	C-1	6.6	0.5	15	49.5
68	W-2	620	4.2	15	39060
69	M-1	155	2.5	15	5812.5
70					230674.013
71	In Centifuge:-				
72	Componer	m	Cp	T	Energy(J/k
73	Material(from	5977.14	0.5	5	14942.85
74	ML	-5600	0.5	5	-14000
75					942.85
76	In ANFD:-				
77	Componer	m	Cp	T	Energy(J/k
78	Wet A-1	377.14	0.5	10	1885.7
79	Moisture rem	-226.284	0.5	10	-1131.42
80					754.28

Appendix C:- Daily Diary

- Day 1 (19/01/24):- Derivation of Fenske Equation.
- Day 2 (20/01/24):- General overview of the plants and information about the products.
- At home (21/01/24 - 25/01/24):- Studied about various MOC's of the reactors, and their applications.
- Day 3 (27/01/24):- Visit of the mini plant and get the information about the components of reactor.
- At home (28/01/24-01/02/24):- Studied about various types of filters and their applications.
- Day 4(09/02/24):- Solved the problem of finding area of condenser.
- Day 5(10/02/24):- Visit MPP-1 plant to get the overview of the manufacturing process of Atorvastatin Calcium.
- From (11/02/24-15/02/24):- Prepare the flowsheet of the manufacturing process of Atorvastatin Calcium.
- Day 6(16/02/24):- Again visit the MPP-1 plant to get the input and output details from the shift officer.
- Day 7(17/02/24):- Collected the remaining output details from MPP-1.
- From (18/02/24-22/02/24):- Prepare the excel sheet of mass balancing of Atorvastatin Calcium.
- Day 8(23/02/24):- Show the prepared excel sheet to the Industrial mentor and worked on the mistakes.
- 24/02/24:- Holiday on account of Sant Ravidas Jayanti.
- Day 9(01/03/24):- Solved the problem of preparing VLE diagram between ethanol-water.
- Day 10(02/03/24):- Prepared the VLE Diagram and it's calculation by Antoine equation on excel sheet.
- From (03/03/24-07/03/24):- Study about different types of pumps used in Industries and their applications.
- 08/03/24:- holiday on account of Mahashivratri.
- Day 11(09/03/24):- Industrial mentor gave the problem of preparing VLE diagram between three components (ethanol,water and SO2).

- From (10/03/24):- Worked on the problem given by Industrial mentor.
- (15/03/24-16/03/24):- Take leave due to BARC Exam.
- Day 12(22/03/24):- Industrial mentor explained how to find VLE among three components.
- Day 13(23/03/24):- leave
- From (24/03/24-28/03/24):- Studied different types of jackets used in reactors.
- Day 14&15(29/03/24-30/03/24):- Visit the ETP Plant.
- From (01/04/24-04/04/24):- Studied about different types of crystallisation methods.
- Day 16&17(05/04/24-06/04/24):- Visit the Solvent recovery plant.
- From (07/04/24-11/04/24):- Studied about different types of inertization methods.
- Day 18&19(12/04/24-13/04/24):- Visit the MPP-1 plant for collecting data for doing energy balance.
- From (14/04/24-18/04/24):- Performed the energy balance of Atorvastatin Calcium on excel sheet.
- Day 20(19/04/24):- Visit the MPP-1 plant to understand the manufacturing process of Quetiapine API.
- Day 21(20/04/24):- Industrial mentor gave the problem of finding the time taken for distillation of Atorvastatin Calcium.
- From (21/04/24-24/04/24):- Worked on the problem given by Industrial mentor.