

# IMPLEMENTATION OF GREEN TECHNOLOGY & GREEN CHEMISTRY IN PHARMACEUTICAL INDUSTRY: A NEWER APPROACH FOR SUSTAINABILITY IN PHARMACEUTICAL INDUSTRY

## Abstract

Emerging trends have nowadays been involved for the sustainability in Pharmaceutical industry. The concept of Green technology, Green Chemistry are growing attentions as the industries produces a significant amount of wastes and Green house gases with the utilization of large volume of water. The implementation of energy efficient system, using electric vehicles in logistics operations and independent verifications such as leadership in energy, environmental design certifications that focuses on company's building designs, construction are considered to be resource efficient which minimizes its carbon footprint. In order to minimize the impact on environment in a cost effective manner the designing of the chemical process with reduction in the use and creation of hazardous substances should be incorporated.

To achieve sustainability in operational perspectives integration of Green supply chain (GSC) can also be adopted. However, the potential risk and finalizing the risks involved in adopting the GSC initiatives within the pharmaceutical industry depends on fuzzy Delphi approach and fuzzy Analytical Hierarchy process (AHP).

According to the data obtained during a survey conducted in top global pharmaceutical companies, the two main obstacles to GC adoption are affairs related to regulatory bodies and pressures to deliver new medications. Hence, it is necessary to

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apply life cycle assessment metrics, enhance GC education, build effective supplier management programmes, and increase the application of green chemistry throughout the entire supply chain. Large decline in Toxics Release Inventory (TRI) release from the pharmaceutical industry in U.S. have been observed with the adoption of GC as per the reports of researchers.

Despite not being publicly disclosed, generic medication companies, API manufacturers, and smaller R&D pharmaceutical businesses show interest in and advancements in GC principles, according to the global pharmaceutical supply chain. The current chapter aims to focus new technologies adoption of GC by pharmaceutical companies and API manufactures, to examine the drivers and barriers to greater adoption of GC by industry and to identify opportunities for wider acceptance of GC by pharma industry and API manufacturers in India.

**Keywords:** Green Chemistry, Green technology, Green Supply Chain, Pharmaceutical Industry, Active Pharmaceutical Ingredients.

## I. INTRODUCTION

Pharma companies have traditionally pledged to provide ground-breaking medicines to raise living standards around the globe [1]. During this process, from chemicals and waste management perspective, health and environmental concern in this are mainly related to release of pharmaceutical in the environment. Direct emissions from drug manufacturing, patient and animal excretion, aqua farming and disposal of unused or expired medicines are found to be various sources of release of pharmaceuticals to the environment [2]. In the recent times, many large pharmaceutical companies have moved to using green-chemistry practices for drug discovery, development and manufacturing. Their approach mainly focuses on profit, people and planet in contribution to the 12 principles of green chemistry which comprises of minimizing ingredients, waste, toxicity and energy [3]. To quantify the waste generated from various process, the chemical industries includes the terms "E-factor" and "PMI" refer to the unit of waste produced per unit of product (API) and the unit of raw material consumed per unit of product, respectively. A lower value on both is desirable, and is the goal that the pharmaceutical industry is driving towards [4]. In a report published in recent times by UK water Research Industry found several common drugs were present in the final effluent in high concentration enough to potentially affect our ecosystem upon a study conducted on 160 sewage treatment works. According to forecasts made by the Delft Institute for Water Education in the Netherlands, before the middle of the century, the amount of pharmaceutical effluence entering rivers could be increase. Antimicrobial resistance (AMR), which is connected to the release of antibiotics and other chemicals into the environment, is a particular cause for concern. Although antibiotics are essential for medical treatment, AMR has been labelled by the World Health Organisation as a "major threat to public health" and is expected to cause 10 million deaths annually by the year 2050 [5]. The field of chemistry known as ecological methods focuses on minimising or completely eliminating the use of harmful compounds in chemical processes as well as poisonous and harmful intermediates and end products. Solvent, Reagent/catalyst and energy consumption are the three key components for a reaction to be called as "Green". "Use and generation" is an another new aspect in the definition of "Green Chemistry" [6].

In 2005 the Pharmaceutical Roundtable started which was initially collaboration between the ACS Green Institute and the pharma industry as a start-up to include green chemistry in the process. Solvents were identified as the source of the majority of waste in the synthesis of small molecules by the Roundtable's benchmarking exercise, which was useful because this is a relatively non-competitive market. The Roundtable had focused on encouraging solvent providers to develop new solvents by using renewable raw materials and creating solvents with better environmental profiles, as well as on assisting chemists in making better solvent choices from the standpoints of the environment, health, and safety [7].

The cost of finding new chemical entities (NCEs) does not significantly decrease with the application of Green Chemistry (GC) principles. Designing APIs is one of GC's most important contributions to the drug discovery process. One issue that has not received much attention up to this point is the downstream persistence of medicines and their active metabolites in the environment. Environmental studies that consider the possibility of harming fish and plant life are required as part of marketing applications by the FDA, EMEA, and the Ministry of Labour, Welfare and Health (MLWH), Japan. To evaluate the

potential for endocrine disruption, till date no good tests are available. As an additional parameter in the drug discovery process, information related to rapid degradation of the designed NCEs after release to the environment should be included. This serves to be an important area of research at the Carnegie Mellon Institute for Green Science, PA, and USA [8].

The Green Aspiration Level (GAL) which is defined as the expected environmental impact for producing any pharmaceutical agent by assessing the complexity of its ideal synthetic route is one of the first significant green efficiency goal for any given manufacturing process. Here the direct route with the minimum number of synthetic stages is designed using commodity chemicals at the beginning of the drug development programme [9].

AstraZeneca in their article have mentioned some of the key features which they have adopted in maintaining sustainability in the drug discovery process for saving our planet. They have mentioned the modified technique of incorporating light into the development process, for photo catalysed carboxylation reaction the use of carbon dioxide in addition with visible light, use of easily and readily available greener materials by our chemists to synthesize the APIs will definitely proved to reduce the environmental footprint of the industry and along with late stage molecule modification techniques the labs , production will be more efficient with the vision to save the resources for future generations[10].

The most crucial variables to take into account for greener techniques are solvents and stoichiometric reagent. Various traditional solvents such as halogenated petroleum-based ones can be substituted with glycerol, ethyl lactate, water which will be more environmentally friendly. Another important factor that lowers the quantity of inorganic salts and/or reagents is a catalyst. Pharmaceutical businesses have thought about using a catalyst as a green alternative to consuming stoichiometric salts and chemicals. However, the application of catalysts to be widely employed has been constrained by the desire for the least expensive reagents [11].

In chemical reactions, solvents are essential for dissolving solids, diminishing viscosity, adjusting temperature, retrieving products by extraction and recrystallization, as well as for cleaning. They may also have an impact on the API's particle size and manufacturing costs by making isolations challenging or necessitating milling. Considering their benefits, these solvents have a number of negative impacts on both human health and the environment. Solvents are mostly derived from non-renewable resources like petroleum which are in contradictions to the basics of Green Chemistry. The only alternative to substitute these environmentally harmful solvents is with some use of benign solvents. The following four directions for the development of green solvents were discussed by Hungerbuhler et al.

- Harmful solvents can be substituted with safer alternatives having superior EHS (Environment, Health, and Safety) characteristics, as improved biodegradability or a lower propensity for ozone depletion.
- Use of renewable resources or “bio-solvents” such as ethanol produced by fermentation of feed materials which contains sugar, starch or lignocellulosic compounds.

- Supercritical CO<sub>2</sub> can replace organic solvents in polymer production, avoiding the usage of chlorofluorocarbons and reducing ozone depletion.
- There are fewer emissions to the air when using ionic liquids, which exhibit low or negligible vapour pressure [12].

Four classes of solvents have been listed by the Centre for Drug Evaluation and Research (CDER) under US FDA (USA Food and Drug Administration). Based on their unacceptable toxicity or deleterious environmental impact Class I solvents includes benzene, carbon tetrachloride, 1,2-dichloroethane, 1,1-dichloroethylene and 1,1,1-trichloroethane. Class II solvents include acetonitrile, methanol, methylene chloride, tetrahydrofuran, toluene, and hexane. The least harmful potential are class III solvents, such as acetic acid, acetone, ethanol, ethyl acetate, heptane, and dimethyl sulfoxide. There are insufficient toxicological data on Class IV solvents, which include isooctane, isopropyl ether, petroleum ether, and 2-methyltetrahydrofuran [13].

There is more than one way to address the complex issue of pharmaceutical industry pollution. Since scientists are trying to find solutions to stop the production of waste, the issue is extremely important everywhere in the globe. With a view to advancing the idea of green chemistry to safeguard human health and the environment while retaining commercial viability, the US has created the American Chemical Society. Dr. Verma emphasised the microwave energy as an alternative source and said it could be utilised for reactions that can create a library of chemicals, particularly in the context of an environment-free solvent strategy for the treatment of waste, alkane, breakdown, and targets for drug discovery. Reducing the use of solvents is the basic idea behind green chemistry [14].

The environmental impact of solvents has been acknowledged, especially with regard to their synthesis and source, as well as their use and potential for accidental discharge. The choice of solvent can have a significant impact on the result of a reaction. This means that switching from a "non-green" solvent to a "green" solvent may have unintended consequences. These unintended consequences includes either a greater need for severe working conditions or an increase in waste. In certain circumstances, the process may end up being less environmentally friendly overall. It is essential to take into account all of a solvent change's effects on the entire process in order to fully comprehend how it can damage a process's potential to be sustainable. In light of this, it is foolish and possibly unimportant to think that a liquid can be considered to be fundamentally "green." Use of a single solvent or a solvent system, rather than a combination of both, is what matters [15].

Based on rigorous solvent selection and consideration of the solvent's role throughout the entire process, traditional organic solvents are primarily used by industrial chemical processes. Neoteric solvents are gradually being included into different industrial processes because they have advantages over organic or aqueous solvents by increasing the product separation. Ionic liquids, deep eutectic solvents, liquid polymers, supercritical carbon dioxide (scCO<sub>2</sub>), gas expanded solvents (GXLs) and switchable solvents are examples of neoteric solvents. Price, availability, purity, restrictions, disposal processes, recycling procedures, and costs must all be taken into account before neoteric solvents are used by the chemical [16].

## II. DEPLOYING GREEN CHEMISTRY IN API SYNTHESIS

Pharmaceuticals are only one of several businesses that have made it a priority to find ways to enhance the environmental profile of production methods and finished goods. By deploying the concept of green chemistry at the time of manufacturing active pharmaceutical ingredients, intermediates or active compounds, waste reduction, increase yield, reaction efficiency with minimal use of solvents and reagents can be achieved. The various submissions to the Presidential Green Chemistry Challenge Awards organised by the US environmental Protection agency provide strategies for green chemistry which can be further applied to the pharmaceutical sector.

In order to increase the catalytic activity and effectiveness of chemical reactions, Professor Bruce H. Lipshutz of the Department of Chemistry and Biochemistry at the University of California, Santa Barbara, developed a technique to reduce the need for organic solvents in the reactions. With a maximum yield of isolated products, Lipshutz and his team came to the conclusion that a derivative of sebacid acid called mono-PEGylated, alpha-tocopherylated derivative (PTS) will be useful to carry out various organic reactions catalysed by transition metals like palladium and ruthenium. Water can be used as the only solvent, at room temperature. The Suzuki, Heck, and Sonogashira cross-couplings, among other olefin metathesis processes and reactions, can be catalysed using this sebacid acid derivative. This derivative enables the catalysis under aqueous environment by eliminating the use of organic solvents in these processes.

Leonard R. Mac Gillivray developed a technique for managing chemical reactivity in organic solids wherein olefins are assembled using templates of small molecules (which go through intermolecular [2+2] photo dimerization) in separate units for solid-state reactions. Instead of long-range crystal packing, this template controls how the olefins are arranged in solid state. This technique was utilised to create ladderanes, which are the building blocks of natural products, in the solid state with region specificity, 100% yield, and no waste by allowing the molecules to interact in orientations and geometrical configurations that are not possible in solution.

Professor V. Ranjan Babu and his colleagues from the Department of Chemistry at Ohio State University developed a new codimerization of ethylene that produced a variety of functionalized vinylarenes, 1,3-dienes, and strained alkenes (i.e., asymmetric hydrovinylation). This idea is applicable to the enantioselective synthesis of NSAIDs from styrene and ethylene. Under mild circumstances, 3-arylbutenes are produced by the codimerization of ethylene with different functionalized vinylarenes, 1, 3-dienes, and strained alkenes, which are then used to synthesise NSAIDs such naproxen, fluriprofen, ibuprofen, and fenoprofen. The synthesis of steroids and their derivatives can also be done using this method. With yields of up to 99%, certain 1-vinylcycloalkenes and 1-substituted 1,3-butadienes can also be effectively heterodimerized with ethylene. In an asymmetric variant of this reaction, phospholanes and phosphoramidites can be employed as ligands with certain substrates, producing yields of up to 99% and an enantiomeric excess of 95%. The ring can have stereo centres implanted using an exocyclic chiral centre. Hemilabile ligands with highly dissociated counterions can be made to increase selectivity and various novel ligands can be made to increase enantio selectivity.

Paul Wender, a chemistry professor at Stanford University in Palo Alto, California, devised function-oriented synthesis (FOS), a method that combines phase economy for the synthetic production of biologically active chemicals acquired from natural sources. FOS attempt to improve or the physiologically active lead compounds should be improved by simple scaffolds which are more easily synthesized. Although promising therapeutic targets can be found in natural products, it can be challenging to create cheap synthetic approaches to these complex molecules. These include simplified bryostatin analogues, which are also used as potential anticancer agents, arenes, Laulimalide analogues with simplified structures that remove the inherent functional instability of natural laulimalide, compounds for the treatment of cancer, compounds that regulate protein kinase C and resemble complicated phorbols and the design, synthesis, and optimisation of polyarginine drug transporters, which are used to enhance potency and prevent multidrug resistance [17].

### III. COST REDUCTION THROUGH GREEN CHEMISTRY

The most effective way to cut the price of a medicine is to reduce the price of its most expensive component i.e. API. Raw materials which are simple and commercially available easily can be used to produce APIs with chemical reactions. As a result, the cost of this process is primarily determined by the price of raw materials and the efficiency of the chemical process used to convert those materials into API. The amount and type of waste produced during drug manufacturing can be determined by factors such as selection of raw material, number of synthetic steps, and efficiency of the API production process. It is necessary to establish and clearly define the manufacturing method for an API before the Phase III clinical trials is initiated. In such scenario the initial components, synthetic schemes, catalysts (if necessary), solvents, reaction and isolation conditions, etc., are fixed. In context of the regulatory affairs, prior to process validation the information comprising the compounds present, residual solvent levels and physicochemical characterization of the API should be defined within the limitations. With process research the production methods are established prior to peak efficiency as limitation of time exists in getting approval of medicine by means of clinical trial and other approval processes.

However, the drug's production company can frequently increase the efficiency with which the raw components are turned into the API by optimising its processes. The finance as well as impact on the environment can be reduced to a great extent by proper application of the improvement and regulatory approval. It may be possible in some circumstances to change the process more drastically by using entirely or largely new synthetic beginning materials or approaches [18].

Green chemistry is an innovative approach to chemical design and manufacturing that aims to minimize the negative impact of chemical processes on human health and the environment. It involves the application of twelve fundamental principles that guide chemists in the development of sustainable and environmentally friendly processes. This chapter provides an overview of the principles of green chemistry and their significance in promoting a more sustainable future.

- 1. Atom Economy:** The principle of atom economy encourages the maximum utilization of atoms in a chemical reaction. It promotes the design of synthetic routes that minimize waste generation by emphasizing the use of renewable feedstock's and efficient catalysts. By improving atom economy, chemists can reduce the amount of waste produced and enhance resource efficiency.
- 2. Pollution Prevention:** Pollution prevention focuses on avoiding the generation of hazardous substances altogether, rather than managing or treating them after they are produced. It advocates for the creation of procedures that reduce or do away with the need of toxic chemicals, thereby reducing the potential for environmental contamination and human health risks.
- 3. Safer Chemicals:** This principle emphasizes the use of inherently safer chemicals, which are less toxic or non-toxic to humans and the environment. Green chemists strive to develop alternative compounds that possess desired properties while minimizing hazards associated with toxicity, persistence and bioaccumulation. Safer chemicals contribute to the reduction of risks throughout a chemical product's life cycle.
- 4. Design for Energy Efficiency:** Energy efficiency is a crucial aspect of green chemistry. Chemists are encouraged to design chemical processes that minimize energy consumption, utilize renewable energy sources, and optimize reaction conditions to reduce energy requirements. By doing so, they can contribute to the conservation of energy resources and reduce greenhouse gas emissions.
- 5. Application of Biodegradable Materials:** The use of biodegradable materials, such as biomass and bio-based materials is an essential principle of green chemistry. By replacing non-renewable resources derived from fossil fuels, chemists can reduce the dependence on petrochemicals and mitigate the associated environmental impacts. This principle promotes the development of sustainable and bio-based alternatives for various chemical processes.
- 6. Reduce Derivatives:** Minimizing the production of unnecessary derivatives during chemical synthesis is an important principle in green chemistry. By designing synthetic routes that require fewer steps and produce fewer by-products, chemists can reduce waste generation, increase efficiency, and conserve resources. This principle also facilitates the development of more sustainable manufacturing processes.
- 7. Catalysis:** Due to its ability to facilitate effective chemical reactions, catalysis is crucial to green chemistry. Green chemists strive to develop and utilize catalytic systems that are selective, efficient and use non-toxic and readily available catalysts. Catalysts enhance reaction rates, reduce energy requirements and minimize waste production, contributing to the overall sustainability of chemical processes.
- 8. Planned Deterioration:** After their intended use, chemical compounds should be made to break down into harmless components. By minimising the permanence of chemicals in the environment and lowering their potential for bioaccumulation, this principle seeks to



protect human health. Designing items that easily biodegrade or break down into non-toxic components encourages environmental sustainability and reduces long-term effects.

- 9. Real-time Analysis to Stop Pollution:** The principle of real-time analysis involves the development and implementation of in-process monitoring techniques to ensure the early detection and prevention of potential environmental and health hazards. By continuously monitoring chemical processes, chemists can identify deviations from the desired conditions and take corrective measures to prevent the formation of unwanted by-products or toxic substances.
- 10. Auxiliaries and Safer Solvents:** Green chemistry encourages the use of environmentally friendly solvents and auxiliary materials. Chemists strive to identify and employ solvents that are non-toxic, non-flammable, and have low environmental impact. This principle promotes the development of sustainable alternatives to traditional solvents, such as water or bio-based solvents, which reduce potential hazards during chemical processes.
- 11. Design for Sustainability:** Designing chemical products and processes with sustainability in mind is a core principle of green chemistry. It entails taking into account a product's whole life cycle, from the extraction of raw materials to disposal. Chemists aim to develop sustainable processes that minimize waste, conserve resources, reduce energy consumption and have a minimal environmental impact.
- 12. Education and Collaboration:** The final principle of green chemistry emphasizes the importance of education, collaboration and dissemination of green chemistry knowledge. It encourages chemists to share information, promote green chemistry principles, and collaborate across disciplines to develop innovative solutions for sustainable chemistry. Education and awareness play a crucial role in fostering a greener and more sustainable chemical industry [19, 20, 21, and 22].

#### IV. SYNTHETIC STRATEGIES USING GREEN SOLVENTS

The development of green solvents has gained significant importance in recent years due to their capability to mitigate the environmental impact of chemical processes. Green solvents, also known as environmentally benign solvents or sustainable solvents, offer several advantages over traditional solvents, such as lower toxicity, reduced waste generation, and improved energy efficiency. Here are many synthetic strategies employed to design green solvents.

- 1. Replacement of Conventional Solvents:** One of the primary strategies for designing green solvents is the substitution of conventional solvents with more environmentally friendly alternatives. For example, volatile organic compounds (VOCs) with high toxicity and significant contribution to air pollution can be replaced with non-toxic and non-volatile solvents. Water as green solvent is a prominent example of this strategy, as water is abundant, non-toxic, and possesses unique properties that make it suitable for a wide range of applications [23].

2. **Renewable and Bio-Based Solvents:** Another approach to developing green solvents is the utilization of renewable and bio-based feedstock's. Renewable solvents are derived from biomass or other renewable sources, minimizing the reliance on fossil fuels. Various natural products, such as vegetable oils, terpenes, and sugars, can serve as precursors for bio-based solvents. These solvents exhibit low toxicity, are readily biodegradable, and contribute to a reduced carbon footprint [24].
3. **Design of Task-Specific Ionic Liquids (TSILs):** Ionic liquids (ILs) are the solvents composed of ions. Task-Specific Ionic Liquids (TSILs) are tailor-made ILs designed to possess specific properties suitable for targeted applications. By carefully selecting the cation and anion components, researchers can optimize the physicochemical properties of TSILs, making them efficacious and sustainable solution. TSILs have been successfully employed in various applications, including catalysis, separation processes, and as media for reaction. [25].
4. **Supercritical Fluids:** Supercritical fluids are substances maintained above their critical pressure and temperature, where they exhibit both gas-like and liquid-like properties. SCFs, such as carbon dioxide (CO<sub>2</sub>) and water, are considered green solvents due to their low environmental impact and unique solvent properties. SCFs offer advantages such as high diffusivity, tunable density and selective solvation capabilities. They are particularly useful for extraction processes and as reaction media in various synthetic applications [26].
5. **Solvent-Free or Solid-State Reactions:** Eliminating the need for solvents altogether is an ideal approach to achieving greener chemistry. Solvent-free or solid-state reactions involve conducting chemical transformations without the presence of a liquid solvent. These reactions offer benefits such as improved reaction rates, reduced waste generation, and simplified purification processes. Solid-state techniques, such as ball milling and mechanochemistry, have emerged as efficient alternatives for conducting solvent-free reactions [27].

Various bio solvents have been used for the production of natural products, medicinal compounds and different intermediates which are used for further synthesis.

6. **Vegetable oils:** Vegetable oils are obtained from the different parts of a variety of plants. They are having structure like triglyceride in which substitution of three hydroxyl groups of glycerol can be done with different fatty acids to produce solids or liquids [28] and can be renewed. Vegetable oils are an essential component of many foods. We detected the acylation and cyclization reactions in vegetable oil, specifically maize oil. The use and benefits of vegetable oil have been investigated. The yield, time of reaction, and also sustainability of vegetable oil have been compared to the toxic solvent xylene. Less price and efficacy of vegetable oils, leads to this reaction as first example of a reaction involving vegetable oils, and this concept is helpful for more synthetic ways [29].
7. **Glycerol as a Bio Solvent:** Glycerol is a polyalcohol and the second component of oleochemicals generated from natural oils. Glycerol has been using in industries, including the pharmaceutical industries, food industries and cellulose films [30]. It is

considered as a good green solvent because of its sustainability and less price. In this context, pharmaceutical business and scientists have become more interested in glycerol as an alternative to other organic solvents that are dangerous, volatile, poisonous, and harmful. Glycerol is a solvent that is utilised in many reactions, chemists and medical scientists must overcome a number of obstacles : (i) Glycerol should be fluidities with a co-solvent due to its viscosity. Glycerol has the advantage that it is less viscous at 60°C and at higher temperatures also the reactions can take place; (ii) glycerol may participate as a reagent in the reaction because it has three hydroxyl groups which are acidic groups; and (iii) the length of glycerol is more and donor atoms are present to form metal catalysts complexes. It results some unwanted secondary products or un reactivity of catalysis. There are two sides to glycerol, which may be applied to any solvents and reagents utilised in research. However, Safaei et al. synthesised 4H-pyrans utilising glycerol as the green solvent in a catalyst-free, one-pot, three-component method [31]. The reactions yielded a variety of pyran derivatives and had a high yield of up to 93%. Additionally, the reaction was carried out in water, and it was found that the reaction yield had decreased to 70%. Cyclization processes under green solvent procedures are quite vital, prompting medicine experts to reorganise their medication design strategy.

Gu et al. recently disclosed a three-component glycerol cyclization process for producing pyran derivatives [32]. In the processes, styrene, dimedone, and p-formaldehyde were utilised. The solvent utilised determined the yield of the product, and the best solvent was glycerol, with a yield of 68%. Other solvents produced significantly less as compared to glycerol. Moreover, the sustainability of glycerol was investigated, and the production was determined to be 65% after three cycles. The reaction of dimedone with para formaldehyde yields an intermediate product that cyclizes with styrene to form the pyrane ring. Lu and his colleagues devised a procedure in which styrene analogue, p-formaldehyde and pyrazolone were reacted in glycerol to produce pyrazolo-pyrane derivative [33]. The reaction was carried out at a temperature like 105°-110°C, and the yield was calculated to be 78%. This reaction in solvent-free condition and ionic liquids leads to no result and 48% success rate respectively.

- 8. Water as a Bio Solvent:** Water has different physical and chemical properties, including strong H-bonding, a large dielectric constant, and a broad temperature range. Water as a solvent, has various benefits over typical organic solvents. Water also used as a green solvent because it is cheap, nontoxic, readily available, non-polluting, and non-flammable. Water is not commonly considered as a chemical. Despite its numerous advantages; water is not often used as prime synthetic solvent in research laboratory and industry since most of the organic molecules are insoluble in water. Water has long been avoided by scientists due to an old chemist's idea that insoluble reagents create no product. On the other hand, has replaced this concept with the new concept that because reactions can be performed in water, where the solubility is not critical for processes. Because the reactants were insoluble in water, Sharpless characterised processes such Diels-Alder, cyclo addition, Claisen rearrangement and nucleophilic opening of epoxide as on-water [34]. Organic chemistry basic reactions are utilised to make drugs in medicinal chemistry. Wittig reaction is one of these reactions. The Wittig reaction is important because it forms a new carbon-carbon bond. Scientist proposed a protocol for the Wittig reaction, which is performed in water at 25°C [35]. Sobral described a green

method for producing 2,2'-dipyrrromethane by reacting pyrrole and diethyl ketone in water. According to Sobral, the reaction yielded 80% and was carried out as gram scaled [36].

Xu et al. reported the synthesis of isocoumarin in H<sub>2</sub>O. They discussed the reaction of salicylic acid in presence of ruthenium catalyst with alkyne produced isocoumarin with 85% yield [37]. Pizzo and colleagues disclosed a reaction between aza compound and vinyl ether that produced derivatives of pyridazine as the sole product and derivative of pyrrole as a secondary product (2%). Because of the limited solubility of nitrogenous compound and vinyl ether, the authors described the reaction as an on-water reaction [38]. Patel and colleagues performed the synthesis of benzothiazole ring on water [39]. The reaction began with morpholine and iodo-benzo-isothiocyanate, thiourea derivative was obtained which was not separated. Thiourea derivative undergoes cyclization reaction in presence of water with a CuO-nanocatalyst along with K<sub>2</sub>CO<sub>3</sub> with a 92% yield.

## V. SYNTHETIC STRATEGIES USING CATALYSTS

- 1. Nanocatalysts:** One of the important green chemistry rules that chemists and medical scientists should be careful is catalyst [40]. There are two kinds of catalysts: heterogeneous and homogeneous. In terms of product yield, homogeneous catalysts outperform heterogeneous catalysts. However, due to contamination of products with metal, the separation, reusability of catalysts under homogeneous category are the most serious drawbacks when used for fine chemical synthesis. Because they are recyclable and easier to isolate from the media heterogeneous catalysts are favoured.

Apart from heterogeneous catalysts, nanocatalysts are very popular as semi-heterogeneous catalysts for to their high surface-volume ratio, resulting in more interactions between the catalyst's surface and the reactant. Even if the catalyst is cleansed using specific filtration techniques, contamination still exists.

Recently Magnetism was employed to obtain magnetic nanocatalysts from a solution containing an external magnetic field [41-45]. Then it is observed, they appear to be acceptable options for the active pharmaceutical ingredient (API) and more promising alternatives for the chemical industry. [46].

Sharma et al. developed a nanocatalyzed cyclization reaction [47]. They created oxazole compounds by reacting benzyl amine and methyl acetoacetate. SEM, XRD, and FESEM were used to characterise the nanomagnetic catalyst. They highlighted how the absence of the nanocatalyst reduced the yield of oxazole derivatives to 5%. Nanocatalyst under reaction conditions; the conversion of the process was 100%, indicating that no waste product was created. Gerbino and colleagues created xanthenes in a single step using a copper-based magnetically recoverable nanocatalyst [48]. Salicylaldehyde and different phenol derivatives were reacted in toluene under ligand-free conditions. Copper nanocatalyst which is reusable was found to be 89% effective. The product yield was lowered to 65 and 62%, respectively, when the copper nanocatalyst was substituted with CuCl or CuO.

- 2. Biocatalysts:** A biocatalyst may be an isolated enzyme, an immobilised enzyme or microbial enzyme. These have been utilised in the laboratory to replicate enzyme activity in biological reactions.

Six classes of enzymes have been used by scientists for a variety of purposes. Food, pharmacology, medicine, and textiles are among the industries that use these enzymes. Enzymes have unique properties that man-made organic substances do not always have. Enzymes have excellent stereo selectivity, which results in just one isomeric product, and can thus reduce medicine costs because chirality property has a significant impact on pharmaceutical pricing when the potential medication has multiple chiral centres. This property compels chemists and medical scientists to create biocatalysts for use in reaction flasks [49, 50].

Savile and colleagues discussed an efficient biocatalytic technique for replacing a asymmetric examine which is Rh-catalyzed undergoes hydrogenation for the anti-diabetic drug sitagliptin. Currently sitagliptin synthesis comprises enamine production which is followed by asymmetric hydrogenation at high pressure. Catalyst which are chiral utilised that is Rh-based, in which the drug sitagliptin has been synthesised in 97% ee with few amount of Rh. This synthetic approach demonstrated a green reaction, which is the direct amination of pro-sitagliptin ketone to produce pure enantiomeric sitagliptin (99.95% ee), followed by phosphate salt production to obtain sitagliptin phosphate. [51].

## VI. CASE STUDY

- 1. Case Study: Green Chemistry in the Synthesis of Lipitor:** Lipitor, the first medication in the world with yearly turnover of \$10 billion, contains the active component atorvastatin calcium. It is a medication that lowers cholesterol by preventing the liver's ability to synthesize cholesterol. This medication is an illustration of a competitive 3,5-dihydroxyheptanoic acid-7-substituted HMG-CoA reductase inhibitor. Ethyl (R)-4-cyano-3-hydroxybutyrate is the main chiral building block in all commercialized synthesis of atorvastatin. The initial steps comprises of reaction of an ethyl 3-hydroxy-4-halobutyrate with a cyanide ion in an alkaline solution at a very high temperature. The cyanide ion is then replaced for halide in hot, alkaline conditions, creating a large amount of by-products. The purified product can be obtained by high-vacuum fractional distillation which further reduces the yield. In order to overcome these problems for a workable and affordable procedure, S. K. Ma et al created a green, two-step, three-enzyme process for the synthesis in the production of atorvastatin in 2010. A ketoreductase (KRED) in conjunction with glucose and a NADP-dependent glucose dehydrogenase (GDH) are employed for cofactor renewal in the first step of the biocatalytic reduction of ethyl-4-chloroacetoacetate. The (S) ethyl-4-chloro-3-hydroxybutyrate product has an isolated yield of 96% and >99.5%ee, respectively. A halohydrin dehalogenase (HHDH) is used to catalyse the replacement of the chloro substituent with cyano in the second phase at neutral pH and room temperature by interacting with HCN. This allowed for the cost and environment-efficient production of the crucial hydroxynitrile intermediate [52].

- 2. Case Study: The Green Synthesis of Artemisinin:** Artemisinin is a highly effective antimalarial drug derived from the Chinese herb *Artemisia annua*. Traditionally, artemisinin was extracted from the plant using organic solvents, which resulted in low yields and a negative environmental impact. In the early 2000s, researchers at the University of California, Berkeley, led by Professor Jay Keasling, embarked on a project to develop a greener and more sustainable synthesis route for artemisinin. The team employed synthetic biology techniques to engineer a strain of yeast, *Saccharomyces cerevisiae*, to produce artemisinic acid, a precursor of artemisinin. This approach eliminated the need for plant cultivation and reduced reliance on natural resources. The genetically modified yeast was designed to convert inexpensive and widely available sugars into artemisinic acid, providing a scalable and sustainable source of the precursor.

To optimize the process further, the researchers collaborated with pharmaceutical company Sanofi. Sanofi developed a green chemical conversion method, replacing the use of hazardous solvents with a greener solvent, which significantly reduced the environmental impact. This joint effort resulted in the successful production of semisynthetic artemisinin on a large scale, ensuring a stable supply of the life-saving drug [53].

- 3. Case Study: Green Chemistry in Ibuprofen's Synthesis:** Ibuprofen is a widely used nonsteroidal anti-inflammatory drug (NSAID) that offers pain relief and anti-inflammatory effects. The traditional synthesis of ibuprofen involves multiple steps, which often require the use of toxic solvents and reagents, leading to significant environmental concerns. However, a notable case study demonstrates the successful implementation of green chemistry principles in the synthesis of ibuprofen. Researchers from the University of York in the United Kingdom developed a greener synthesis route for ibuprofen using catalytic processes. They employed a catalyst composed of a readily available, non-toxic material called 2-methyl-1,3-propanediol (MPD) in the conversion of a precursor molecule into ibuprofen. This green catalytic process eliminated the need for hazardous solvents and reduced waste generation, leading to a more sustainable manufacturing method for the drug [54, 55, 56, 57].
- 4. Case Study: Green Chemistry in the Synthesis of Valsartan:** Angiotensin II (AT-II) receptor antagonists, of which valsartan is a part, are a class of drugs. This class combines a high safety and tolerability profile with potent anti-hypertensive action. The outer protective layer of heart and artery smooth muscle cell membranes contains AT-II receptors, which when activated cause the tissues to contract. Despite variations in one's level of hydration, sodium intake, and other physiological factors, AT-II aids in the maintenance of constant blood pressure. Additionally, it performs regulatory tasks such as preventing sodium from being excreted by the kidneys, preventing the re-uptake of norephedrine, and encouraging the production of aldosterone. Valsartan is used to treat cardiovascular issues and heart failure because it reduces the rise in blood pressure brought on by hormone receptor interactions by inhibiting the effects of AT-II on its receptors. The multistep synthesis of Valsartan/hydrochlorothiazide was first described in 1994. Most of the reported works share the biphenyl unit as a structural component, and the production of this unit is a crucial step in the synthesis. Suzuki-Miyaura couplings are used in the documented preparation techniques for valsartan. The major flaw is found

to be the use of costly substrates of boronic acid while synthesizing valsartan particularly in the cross-coupling step. In order to boost throughput and decrease the use of halogenated solvents, Goossen and colleagues published a four-step method for the synthesis of valsartan in 2007. They did this by using decarboxylative coupling. The original synthesis's three chemical stages were altered by Beutler and colleagues. In contrast to the more expensive organoboronic acid coupling, Gosh and colleagues (2010) developed a quick and simple method to produce valsartan using Negishi coupling of oxazoline moieties. According to Pandarus et al. (2013), a heterogeneous Suzuki-Miyaura coupling reaction between 2-chlorobenzonitrile and 4-tolylboronic acid produced 4-methyl-2-biphenylcarbonitrile over the functionalized organosilica matrix [52].

## VII. FUTURE PROSPECTS

The pharmaceutical industry, like many other sectors, has been increasingly recognizing the importance of sustainability and environmental responsibility. As worries about resource depletion and climate change intensify, there is a growing demand for eco-friendly practices in all industries, including pharmaceuticals. The adoption of green chemistry and technology in the pharmaceutical industry has the potential to bring about a number of advantages:

- **Reduced Environmental Impact:** The adoption of green technology and green chemistry can lead to a reduction in harmful emissions, waste generation, and the consumption of non-renewable resources. This can significantly lower the industry's carbon footprint and can combat climate change as a contribution to global efforts.
- **Cost Savings:** Many green technologies and practices are designed to be more efficient and less resource-intensive. By adopting these approaches, pharmaceutical companies can potentially reduce operational costs, improve energy efficiency, and optimize resource utilization.
- **Enhanced Reputation and Market Appeal:** As consumers and investors become more environmentally conscious, companies that prioritize sustainability are likely to gain a competitive advantage. Emphasizing green initiatives can improve a pharmaceutical company's reputation and attract environmentally-conscious customers and investors.
- **Regulatory Incentives:** Governments and regulatory bodies worldwide are increasingly promoting sustainable practices. By incorporating green technology and green chemistry into their operations, pharmaceutical companies may be eligible for incentives, tax benefits, or preferential treatment when seeking approvals for new products.
- **Innovation and Research Opportunities:** Embracing green technology and green chemistry requires continuous research and development of new sustainable methods and materials. This opens up opportunities for collaboration and innovation within the pharmaceutical industry and with other sectors that focus on sustainability.
- **Access to New Markets:** Some countries and regions have stricter environmental regulations, making it challenging for conventional pharmaceutical products to enter

those markets. By adopting green practices, companies can gain access to new markets and expand their global reach.

- **Risk Management:** Implementing sustainable practices can help pharmaceutical companies mitigate potential risks associated with climate change, resource scarcity, and changing regulatory landscapes

In summary, the implementation of green technology and green chemistry in the pharmaceutical industry presents an innovative approach for sustainability. By embracing eco-friendly practices, pharmaceutical companies can not only contribute to a healthier environment but also position themselves for long-term success by attracting environmentally-conscious customers, investors, and partners. As technology and awareness continue to advance, the future prospects for sustainable practices in the pharmaceutical industry appear promising.

## VIII. CONCLUSION

In conclusion, the adoption of green chemistry and technologies in the pharmaceutical sector represents a transformative and imperative approach towards sustainability. This newer approach not only addresses the pressing environmental challenges facing our planet but also lays the foundation for a more resilient and responsible pharmaceutical sector.

Throughout this chapter, we have delved into the multifaceted benefits that arise from embracing eco-friendly practices in pharmaceutical manufacturing, research, and development. By adopting green technologies, pharmaceutical companies can significantly reduce their ecological footprint, minimize waste generation, and optimize resource utilization. These endeavours not only align with the global call for environmental stewardship but also position these companies as leaders in the pursuit of a greener future.

Furthermore, we have explored the potential cost savings and long-term economic advantages associated with sustainable practices. By employing more efficient and resource-conserving methods, pharmaceutical companies can not only improve their bottom line but also foster a culture of innovation, spurring the development of new and cutting-edge green technologies.

The shift towards sustainability is not only driven by ethical considerations but also by the demand from consumers, investors, and regulatory bodies. Companies that prioritize environmental responsibility and invest in green chemistry will undoubtedly gain a competitive advantage, attracting a growing cohort of eco-conscious customers and investors who seek to support business aligned with their values.

While the journey towards a fully sustainable pharmaceutical industry may present challenges, the potential rewards are both tangible and intangible. Governments and regulatory bodies worldwide are increasingly recognizing the significance of green initiatives, offering incentives and favourable treatment for companies that incorporate sustainable practices into their operations.



As the pharmaceutical industry embarks on this transformative path, collaboration, research, and continuous innovation will be essential. By fostering cross-industry partnerships and sharing knowledge, the sector can overcome obstacles and create a more sustainable and interconnected ecosystem.

In closing, the adoption of green chemistry and technologies in the pharmaceutical sector is not just a means to an end; it is a pivotal step towards safeguarding the health of our planet and its inhabitants. Through our collective commitment to sustainability, we can usher in a new era of pharmaceutical excellence—one that balances medical progress with environmental responsibility, securing a brighter and healthier future for generations to come.

## REFERENCE

- [1] Mishra M; Sharma M; Dubey R; Kumari P; Ranjan V; Pandey J. Green synthesis interventions of pharmaceutical industries for sustainable development. *CRGSC*, 2021, 4, 100174. <https://doi.org/10.1016/j.crgsc.2021.100174>
- [2] <https://www.unep.org/explore-topics/chemicals-waste/what-we-do/emerging-issues/environmentally-persistent-pharmaceutical> (accessed Nov 26, 2022)
- [3] Tucker J.L; Faul M.M. Drug companies must adopt green chemistry. *NATURE*, June 2016, 534, 27-29. DOI:10.1038/534027a
- [4] Sharma V. Applicability of Green Chemistry in Pharmaceutical Processes. *Pharma Bio World*, March 2015, pp 34-36.
- [5] Brown A. Pharma industry confronts growing problem of pharmaceutical waste. *Nordic Life Science News*, June 2020.
- [6] Patel M; Patel H; Mevada S; Patel O; Chemistry Goes Green: A Review On Current And Future Perspectives of Pharmaceutical Green Chemistry. *Wjpmr*, 2020, 6(7), 125-131.
- [7] Sutton S. From savings patients to saving the planet. *The Medicine Maker*, May 2022.
- [8] Fortunak M. J. Current and future impact of Green Chemistry on the Pharmaceutical Industry. *Future Med. Chem*, 2009, 1(4), 571-575. 10.4155/fmc.09.60
- [9] Elder D. Green Chemistry. *EPR (Online)* 2022 (1). <https://www.european-pharmaceutical-review.com/article/168537/green-chemistry/> (accessed Nov 24, 2022)
- [10] Johansson M; Douglas J. Striving for sustainable drug discovery using Green Chemistry, May 2022.
- [11] <https://www.astrazeneca.com/what-sciencecando/topics/sustainability/Striving-for-sustainable-drug-discovery-using-Green-Chemistry.html> (accessed on Nov 24, 2022)
- [12] Ratti R. Industrial applications of green chemistry: Status, Challenges and Prospects. *SN Applied Sciences*, Jan 2020. DOI:10.1007/s42452-020-2019-6
- [13] Menges N. The Role of Green Solvents and catalysts at the future of Drug Design and of synthesis. *Green Chemistry*, Dec 2017. DOI:10.5772/intechopen.71018
- [14] Cue B.W; Zhang J. Green process chemistry in the pharmaceutical industry. *GCLR*, Dec 2009, 2(4), 193-211. DOI:10.1080/17518250903258150
- [15] Indian pharma sector looks at 'green chemistry' processes to save environment. *PHARMABIZ.com*. [Online] 2002, <http://test.pharmabiz.com/news/indian-pharma-sector-looks-at-green-chemistry-processes-to-save-environment-13288> (accessed Dec 5, 2022)
- [16] Welton T. 2015 Solvents and sustainable chemistry. *Proc. R. Soc. A* 471:20150502.
- [17] DOI: <https://doi.org/10.1098/rspa.2015.0502>
- [18] Clarke C.J; Tu W.C; Levers O; Brohl A; Hallett J.P. Green and Sustainable Solvents in Chemical Processes. *Chem. Rev*, September 2017. DOI: 10.1021/acs.chemrev.7b00571
- [19] Arnum P.V. Deploying Green Chemistry in API Synthesis. *PTSM*, Aug 2009, 5(7).
- [20] Joarder D.D; Sarkar R; Mukhopadhyay C; Sustainable green technologies for synthesis of potential drugs targeted toward tropical diseases. *Green Approaches in Medicinal Chemistry for Sustainable Drug Design. Advances in Green and Sustainable Chemistry*, 2020, 75-93. DOI:10.1016/B978-0-12-817592-7.00004-6
- [21] Anastas, P. T., & Warner, J. C. (1998). *Green chemistry: Theory and practice*. Oxford University Press.
- [22] Clark, J. H., & Macquarrie, D. J. (Eds.). (2002). *Handbook of green chemistry and technology*. Wiley.

- [23] Lancaster, M. (2010). Green chemistry: An introductory text. Royal Society of Chemistry.
- [24] Sheldon, R. A. (2017). The twelve principles of green chemistry: In practice. *Green Chemistry*, 19(1), 18-43.
- [25] Xu L, et al., "Water as a Green Solvent: Recent Developments and Applications," *Chem Rev*, 117,2017.
- [26] H. James, Clark, J. Thomas, Farmer, J. Andrew, Hunt and S. James, Opportunities for Bio-Based Solvents Created as Petrochemical and Fuel Products Transition towards Renewable Resources."
- [27] L. Rohit, "A review of ionic liquids: Applications towards catalytic organic transformations," 227, pp. 44-60, 2017.
- [28] Željko et al., "Are supercritical fluids solvents for the future?" *Engineering & Processing: Process Intensification*, 141, pp.1-8, 2019.
- [29] M. Hiren, Marvaniya, N. Kaumil and S. Dhruvo Jyoti, "Greener reactions under solvent free conditions," *International Journal of Drug Development & Research*, 3( 2), 2011.
- [30] R.D. O'Brien, "Fats and Oils: Formulating and Processing for Applications," CRC Press; Boca Raton, USA, 3rd ed. 2005.
- [31] N. Menges and E. Şahin, "Metal- and base-free combinatorial reaction for C-acylation of 1,3-diketone compounds in vegetable oil: The effect of natural oil," *ACS Sustainable Chemistry & Engineering*, 2, pp.226-230, 2014.
- [32] Claude S. Research of new outlets for glycerol – recent developments in France. *Fett/ Lipid*. 1999;101:101-104
- [33] H.R. Safaei, M. Shekouhy, S. Rahmanpur and A. Shirinfeshan, "Glycerol as a biodegradable and reusable promoting medium for the catalyst-free one-pot three component synthesis of 4H-pyrans," *Green Chemistry*, 14, pp.1696-1704, 2012.
- [34] M. Li, C. Chen, F. He and Y. Gu, "Multicomponent reactions of 1,3-cyclohexanediones and formaldehyde in glycerol: Stabilization of paraformaldehyde in glycerol resulted from using dimedone as substrate," *Advanced Synthesis and Catalysis*, 352, pp.519-530, 2010.
- [35] J-N. Tan, M. Li and Y. Gu, "Multicomponent reactions of 1,3-disubstituted 5-pyrazolones and formaldehyde in environmentally benign solvent systems and their variations with more fundamental substrates," *Green Chemistry*, 12, pp.908-914, 2010.
- [36] S. Narayan, J. Muldoon, M.G. Finn, V.V. Fokin, H.C. Kolb and K.B. Sharpless, "On Water": Unique reactivity of organic compounds in aqueous suspension," *Angewandte Chemie International Edition*, 44, pp.3275-3279, 2005.
- [37] L.A. Morsch, L. Deak, D. Tiburzi, H. Schuster and B. Meyer, "Green aqueous Wittig reaction: Teaching green chemistry in organic teaching laboratories," *Journal of Chemical Education*, 91, pp.611-614, 2014.
- [38] AJFN. Sobral, "Synthesis of meso-diethyl-2,2'-dipyrromethane in water," *Journal of Chemical Education*, 83, pp.1665-1666, 2006.
- [39] Li et al., "Water as a green solvent for efficient synthesis of isocoumarins through microwave-accelerated and Rh/Cu-catalyzed C-H/O-H bond functionalization," *RSC Advances*, 3, pp.3402, 2013.
- [40] Attanasi et al., "Inverse-electron-demand Diels-Alder reactions of (E)-3-diazenylbut-2-enes in water," *Helvetica Chimica Acta*, 84, pp.513, 2001.
- [41] S. Kumar, S. Guin, J. Nath and B.K. Patel, "An "on-water" exploration of CuO nanoparticle catalysed synthesis of 2-aminobenzothiazoles," *Green Chemistry*, 14, pp.2491, 2012.
- [42] Q. Sun, X-Q. Zhang, Y. Wang and A-H. Lu, "Recent progress on core-shell nanocatalysts," *Chinese Journal of Catalysis*, 36, pp.683-691, 2015.
- [43] D. Wang and D. Astruc, "Fast-growing field of magnetically recyclable nanocatalysts," *Chemical Reviews*, 114, pp.6949-6985, 2014.
- [44] V. Polshettiwar, R. Luque, A. Fihri, H. Zhu, M. Bouhrara and J-M. Basset, "Magnetically recoverable nanocatalysts," *Chemical Reviews*, 111, pp.3036-3075, 2011.
- [45] M. Hu, Z. Yao and X. Wang, "Graphene-based nanomaterials for catalysis," *Industrial & Engineering Chemistry Research*, 56, pp.3477-3502, 2017.
- [46] Liu J, Sun W. *Magnetic nanoparticles in catalysis, magnetic nanomaterials: Applications*
- [47] *in catalysis and life sciences*, Chapter 3. RSC Publishing, Cambridge. 2017:59-98
- [48] L. Pena and D. Wang, "Recyclable magnetic materials for biomass conversion, magnetic nanomaterials: Applications in catalysis and life sciences" *The Royal Society of Chemistry*, 5, pp.120-141, 2017.
- [49] R. Ciriminna and M. Pagliaro, "Green chemistry in the fine chemicals and pharmaceutical industries," *Organic Process Research and Development*, 17, pp.1479-1484, 2013.

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- [50] S. Dutta, S. Sharma, A. Sharma and R.K. Sharma, "Fabrication of core-shell-structured organic-inorganic hybrid nanocatalyst for the expedient synthesis of polysubstitutedoxazoles via tandem oxidative cyclization pathway," *ACS Omega*,2,pp.2778-2791,2017.
- [51] C.A. Menendez, F.Nador, G. Radivoy and D.C. Gerbino, "One-step synthesis of xanthenes catalyzed by a highly efficient copper-based magnetically recoverable nanocatalyst,"*Organic Letters*, 16,pp.2846-2849,2014.
- [52] L. Botta, B.M. Bizzarri, x. M. Bizzarri and R. Saladino, "Advances in biotechnological synthetic applications of carbon nanostructured systems," *Journal of Materials Chemistry B*, 5, pp.6490-6510, 2017.
- [53] W-L. Liu, S. Lirio, H-Y. Huang and S. Ma, "Functional metal-organic frameworks for enzyme/ protein immobilization, functional supramolecular materials: From surfaces to MOFs," RSC Publishing, Cambridge,5,pp.281-296,2017.
- [54] Savile et al., "Biocatalytic asymmetric synthesis of chiral amines from ketones applied to sitagliptin manufacture," *Science*, 329,pp.305-309,2010.
- [55] Gupta, P., & Mahajan, A. (2015). Green chemistry approaches as sustainable alternatives to conventional strategies in the pharmaceutical industry. *RSC Advances*, 5(34), 26686–26705. <https://doi.org/10.1039/C5RA00358J>
- [56] Newman, D. J., & Cragg, G. M. (2020). Natural Products as Sources of New Drugs over the Nearly Four Decades from 01/1981 to 09/2019. *Journal of Natural Products*, 83(3), 770–803. <https://doi.org/10.1021/acs.jnatprod.9b01285>
- [57] Clark, J. H., &Macquarrie, D. J. (2002). Handbook of green chemistry and technology. Blackwell Publishing.
- [58] Kozłowska, M., Baran, T., &Grymel, M. (2019). Green chemistry in the synthesis of nonsteroidal anti-inflammatory drugs. In *Advances in Industrial Mixing* (pp. 341-362). CRC Press.
- [59] Wells, A. S., Hanefeld, U., &Poliakoff, M. (2006). Green chemistry in the pharmaceutical industry. *Green chemistry*, 8(5), 411-420.
- [60] Kleinman, M. T., & Caputo, R. K. (2010). Green chemistry in the pharmaceutical industry. *Organic Process Research & Development*, 14(4), 935-939.