OPEN ACCESS Freely available online

Journal of Pollution Effects & Control

ISSN: 2375-4397

Review Article

Industrial Pollution Control Employing Green Metrics: A Review

Asnake Gudisa Ede*, Tadesse Weyuma Bulto, Getachew Yigezu Juta, Mignot Getachew Bedada

Department of Urban Environmental Management, Kotebe University of Education, Addis Ababa, Ethiopia

ABSTRACT

The 2001 Chemistry Nobel Laureate, Ryōj Noyori, said Chemists must pursue Practical Elegance”: that is chemical synthesis must be intellectually logical and technically truly efficient. Neither 100% atom economy nor 100% yields evaluate the efficiency of industrial processes. Consequently, the present review details the complete quantification of major Green Metrics parameter such as Reaction Mass Efficiency (RME), Atom Economy (AE) , Material Recovery Parameter (MRP), Stoichiometric Factor (SF) and Yield(Y) for well recognized and in some cases industrially applicable organic synthesis such as Suzuki cross coupling, Wittig reaction, Grignard reaction, Aldol condensation, Michael addition and Bachman rearrangement under different scenarios .It also assesses the Environmental factors (E-factors) indicating the waste footprint per product formed. Finally, the Radial Pentagon comprising AE, RME, MRP, SF and Y is depicted and all together measures the efficiency of synthetic methods or processes. Moreover, the review details not only green processes but also alternative green products. This sustainability-based approach allows chemists to clearly assess whether or not chemical products or processes are sustainable or not.

Keywords: Green metrics; Green processes and products; Sustainability; Radial pentagon

INTRODUCTION

Green chemistry aims at designing of products and processes that reduce or eliminate the use and generation of hazardous substances [1-3]. Principle 2 of Green Chemistry, Atom Economy (AE), states that synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product [4-5]. Chemists have traditionally measured the efficiency of a reaction by determination of the percentage yield (% yield) of the reaction. However, the % yield deals with only the amount of the desired product(s) that is isolated (relative to the limiting reagent) and does not consider the efficiency of the reaction relative to (waste) that are formed [6-7]. And AE measures only the atoms incorporated into the desired product and cannot measure the excess of reagents used and the nature of wastes generated. In this regard, neither 100% atom economy nor 100% yields evaluate the efficiency of industrial processes. RME is relatively the better way to study the efficiency of the reaction over atom economy [8-9]. Among the three 2001 Chemistry Nobel Laureates, Ryoji Noyori, said Chemists must pursue “Practical Elegance”: that is chemical synthesis must be intellectually logical and technically truly efficient [10-11].

LITERATURE REVIEW

Table 1 shows the E-factors of various chemical industries. Pharmaceutical industry annual production capacity (10-100 tones) is less than oil refining, bulk and fine chemicals but its waste footprint, the E-factor, is higher than all (25-100 kg waste/kg product) [12-13]. Annual production oil is higher but its refining left minimum waste to the environment. However, it is important to consider the nature of waste not only the quantity of waste. The E-factor value indicates only the quantity of waste generated not the nature of waste. But, Environmental Quotient (EQ), =Q × E. How to derive a real objective value for Q for every chemical known? This is still open for further investigation. However, Q equals to 100 for salts of heavy metal and 1 for NaCl and other benign wastes like water.

Table 1: E-factors of various chemical industries.

Industrial sector	Annual production(tones)	E-factors
Oil refining	10^6-10^8	<0.1
Bulk chemicals	10^4-10^6	0-1
Fine chemicals	10^2-10^4	5-50
Pharmaceuticals	10^1-10^2	25-100

Correspondence to: Asnake Gudisa Ede, Department of Environmental Science, Kotebe Metropolitan University, Addis Ababa, Ethiopia, E-mail: astuasnegude@gmail.com

Received: 30-May-2022, Manuscript No. JPE-22-001-Pre Qc 22; **Editor assigned:** 03-Jun-2022, PreQC No. JPE-22-001-Pre Qc 22 (PQ); **Reviewed:** 17--Jun-2022, QC No. JPE-22-001-Pre Qc 22; **Revised:** 24-Jun-2022, Manuscript No. JPE-22-001-Pre Qc 22 (R); **Published:** 01-Jul -2022, DOI: 10.35841/2375-4397.22.10.343

Citation: Ede AG, Bulto TW, Juta GY, Bedada MG (2022) Industrial Pollution Control Employing Green Metrics: A Review. J Pollut Eff Cont. 10: 343.

Consequently, the present review details the complete quantification of major Green Metrics parameter [14-15] such as RME, AE, Material Recovery Parameter (MRP), Stoichiometric Factor (SF) and Yield (Y) for well recognized and industrially feasible organic syntheses. It also assesses the Environmental factor (E-factor) indicating the waste footprints per product formed. Five of the green metrics all together display the "greenness" or sustainability of the chemical reaction or industrial processes. In this regard, Google Scholar, SciFinder, Royal Society of Chemistry, American Chemical Society, Science Direct and US Presidential Green Chemistry Challenge Awards were the main search engines used. The search terms used included: Principle of Green Chemistry, Sustainable Chemistry, Green Metrics, Alternative Green Products, Green Synthetic Strategies, The Algebra of Organic Synthesis and Sustainable Chemistry Processes.

Green Metrics

In this section, the major Green Metrics such as RME, AE, MRP, SF and Yield (Y) was quantified for well recognized organic syntheses such as Suzuki cross coupling, Wittig reaction, Grignard reaction, Bachman rearrangement, Michael addition and others. Environmental factor indicating the waste footprint was also included. Five of the green metrics all together display the "greenness" of the chemical reaction or industrial processes.

The wittig reaction

Wittig reaction was, and probably still is, one of the most used academic reaction for the carbon-carbon double bond construction starting from aldehydes and using phosphorus yields [14-18]. The procedure for this reaction for synthesis of styrene is as follows: To a solution of methyltriphenylphosphonium bromide (1.96 g, 5.5 mmol) in dry THF (30 ml) was added n-butyllithium (2.2 ml of 2.5 M in n-hexane, 5.5 mmol) at 0°C and the solution was stirred at 0°C for 1 h. To this mixture was added benzaldehyde (0.51 mL, 5 mmol) in THF (10 ml) and the resulting mixture was stirred at room temperature for 1h. The reaction was then quenched with water and extracted with ethyl acetate. The organic layers were washed with water and brine and dried over sodium sulfate. After removal of solvent in vacuo, the residue was purified by column chromatography with n-hexane:ethyl acetate to afford the styrene as a liquid (442 mg, 85%). Benzaldehyde: d=1.044 g/mL; n-BuLi MW=64.1 g/mol: 5.5 mmol=0.35g.

Atom Economy (AE)

In the calculation of Atom Economy (Equation 1) for multi-step processes, intermediates that are formed in one step and consumed during a later step are neglected. Thus, Molecular Weights (MW) are

- MW of $P(ph)_3$=C18H15P =262.26 g/mol
- MW of CH_3Br=94.94 g/mol
- MW of n-BuLi=C_4H_9Li=64.06
- MW of Benzaldehyde=C_7H_6O=106.12
- MW of styrene=C_8H_8=104.15

$$AE(\%)\left[\frac{\text{Molecular weight of desired product}}{\text{Molecular weight ofreagents}}\right]\times 100$$

For the Wittig reaction

$$AE(\%)=\left[\frac{104.15}{262.29+94.94+106.12}\right]\times 100$$

19.7% ≈ 20%

This show only 20% of the atoms of the reactants are incorporated into the final products and 80% are wastes or byproducts. To prepare 104.2 Kg of product we need to use 262.3+94.9+64.1+06.1= 27.4 Kg of reagents. In preparing 104.2 Kg of product we will produce 278.3+58.1+86.8=423.2 Kg of waste.This shows that 4 Kg of wastes per 1 Kg of desired products. The wastes have effects on pillars of sustainable development. They can pose health impacts, environmental problem and economic loses. AE depends on which reactants are selected for synthesizing the desired product. AE calculation implies that all reactants are used in exactly stoichiometric amounts. But it is quite common in real experimental procedures to use slight excesses of one or more reagents. AE calculation implies that the desired product is obtained with an ideal yield of 100%. But, in practice a 100% yield is almost impossible to achieve.

Reaction Mass Efficiency (RME)

To overcome some of the limitations of AE, the actual masses of the desired product and all of the reagents used can be simply used instead of molecular weight which is called RME. In its most simple form, RME [9] is calculated as:

$$\text{RME}(\%)=\left[\frac{\text{mass of isolated desired product}}{\text{mass of all reagents used}}\right]\times 100$$

Therefore, RME accounts for the excesses of reagents used unlike AE as the former includes other green metric parameters detailed below. Thus, the RME of the Wittig reaction is

$$\text{RME}(\%)=\left[\frac{0.44\text{ g}}{1.96\text{ g}+0.35\text{ g}+0.53\text{ g}}\right]\times 100$$

This is lower value than AE (20%). This shows that the Sheldon E-factor is 16 kg of desired product for 84 kg of byproducts or wastes. The implication is that the wastes can have socio-economic and environmental impacts. However, it is possible to reduce the impacts *via* recycling, recovery; reuse or reclaiming the wastes and that depends on the different scenarios employed such as partial reclaiming scenario, all organic reclaiming or complete reclaiming that can be disclosed below.

The Stoichiometric Factor (SF)

It can be accounted for reagents used in excess by calculation of the SF as:

$$SF = 1+\left[\frac{\text{Excess mass of reagents}}{\text{stoichiometric mass of reagents}}\right]$$

If no reagent is used in excess, the numerator in this equation will be zero and so stoichiometric factor will be 1, the best possible value. SF=1 for stoichiometric reactions carried out with no excess reagents; SF>1, otherwise. For the real Wittig reaction example benzaldehyde (5 mmol) is the limiting reagent. Methyl triphenyl phosphonium bromide (5.5 mmol) and n-butyl lithium (5.5 mmol) are used in excess.

- Methyl triphenyl phosphonium bromide, MW=357.2 g/mol
- n-butyl lithium, MW=64.1 g/mol

- Benzaldehyde, MW=106.1 g/mol

$$SF = 1+\left[\frac{0.5\times\ 357.2+0.5\times 64.1}{5\times (357.2+64.1+106.1}\right]=1.08$$

The closer value of SF to 1 indicates that the excess reagents and stochiometric reagents are closer to each other. The stoichiometric reactions were carried out with less excess reagents and are better with respect to this metrics.

Curzon's RME

As defined by Curzon, RME is an improvement with respect to AE, but is it enough? The amounts of chemical used for Witting case example are:

- Methyl triphenyl phosphonium bromide: 1.96 g
- n-butyl lithium solution (d=0.693 g/mL), 2.2 mL, 1.52 g
- benzaldehyde (d=1.044 g/mL): 0.51 mL=0.53 g
- tetrahydrofuran (THF, d=0,889 g/mL): 40 mL=35.6 g
- water and ethyl acetate for quenching.
- n-hexane and ethyl acetate for purification.

This will take us to another form of RME as detailed here under.

Andraos's RME

In 2005 Andraos proposed a better definition of the RME that takes into account all the masses of the chemicals used in a reaction, including the mass of catalysts, solvents, and work-up/purification materials. This is an improvement over Curzon's RME.

$$\mathrm{RME}(\%)=\left[\frac{\text{mass of isolated desired product}}{\text{mass of all chemicals used}}\right]\times 100$$

To relate this new metric with AE, a supplementary metric, the Material Recovery Parameter (MRP), is important to account for catalysts, solvents, and work-up/purification materials.

Material Recovery Parameter (MRP)

$$MRP=\left[\frac{1}{1+\left\{\mathrm{Y}\times\ \mathrm{AE}\times\frac{(\mathrm{c}+\mathrm{s}+\mathrm{w})}{(\mathrm{p}\times\ \mathrm{SF})}\right\}}\right]$$

Where,

Y = yield

AE = Atom Economy

c = mass of catalysts used

s = mass of reaction solvents

w = mass of auxilliary materials used (isolation, purification)

p = mass of desired isolated product

SF = stoichiometric factor

$$\mathrm{RME}=\left|\frac{\mathrm{Y}\times\mathrm{AE}\times\mathrm{MRP}}{\mathrm{SF}}\right|\times\ 100$$

It is quite difficult to derive an analytical form of MRP, since it depends on many different parameters. Just consider that for a solventless reaction (s=0), without any catalyst (c=0) and that requires no work-up or purification step (w=0), the MRP is 1, the best possible value. On the other hand, a reaction using a huge amounts of solvents (very big s+w), will have a value of MRP near 0, its worst value.

The general form of RME (Andraos' RME) is related to MRP, yield, AE and SF as:

$$\mathrm{RME}=\left[\frac{\mathrm{Y}\times\mathrm{AE}\times\ \mathrm{MRP}}{\mathrm{SF}}\right]\times 100$$

In this example of the Wittig reaction, calculation of the exact value of RME and MRP is not easy since the amounts of auxiliary solvents used are not reported in the experimental procedure. This is the pitfalls of organic synthesis. However, an approximate RME value can be calculated taking into account only the mass of reaction solvents used.

Therefore, the (approximate) general RME for the Wittig reaction

- Methyl triphenyl phosphonium bromide: 1.96 g
- n-butyl lithium solution (d=0.693 g/mL), 2.2 mL, 1.52 g
- Benzaldehyde (d=1.044 g/mL): 0.51 mL=0.53 g
- Tetrahydrofuran (THF, d=0,889 g/mL): 40 mL=35.6 g
- Isolated product (85% yield): 0.44 g

$$\mathrm{RME}(\%)=\left[\frac{0.44}{1.96+1.52+0.53+35.6}\right]\times 100=1.1\%$$

This very low value is indeed due to the mass of reaction solvents because in an organic transformation, the greater amounts of chemicals usually used are solvents (reaction, isolation and purification solvents). This shows a supplementary factor is needed. Thus, the (approximate) MRP for the Wittig reaction is calculated as

- Yield: 85%=0.85
- AE: 19.7%=0.197
- SF: 1.08
- Solvents used (s): 35.6 g (THF)+1.2 g (n-Hexane)=36.8 g
- Isolated product (p): 0.44 g
- It is assumed c and w to be zero.

This is common pitfalls of organic synthesis. Missing information in synthetic plans (amounts of drying agents used, amounts of stationary phases used in purifications, masses of extraction and purification solvents, exaggerated claims of efficiency, amplified reaction performances) are the pitfall.

$$\mathrm{MRP}=\left[\frac{1}{1+\frac{(0.85+0.197\times 36.8)}{0.44\times 1.08}}\right]=0.072$$

RME, MRP, AE, 1/SF and yield can be used altogether visually display the efficiency of an organic transformation. Therefore, the Radial Pentagon for the real Wittig Reaction (Y=0.85; AE= 0.197; SF=1.08; RME=0.011, MRP=0.072) is as depicted in Figure 1.

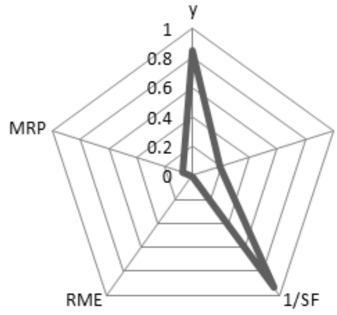

Figure 1: Radial pentagon of Witting reaction.

In addition to Green metrics parameters, it is important to consider the waste footprints of chemical or industrial processes. In this regard, consideration of Environmental factor is important. The normal formula of E-factor is described in terms of Molecular Weight (MW).

$$\text{EMW}(\%) = \text{kg waste / kg product)} = \left[\frac{\text{MW of all wastes}}{\text{MW of Desired Product}}\right] \times 100$$

However, more than MW it is better to express in terms of molecular mass a new Sheldon's Environmental Factor. In the same way we can derive a general form of RME from AE, it is possible also to define a new form of Sheldon's Environmental factor in order to take into account the yield and excesses of reagents, simply using masses instead of molecular weights:

$$\text{RME} = \left[\frac{1}{1+\text{Em}}\right]$$

Therefore, the different forms of RME under various scenarios can be summarized as follows: Excess reagents used, reaction catalyst, reaction solvent, work-up and purification materials destined for waste

$$RME = \frac{Y \times AE}{SF} \quad \frac{1}{1+\dfrac{y \times AE\,(c+s+w)}{p \times SF}}$$

No excess reagents used, reaction solvent, work-up and purification materials recycled (recovered), reaction catalyst destined for waste.

$$RME = Y \times AE \times \frac{1}{1+\dfrac{y \times AE \times c}{p}}$$

Excess reagents used reaction solvent, reaction catalyst, work-up and purification materials recycled (recovered).

$$RME = \frac{Y \times AE}{SF}$$

No excess reagents used reaction solvent, reaction catalyst, work-up and purification materials recycled (recovered).

$$RME = Y \times AE$$

Suzuki cross coupling

Furthermore, the Radial Pentagon for the synthesis of 1, 1'-Biphenyl using Suzuki cross coupling catalyzed by Palladium (0) is given below in Figure 2 [19-21].

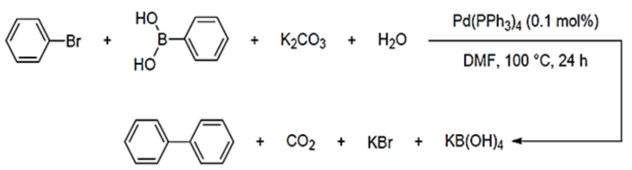

Figure 2: Cross coupling catalysed by Palladium reaction.

Procedure: Bromobenzene (2.1 mL, 20 mmol) was added to a mixture of palladium (0) catalyst (0.023 g, 0.02 mmol), phenylboronic acid (3.66 g, 30 mmol) and K_2CO_3 (5.53 g, 40 mmol) in H_2O (10 mL) and DMF (80 mL). The reaction was stirred under reflux for 24 hours at 100°C. After cooling to room temperature water was added (10 mL) and the aqueous layer was extracted twice with a 1:1 mixture of n-hexane/diethyl ether (2 × 50 mL). The organic layer was washed with brine (40 mL), dried over $MgSO_4$ (5 g), filtered and concentrated under vacuum. The product (2.87 g) was obtained as a white crystalline solid after crystallization from n-hexane (60 mL). The green metrics parameters are tabulated below Table 2. Under no reclaiming scenario (Em=89.9 kg waste/kg product) the waste footprint is the highest than the other scenarios whereas it is the least in complete reclaiming scenarios (Em=6.75 kg waste/kg product). This implies recovering of all post reaction materials considerably reduce the waste generated. This has environmental and socio-economic merits (Figure 3).

Table 2: Green Metrics and E-factors of Suzuki cross coupling under different scenarios.

Metrics	No reclaiming	Partial organic reclaiming	All organic reclaiming	Complete reclaiming
AE	0.354	0.354	0.354	0.354
Em	89.9	65.7	28.4	6.75
RME	0.011	0.015	0.034	0.129
1/SF	0.389	0.389	0.389	0.389
Y	0.933	0.933	0.933	0.933
MRP	0.083	0.116	0.262	1

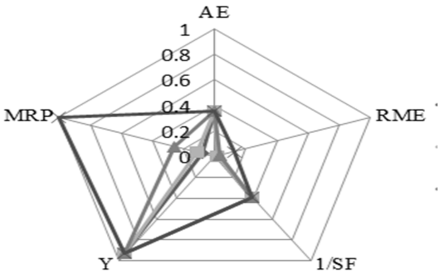

Figure 3: Radial pentagon representing RME values for the synthesis of 1, 1-Biphenyl using the suzuki cross-coupling under various scenarios.

Note: ◆ No reclaiming ■ Partial organic reclaiming ▲ All organic reclaiming

Grignard reaction

In addition, the green metrics-factor and radial pentagon for the synthesis of diphenylmethanol using the Grignard methodology is summarized as follows [7].

Procedure: To a 25 mL rounded bottom flask charged with 0.4 g dry magnesium turnings is added drop wise a solution of 1.8 mL of bromobenzene in 9 mL of dry ether over 20 minutes. The reaction solution was gently refluxed for a further 20 minutes. A second solution of 1.5 mL of benzaldehyde in 4 mL of dry ether was added drop wise over a period of 20 minutes. After addition was complete the mixture was refluxed for 15 minutes then cooled. The reaction mixture was then poured over 10 g of crushed ice followed by addition of 3 mL of 5% aqueous HCl solution. The ether layer was separated and washed successively with water (30 mL), saturated sodium bisulfite ($NaHSO_3$) solution (30 mL), and again with water (30 mL). After drying with 5 g $MgSO_4$, filtration, and evaporation of the solvent, the crude product was recrystallized from petroleum ether (100 mL) providing 2.18 g of pure diphenylmethanol (Figure 4).

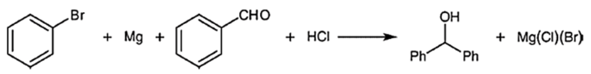

Figure 4: Recrystallized reaction.

RME is calculated under three various scenarios: i) under reclaiming reaction solvents, catalysts, and byproducts, and all post-reaction materials (complete reclaiming metrics); under reclaiming ether from reaction and petroleum ether from purification (partial reclaiming metrics); iii) under committing all reaction solvents, catalysts, and byproducts, and post-reaction materials to waste (no reclaiming metrics). For the synthesis of diphenylmethanol using the Grignard methodology, AE=0.569; yield=0.8004, SF=1.611 and the other metrics are evaluated and Tabulated in Table 3.

Table 3: Green Metrics of Grignard reaction under different scenarios and the pentagon.

Complete reclaiming metrics	
MRP	1
Em	2.541
RME	0.282
Partial reclaiming metrics	
MRP	0.6195
Em	55.45
RME	0.018
No reclaiming metrics	
MRP	0.02416
Em	89.034
0.083	0.083

In general, Table 4 summarizes of Green Metrics analyses for various reaction types .The waste footprint per product formed (Em) depends on the RME under different scenarios. As RME increases under different scenarios, Em correspondingly decreases. However, the quantities of wastes are different from the nature of wastes. The implication is that decreasing the dose decreases the toxicity according to the father of toxicology (Paracelsus) who states that all substances are poisons; there is none that is not a poison. The right dose differentiates a poison and a remedy. This can make the Predicted Environmental Concentration (PEC)- a concentration of a material in the environment lesser and lead to Predicted No Effect Concentration (PNEC). This can reduce the Risk Quotients (RQ=PEC/PNEC) and the hazard if exposure happens. This implies that no adverse effects are anticipated.

RESULTS AND DISCUSSION

Alternative green products

Green diesel: Despite the fact that most of the current biodiesels are produced through a transesterification process, these Fatty Acid Methyl Esters (FAMEs) have high oxygen content, poor flow property at low temperatures and poor oxidative stability. To solve such problems, catalytic cracking [22], hydrotreating [22-23], and deoxygenation [24] have been attempted to produce green diesel (Figure 5). The claims of green diesel over biodiesel are the following: Green diesel is sulphur free; its cerana number and calorific values are higher than biodiesel and even petro-diesel; and have improved cold filter plug point.

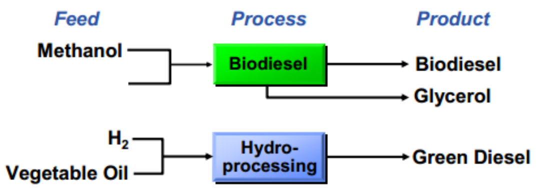

Figure 5: Vegetable oil processing routes.

Green pesticides: Spinosins are the best among green pesticides. Because, it stays in the environment for six months killing malaria causing mosquitoes at any metamorphosis cycle and degrades into environmental friendly products [25].

Green surfactant: Bio surfactants show unique properties (e.g., mild production conditions, lower toxicity, higher biodegradability and environmental compatibility compared to their chemical counterparts [26]. The numerous advantages of bio surfactants have applications not only in the food, cosmetic, and pharmaceutical industries but in environmental protection (soil washing, oil spills cleaning). Biosurfactants are the most promising due to high productivity from the renewable resources (Figure 6). They are safer, degradable and renewable unlike alkyl phenol ethylates that are endocrine disrupting compounds [26].

Green drug carriers: Phospholipids from microalgae can be used as drug delivery system as liposome. Therapeutic agents such as proteins/peptides, nucleic acids, ant carcinogens, and other drugs have the drawbacks of low bioavailability, rapid clearance, and high toxicity. Liposomes have many advantages being able to deliver hydrophilic and lipophilic drugs, targeting and tissue compatibility, reducing drug toxicity and improving its stability (Figure 7). Liposomes can serve as the carriers of antitumor, antifungal, analgesic, in gene therapeutics and vaccines [26-27].

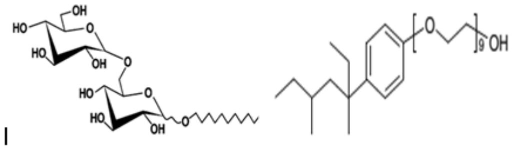

Figure 6: Alkyl polyglycoside (left) and Nonylphenol ethoxylate(right).

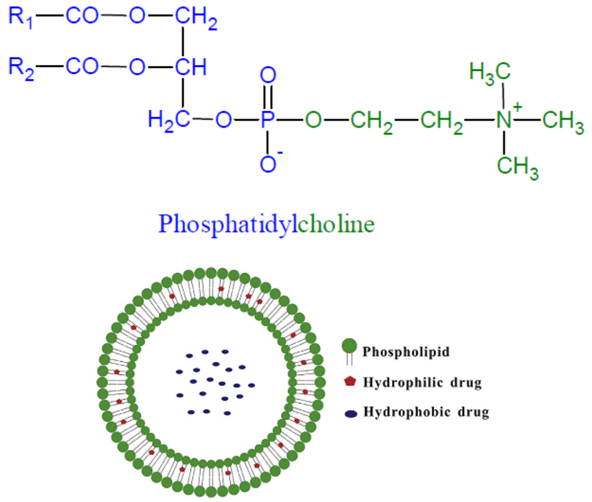

Figure 7: Structure of Phosphatidylcholine (left) and liposome (right) [27].

Green polymers: Bio plastics are plastics derived from renewable biomass sources. The increasing application of bio plastics is vital in the quest for a bio based economy for the nearest future. With the increasing scarcity of fossil raw materials and global warming, the use of renewable raw materials is an obvious solution and promises huge potential. One of the decisive advantages in the replacement of conventional plastics with bio plastics is the contribution to the reduction of atmospheric greenhouse gases, thus plays a major role in the mitigation of global warming. Another advantage is that most biopolymers are also biodegradable, renewable and compostable.

Worldwide Poly Hydroxy Alkanoates (PHAs) producing and research companies and the commonly used bacterial strain PHAs possess highly favorable technological properties similar to conventional petro-based plastics, sometimes superior to other biodegradable polymers such as chemically synthesized plastics. Their versatility, biodegradability and immunological inertness have made them potential candidates in several applications, from biomedical/medical fields to food, packaging, textiles and household materials [28].

Green Catalysis-Biocatalyst: Synthesis of Sitagliptin *via* first generation route involves deprotection of the amino group, 52% overall yields, eight steps, poor atom economy and poor Reaction Mass Efficiency (RME)=0.4% , E-factor of 250 kg waste/kg product, 81% e.e , generations of liquid wastes, uses of corrosive NaOH ,HCl and Pd catalyst loading. Second generation utilizes precious and toxic transition metal, high-pressure equipment, crystallization to obtain optically pure Sitagliptin, which are significant cost drivers. A one-pot process, an improvement over second generation, affords the sitagliptin >99.6 wt%; with as low as 0.15 mol% tBuJOSIPHOS-Rh (I), 65% overall yield, RME=1.9% that is 5 times improvement over 1st generation, E-factor of 50 and zero aqueous waste. Whereas, third generation engineered biocatalytical process lead to an increase in the overall yield by 13% and productivity by 53% as compared to the second generation process, RME=2.5%, 6 and 2 times improvement over 1st and 2nd generations and reduction of the total waste produced by 19%. Uses H_3PO_4 that is more tolerable than HCl and NaOH. No flammable liquids. It uses renewable feedstock, mild temperature and eliminates precious heavy metals. The enzymatic reaction is run in multi reactors avoiding the need for specialized high-pressure hydrogenation equipment and a reduction in total manufacturing cost. In general, biocatalytical methods of sitagliptin for this case review seem more sustainable than chemocatalytical with respect to most green chemistry principles [29-30].

Green antifoulant: Tributyltin oxide (TBT) was a typical additive for paintings of ship hull, to prevent fouling by corals, sponges, crustaceans and other organisms. But, TBT is persistent and toxic to aquatic organisms. It was banned since 2003 from International Maritime Organization (IMO).Di Chlorooctylisoti OazolIdinon -e (DCOI), new environmentally safe antifouling agent. It reduces toxicity, less biomagnified and rapidly degrades into less toxic form 4 hours after offering the desired applications.

Green solvents: The major reagent used in chemical industry is solvent. This shows, the major waste is solvent. As a result, using green solvents are elegant enough for sustainable industrializations. Reactions that take place in the absent of solvent is given priority [32]. The next better option is to use water as universal solvents [33]. Water can dissolve polar solvents and super critical fluid water dissolute even non-polar solvents [34]. By using appropriate catalysts water can dissolute non-polar compounds and organic syntheses demanding non-polar solvents can take place in polar solvents like water [35]. The good option next water is to use super critical fluid carbon dioxide super critical fluid water and ionic liquids [36-42].However, reaching super critical fluids is expensive and ionic liquids are toxic to aquatic environments.

CONCLUSION

Green metric parameters all together are important to visualize the sustainability of chemical processes and should be applied industrially or laboratory methods. Reaction mass efficiency is a quantity that can be factored into four independent factors: reaction yield, atom economy, inverse of stoichiometric factor accounting for the use of excess reagents, and materials recovery parameter accounting for the use of reaction solvents, catalysts, and other materials used in post-reaction operations such as workup and purification procedures. Results are depicted as a radial pentagon that allows the easy visual inspection of which variables contribute to the attenuation of reaction mass efficiency for a given reaction. However, it is better to include the carbon efficiency and energy required to recover or reclaim reagents or chemicals. It is advisable to incorporate the nature of the waste (Environmental Quotient) not only its quantity. For example, the socio-economic and environmental impacts of 1kg of mercury and 1 kg of calcium are quite different. It is advisable to include the safety data sheet of all reagents summarizing their toxicity, hazard, bioaccumulation or persistence and assess their sustainability with respect to the Twelve Principle of green chemistry. Besides, syntheses of alternative green products are important. For instance, synthesis of alkyl polyglycoside biosurfactants over endocrine disruptor surfactant such as alkyl phenol ethoxylates ,green pesticides like spinosin over persistent pesticides like DDT, alternative antifoulant like DCOI over TBTO, Green diesel over petrodiesel, solventless reaction or use of alternative green solvent like ionic liquids or supper critical fluid CO_2 or H_2O over carcinogenic solvents are awesome. Not only green product design but also green processes design is essential to make chemical industries sustainable.

ACKNOWLEDGEMENT

I am unreservedly grateful to the European Commission for the scholarship funded as Erasmus Mundus Joint Master Degree in Chemical Innovation and Regulation (EMM ChIR). I also heart fully thank the EMM ChIR professors for the novel and updated sciences.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

REFERENCES

1. Illman DL. Environmentally benign chemistry aims for processes that don't pollute. Chem Eng News. 1994;72(36).
2. Lancaster M. Green chemistry: an introductory text. Chem Sci.2020.
3. Poliakoff M, Licence P. Sustainable technology-Green chemistry. Nature. 2007;450(7171):810-812.
4. Anastas P, Eghbali N. Green chemistry: principles and practice. Chem Soc Rev. 2010;39(1):301-12.
5. Trost BM. Atom economy—a challenge for organic synthesis: homogeneous catalysis leads the way. Angew Chem Int Ed Engl. 1995;34(3):259-281.
6. Anastas PT, Warner JC. Green chemistry. Frontiers. 1998;640:1998.
7. Sheldon RA. Metrics of green chemistry and sustainability: past, present, and future.ACS Sustain Chem Eng. 2018;6(1):32-48.
8. Andraos J, Sayed M. On the use of" green" metrics in the undergraduate organic chemistry lecture and lab to assess the mass efficiency of organic reactions. J Chem Educ. 2007;84(6):1004.
9. Curzons AD, Constable DJ, Mortimer DN, Cunningham VL. So you think your process is green, how do you know?—Using principles of sustainability to determine what is green–a corporate perspective. Green Chem. 2001;3(1):1-6.
10. Noyori R. Pursuing practical elegance in chemical synthesis. Chem Commun. 2005(14):1807-11.
11. Noyori R. Facts are the enemy of truth—Reflections on serendipitous discovery and unforeseen developments in asymmetric catalysis. Angew Chem Int Ed. 2013 ;52(1):79-92.
12. Sheldon RA. The E factor: fifteen years on. Green Chemistry. 2007;9(12):1273-1283.
13. Sheldon RA. Fundamentals of green chemistry: efficiency in reaction design. Chemical Society Reviews. 2012;41(4):1437-51.
14. Andraos J. The algebra of organic synthesis: green metrics, design strategy, route selection, and optimization. CRC Press; 2016.
15. Lapkin A, Constable D. Green chemistry metrics. Wiley; 2008.
16. Byrne PA, Gilheany DG. The modern interpretation of the Wittig reaction mechanism. Chem Soc Rev.2013;42(16):6670-96.
17. Ramazani A, Kazemizadeh AR, Ahmadi E, Noshiranzadeh N, Souldozi A. Synthesis and reactions of stabilized phosphorus ylides. Curr Org Chem. 2008 ;12(1):59-82.
18. Wu J, Zhang D, Wei S. Wittig reactions of stabilized phosphorus ylides with aldehydes in water. Synth commun.2005;35(9): 1213-1222.
19. Miyaura N, Suzuki A. Palladium-catalyzed cross-coupling reactions of organoboron compounds.Chem Rev. 1995 Nov 1;95(7):2457-2483.
20. Suzuki A. Recent advances in the cross-coupling reactions of organoboron derivatives with organic electrophiles, 1995–1998. J Organomet Chem. 1999;576(1-2):147-168.
21. Wolfe JP, Singer RA, Yang BH, Buchwald SL. Highly active palladium catalysts for Suzuki coupling reactions. J Am Chem Soc. 1999;121(41):9550-9561.
22. Corma A, Huber GW, Sauvanaud L, O'connor P. Processing biomass-derived oxygenates in the oil refinery: Catalytic cracking (FCC) reaction pathways and role of catalyst. J Catal. 2007;247(2):307-27.
23. Huber GW, O'Connor P, Corma A. Processing biomass in conventional oil refineries: Production of high quality diesel by hydrotreating vegetable oils in heavy vacuum oil mixtures. Appl Catal. 2007;329:120-129.
24. Snåre M, Kubicˇkova I, Mäki-Arvela P, Eränen K, Murzin DY. Heterogeneous catalytic deoxygenation of stearic acid for production of biodiesel. Ind Eng Chem Res. 2006 ;45(16):5708-5715.
25. Hertlein MB, Thompson GD, Subramanyam B, Athanassiou CG. Spinosad: a new natural product for stored grain protection. J Stored Prod. 2011;47(3):131-46.
26. Kitamoto D, Isoda H, Nakahara T. Functions and potential applications of glycolipid biosurfactants—from energy-saving materials to gene delivery carriers. J Biosci Bioeng. 2002;94(3):187-201.
27. Delalat B, Sheppard VC, Rasi Ghaemi S, Rao S, Prestidge CA, McPhee G, et al. Targeted drug delivery using genetically engineered diatom biosilica.Nat Commun. 2015 ;6(1):1-1.
28. Keshavarz T, Roy I. Polyhydroxyalkanoates: bioplastics with a green agenda. Curr Opin Microbiol. 2010;13(3):321-326.
29. Desai AA. Sitagliptin manufacture: a compelling tale of green chemistry, process intensification, and industrial asymmetric catalysis. Angew Chem Int Ed. 2011;50(9):1974-6.

30. Savile CK, Janey JM, Mundorff EC, Moore JC, Tam S, Jarvis WR, et al. Biocatalytic asymmetric synthesis of chiral amines from ketones applied to sitagliptin manufacture. Science. 2010 ;329(5989):305-309.

31. Willingham GL, Jacobson AH. Designing an environmentally safe marine antifoulant.2020.

32. Marvaniya HM, Modi KN, Sen DJ. Greener reactions under solvent free conditions. J Drug Dev Res.2011;3(2):0-10.

33. Pohorille A, Pratt LR. Is water the universal solvent for the life?. Orig Life Evol Biosph. 2012 Oct;42(5):405-409.

34. Woodcock LV. Supercritical water: percolation transitions and a colloidal mesophase. arXiv.2013;1308.4481.

35. Mase N, Nakai Y, Ohara N, Yoda H, Takabe K, Tanaka F, Barbas CF. Organocatalytic direct asymmetric aldol reactions in the water. J Am Chem Soc.2006 ;128(3):734-735.

36. Abdulkhani A, Marvast EH, Ashori A, Karimi AN. Effects of dissolution of some lignocellulosic materials with ionic liquids as green solvents on mechanical and physical properties of composite films. Carbohydr Polym. 2013;95(1):57-63.

37. Hsiao Y, Rivera NR, Rosner T, Krska SW, Njolito E, Wang F, et al. Highly efficient synthesis of β-amino acid derivatives via asymmetric hydrogenation of unprotected enamines. J Am Chem Soc. 2004;126(32):9918-9.

38. Li J, Wang X, Zhang T, Wang C, Huang Z, Luo X, Deng Y. A review on phospholipids and their main applications in drug delivery systems. Asian J Pharm Sci. 2015;10(2):81-98.

39. Liu Q, Janssen MH, van Rantwijk F, Sheldon RA. Room-temperature ionic liquids that dissolve carbohydrates in high concentrations. Green Chem. 2005;7(1):39-42.

40. Moniruzzaman M, Ono T. Ionic liquid assisted enzymatic delignification of wood biomass: a new 'green'and efficient approach for isolating of cellulose fibers.Biochem Eng J.2012;60:156-160.

41. Polaskova M, Cermak R, Verney V, Ponizil P, Commereuc S, Gomes MF, et al. Preparation of microfibers from wood/ionic liquid solutions. Carbohydrate polymers. 2013;92(1):214-217.

42. Shibata M, Teramoto N, Nakamura T, Saitoh Y. All-cellulose and all-wood composites by partial dissolution of cotton fabric and wood in ionic liquid. Carbohydrate polymers. 2013;98(2):1532-1539.