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Applications Of Green Chemistry In The Pharmaceutical Process

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Abstract:

The advancement of new pharmaceutical products by organic synthesis has added to an insurgency in restorative care, empowering sensational decreases in hospitalization, suffering, and death. Nonetheless, this accomplishment is defective if the earth is antagonistically affected. With the raising significance on green chemistry [1], pharmaceutical process chemists give consideration, their concentration and imagination toward limiting the environmental effect. This paper will present a particular outline of valuable intends to accomplish this objective, and converse the successful modification of processes to achieve reduced resource requirements, waste generation and energy consumption. An attempt has been made in this paper to discuss key factors for deriving environment friendly processes in the synthesis of pharmaceutical products. The selection and use of solvents is emphasized as regards methods to limit environmental impact.

Keywords

green chemistry, pharmaceuticals, solvent utilization strategies

1. Introduction

The manufacture of chemicals can possibly create significant amounts of waste by-products and pollutants, for example, contaminated solvents, drained reagents, and air contaminations. Pharmaceutical manufacturers are noteworthy contributor of these factors. The manufacture of drugs generates more waste and by-products in noteworthy to all others (2). This must be taken in perspective, since the medical and administrative necessities of pharmaceutical purity will normally lead to more waste percent product when contrasted with making less sophisticated compounds of less stringent purity; be that as it may, it underlines the challenge and open door for improvement exhibited to the pharmaceutical industry. An existence cycle investigation of waste produced from their Active Pharmaceutical Ingredient (API) manufacturing facilities assessed that 80% of their waste is solvent-related. Expecting other pharmaceutical companies produce a comparative level of solvent waste, this proposes tending to the selection, utilization, recuperation, and disposal of solvents will contribute significantly to mitigating this issue. While by all account not the only means for greening pharmaceutical manufacture, solvent considerations in drug process incorporated in this review.

2. Green Solvents in pharmaceutical process [3]

The selection of solvents for the synthesis of pharmaceuticals is basic on various levels [4]. Beyond the undeniable capacity of solvents to enable compounds to react efficiently in solution, they may additionally effect manufacturing costs by prompting troublesome separations or requiring processing. Solvents often impact the crystal form of the API, which straightforwardly decides dissolution rates, formulation, and bioavailability. The usage of solvents also brings the burden of solvent incorporation into the API. On the off chance that they cannot be evacuated, the amount must be controlled or constrained to levels that are safe to the patient. While the presence of solvents in drugs is not typically viewed as an ecological effect, they might be viewed as a type of contamination for the purposes of this review as they influence directly as does other pollution. To evaluate this danger to our health, solvents have need of categorization. The Center for Drug Evaluation and Research (CDER) of the USA Food and Drug Administration (FDA) records four classes of solvents sorted out by patient safety and ecological contemplations [5]. Class I solvents (i.e. benzene, carbon tetrachloride, 1,2-dichloroethane, 1,1-dichloroethylene, and 1,1,1-trichloroethane) are exceptionally undesired in view of their unacceptable toxicity or pernicious ecological effect. Class II solvents are most commonly organic solvents, for example,acetonitrile, methanol, methylene chloride, tetrahydrofuran, toluene, and hexane (Table 1).

Table 1: Class II solvents with limitations in pharmaceutical products*

Solvent	PDE (mg/day)	Concentration limit (ppm)
Acetonitrile	4.1	410
Chlorobenzene	3.6	360
Chloroform	0.6	60
Cyclohexane	38.8	3880
1,2-Dichloroethene	18.7	1870
Dichloromethane	6.0	600
1,2-Dimethoxyethane	1.0	100
1,4-Dioxane	3.8	380
2-Ethoxyethanol	1.6	160
Ethyleneglycol	6.2	620
Formamide	2.2	220
Hexane	2.9	290
Methanol	30.0	3000
2-Methoxyethanol	0.5	50
Nitromethane	0.5	50
Pyridine	2.0	200
Sulfolane	1.6	160
Tetralin	1.0	100
Toluene	8.9	890
1,1,2-Trichloroethene	0.8	80
Xylene	21.7	2170

* FDA website: http://www.fda.gov/cder/guidance/

Class III solvents (i.e. acetic acid, acetone, ethanol, ethyl acetate, heptane, and dimethyl sulfoxide) have the lowest toxic potential. The lack of proven human toxicity is the primary criterion for being recorded as a class three solvent and the potential for downgrade to class II or I is constantly conceivable. Class IV solvents (i.e. isooctane, isopropyl ether, petroleum ether, and 2-methyltetrahydrofuran) have lacking toxicological information. Regardless of whether any of these solvents are totally environment considerate is begging to be proven wrong, which is another explanation behind carefully considering the utilization of these solvents in pharmaceutical processes.

Since plainly solvents can rarely be avoided for proficient pharmaceutical manufacture, the underlying inquiry turns out to be the means by which to choose as green a solvent as could be expected under the circumstances. Certain solvents might be rejected that pose potential harm to patients, administrators, and the earth. Such rarely utilized solvents alongside potential substitutes are listed in Table 2.

The Environmental Protection Agency (EPA) offers a several valuable sites (6) for outlining green syntheses. The Green Chemistry Expert System (GCES) offers guide-lines and bolster data for contriving a green-chemistry process (7). This incorporates a green solvents/reactions conditions module, which contains data on green solvent alternatives to conventional choices. Acetic acid, Water, Ethanol, Acetone, 1-Butanol, 2-Butanol, t-Butanol, Butyl acetate, Propyl acetate, Methyl acetate, Ethyl acetate, Isobutyl acetate, Isopropyl acetate, Tetrahydrofuran, etc. are generally perceived as green solvents and gives a way to picking eco-friendly solvents for manufacture.

Table 2: Solvents with limited use in pharmaceutical [4].

Solvent	Unfavorable issues	Possible alternative solvent(s)
Ethyl ether	Flammable	MTBE
Chloroform, dichloromethane	Toxicity and environmental	$PhCH_3/CH_3CN$, n-butanol or trifluorotoluene
Benzene	Toxicity	Toluene
Isopropyl ether	Peroxide formation	MTBE
CCl_4, $ClCH_2CH_2Cl$	Mutagenicity and environmental impact	
HMPA	Toxicity	N-methylpyrrolidine
Ethylene Glycol	Toxicity	1,2-propanediol
Hexane	Electrostatic discharge	
Neurological toxicity	Heptane	
Pentane	Flammable	Heptane
Dioxane	Teratogen	Tetrahydrofuran (THF) or 2-Me-THF

There are two monographs that give wellspring of information, one is 'Functional Process Research and Development' [8] and the other is 'Squander Minimization in Pharmaceutical Process Development: Principles, Practice, & Challenges' [9].

3. Conclusion

A significant number of the green chemistry standards are not new to pharmaceutical industry scientists, but rather converse to the way great process improvement is completed. They do represent to another area of focus to additionally decrease production costs, work in more prominent process strength, and to reduce the ecological impression of the pharmaceutical industry. Green chemistry is quickly being accepted by chemists, and not just on the grounds that it is the right, yet cost is likewise a factor. As the pharmaceutical industry keeps on feeling obligated to hold down the cost of medications, the execution of an ecologically kindhearted way to drug synthesis will contribute by lessening the expanding expenses of reagent and waste disposal. In addition, this paper has

given incentives for further work in developing green pharmaceutical processes.

References

[1] Anastas, P.T.; Williamson, T.C., Eds.; Green Chemistry: Frontiers in Benign Chemical Syntheses and Processes; Oxford University Press: Oxford, UK, 1998.

[2] Sheldon, R.A. Chem. Ind. 1992, 23, 903 906; Sheldon, R.A. Chem. Tech. 1994, 24, 38 47.

[3] Clark, J.H.; Tavener, S.J. Org. Pro. Res. Dev. 2007, 11, 149 155.

[4] Anderson, N.G. In Art of Drug Synthesis; Johnson, D.S., Li, J.J., Eds.; John Wiley & Sons: Hobooken, New Jersey, 2007; 1128.

[5] Guidance for Drugs in USA Food and Drugs Administration. http://www.fda.gov/Drugs/

[6] USA Green Chemistry Website. http://www.epa.gov/greenchemistry.

[7] EPA Green Chemistry GCES Tool. http://www.epa.gov/greenchemistry/pubs/gces.html.

[8] Gadamasetti, K.G., Ed. Process Chemistry in the Pharmaceutical Industry; Marcel Dekker: New York, 1999, 317.

[9] Zhang, T.Y. In Handbook of Green Chemistry and Technology; Clark, J., Macquarrie, D., Eds.; Blackwell Science: Oxford, UK, 2002; pp 306 320.