Green Chemistry in Pharmaceutical Industry

A Case Study

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Overview

- E-Factor in Pharma Industry
- Magnitude of Challenge & Impact
- Why Green Chemistry?
- Implementation of GC - Our real concern?
- What’s possible through GC? - A Case Study
- Conclusions
- Industrial Green Chemistry Workshop (IGCW2011)
# E-Factor of Pharma Industry

**E - Factor** = Environmental Impact Factor  
= kgs waste per kg of desired product

<table>
<thead>
<tr>
<th>Sector</th>
<th>E - Factor</th>
<th>Product Tonnage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oil Refining</td>
<td>≤ 0.1</td>
<td>$10^6 - 10^8$</td>
</tr>
<tr>
<td>Bulk Chemicals</td>
<td>1 – 5</td>
<td>$10^4 - 10^6$</td>
</tr>
<tr>
<td>Fine Chemicals</td>
<td>5 – 50+</td>
<td>$10^2 - 10^4$</td>
</tr>
<tr>
<td><strong>Pharmaceuticals</strong></td>
<td><strong>25 – 100+</strong></td>
<td><strong>$10 - 10^3$</strong></td>
</tr>
</tbody>
</table>

Source: R A Sheldon

Need to explore ways to address this challenge of high E-Factor.
1MT of Chemical Intermediate = 10,000 lit of liquid effluents

1lit of liquid effluent (high COD, BOD & toxic sub.) has potential to contaminate = approx. 1000 lit of clean water in rivers, lakes, etc.

1 normal human being consumes = approx. 100 lits water / day

1MT of Chem. Intermediate = 100,000 peoples water security at stake

10’s of millions of tons of Chemical Intermediates we make every year = ????? Serious impact on the water security of all humans

Need to explore ways to accelerate implementation of Green Chemistry & Green Engineering.
Nature of Pharmaceutical manufacturing:

- Complex molecules & multi-step synthesis
- Chemistry Intensive processes
- Stringent quality & regulatory requirements

The above leads to High E - Factor or Environmental Impact Factor
Impact: huge threat to water bodies & human health

- Quantity – 25 to 100 bn kgs per annum only from Pharma
- Outcome – converting one kind of effluent in to other
- Toxicity – not fully known (Ecotoxicity data available for less than 1% of human pharmaceuticals…Ref: journal “Regulatory Toxicology & Pharmacology, April’2004)”
- Degradation – very slow, impact unknown after degradation

Examples:

- Feb 2009, Pharma Zone in Central India – River water sample analyzed by a professor from Sweden. Supposedly treated water is a soup of 21 different APIs.
- 2007, River in China – effluent from a contraceptive manufacturing plant contained 10 times of Oestrogen required to collapse fish population.
Principles of Green Chemistry & Green Engineering can provide a powerful toolbox for innovations which offer Economic & Environmental Competitiveness.

**Why Green Chemistry?**

- **Commercial Reasons:**
  - Shrinking pipeline - generate max. value from successful leads
  - Severe competition - edge over competitors
  - Price Pressures - sustain margins
Implementation of GC: Our Real Concern?

Magnitude of Environmental Challenges

Scale

Urgency
## A Case Study

<table>
<thead>
<tr>
<th>Industry</th>
<th>Pharmaceutical</th>
</tr>
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<tr>
<td>Customer</td>
<td>One of the fastest growing Pharma Company in India</td>
</tr>
<tr>
<td>Product</td>
<td>Anti – Retroviral (or Anti – Aids) Drug</td>
</tr>
<tr>
<td>Application</td>
<td>Prevents transfer of virus from mother to child</td>
</tr>
<tr>
<td>Our Context</td>
<td>Enable our customer to supply drug to patients at affordable price so that our next generation is not contaminated with the virus</td>
</tr>
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</table>

Convert entire API/Drugs synthesis in to **Green**
A Case Study: Environmental Competitiveness

**CONVENTIONAL SYNTHETIC CHEMISTRY PROCESS**

<table>
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<tr>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
<th>Stage IV</th>
<th>Stage V</th>
<th>Stage VI</th>
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</thead>
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<td>Diazo. &amp; Hydrolysis</td>
<td>Nitrilation</td>
<td>Chlorination</td>
<td>Reduction</td>
<td></td>
<td></td>
</tr>
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</table>

- E-Factor: 32  38  28  4
- Effluent: 1920 TPA  2280 TPA  1680 TPA  240 TPA  Total = 6120 TPA (for 60TPA plant)

**GREEN CHEMISTRY SOLUTION BY NEWREKA**

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- E-Factor: 6  6  1  4
- Effluent: 360 TPA  360 TPA  60 TPA  240 TPA  Total = 1020 TPA
A Case Study: Economical Competitiveness

**CONVENTIONAL SYNTHETIC CHEMISTRY PROCESS**

Stage I: Diazot. & Hydrolysis
Stage II: Nitration
Stage III: Chlorination
Stage IV: Reduction
Stage V
Stage VI

- Th. Yield: 1.01
- Yield: 0.80

0.826 = Overall Yield 1.317

**GREEN CHEMISTRY BASED PROCESS**

Stage I: Diazot. & Hydrolysis
Stage II: Nitration
Stage III: Chlorination
Stage IV: Reduction
Stage V
Stage VI

- Th. Yield: 1.01
- Yield: 0.95

0.826 = Actual Yield 1.140 (86% of Th.)

250% Improvement in Yield
Impact:

- Industrial Green Chemistry based Solution impacted:
  1. Economics (RMC down by 40%)
  2. Environment (E-Factor down by 90%)
  3. Safety ($H_2$, Ni, Chloroform, EDC, MeOH avoided)

- Customer gets a breakeven on their investment in < 3 months.

- Enhanced Quality is a Bonus.
Conclusions

- Magnitude of challenge >>...>> current Scale & Urgency of implementing Green Chemistry by Industry

- Green Chemistry is an effective tool to gain both economical & environmental competitiveness

- Need to develop GC Toolbox & expand awareness of industry to use this toolbox

- Green Chemistry - it’s simple & do-able, case study shows that it doesn’t require extraordinary skills, just a shift in mindset

- What’s Required? - expanding awareness about GC within team, providing some freedom to R&D team to experiment & explore, willingness to invest resources & take some risk, being open to collaborate & partner

Rewards of implementing Green Chemistry are Extraordinary.
Roadblock in Implementation of GC

- Academia, Universities, & Research Institutes
- Industry
- Government Bodies, Regulatory Bodies & NGO’s
- Common Man & Society

The GAP
Attempt to bridge the gap

- Academia, Universities, & Research Institutes
- Industry
- Government Bodies, Regulatory Bodies & NGO’s
- Common Man & Society

Industrial Green Chemistry World (IGCW)
IGCW- a global platform for:

- **IGCW Expo**: Showcasing innovations in industrializing GC&E technologies
- **Case-study Presentations**: Sharing emerging & innovative technologies in the Industrial world of GC&E
- **IGCW Innovators’ Award**: Recognizing & Felicitating GC&E Initiatives
- **Exploring A,B,C of GC&E**: Customized one day seminars for Scientists & engineers
- **e-learning GC&E concepts & practices for various stakeholders**
- **e-Connecting GC&E community through online networking platform**
- **Shaping future**: GC&E training workshops for Teachers and Students

Organizer: Green ChemisTree Foundation, [www.industrialgreenchem.com](http://www.industrialgreenchem.com)
Thank You
&
Wish all of You a
“Greener Future”
from
Team Newreka