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Novel manufacturing technologies for the future chemical and pharmaceutical industry

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Abstract: Globalization of chemical and pharmaceutical markets requires the development of new intensified chemical process to be competitive the new environments. This paper reviews some of the recent developments in the area of intensified chemical processes and discusses some challenges in the implementation of these processes. Some discussion of the perspectives of the current chemical processes is given.

Keywords: intensified chemical processes, chemical and pharmaceutical market.

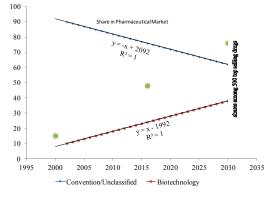
1 Introduction

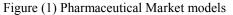
Globalization in recent years has led to raised competition level around the Globe and introduced new challenges and issues related to the mature and newly rapidly developing markets. This new circumstances require novel approaches to sustain business in such sectors as chemical engineering, pharmaceutical and biochemical industry [1]. Several major challenges include limited energy resources, rising energy prices, overwhelming concerns on the greenhouse effect and global warming, political and economic instabilities in the Middle East, Europe and Asia. Given all these concerns, the chemical and pharmaceutical industry must develop and adopt new product development and fabrication concepts which will address new challenges and would allow sustainable growth in the upcoming years.

Old and mature product development and fabrication approaches cannot compete in the environment of agile market. Traditional large production facilities with dedicated and fixed fabrication capacities and defined product lines can no longer quickly adjust to novel demands and quick changes in the pharmaceutical and biochemical industries [2,3].

The need to quickly adopt and react on the changing market demand and supply circumstances

has been increasing quickly and recently becoming much more important.





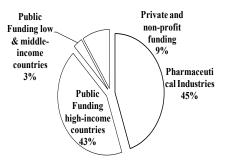


Figure (2) Concentration of Pharmaceutical industries research (The World Medicine Situation taken from World Health Organization and modified according to literatures for 2011)

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One of the important aspects in the rapidly evolving sectors of chemical engineering and pharmaceutical industry is the strategic investment decision making process to choose the most suitable production technology process which would most likely respond and be flexible to changing product specification [1-4]. The investment decision on the fabrication technology is usually made on the very early stages of product development and the risk of failure due to wrong production technology and product specification is very high [4].

2. Technical approach

The need for the process intensification is becoming more and more important whereby new and flexible engineering technological solutions with more smaller, "greener", safer, and scalable and efficient approaches is crucial. A number of recent developments in nanotechnology and nanofabrication sectors, such as micro and nanocatalytic materials, allow further intensification of currently accessible mature chemical processes [5,6]. On of such prominent technology examples would be the reactive distillation, which combines some of the older and mature technological solutions, such as columns heat exchangers etc. with novel and innovative catalytic packing [6].

Micro reaction is another bright example of combining mature technological solutions with new approaches. By introducing micro- and nanoscale technology, much higher concentration gradient becomes accessible, which leads to more efficient and fast mixing processing [7].

It could be emphasizes the need for increased efficiency in industrial processes, specifically addressing chemical and pharmaceutical manufacturing. It employs the term "intensification" to describe the detailed analysis and improvement of all steps in production, in efficiency supply through several manufacturing and approaches and technical knowledge bases. The economic benefits offered by higher efficiencies are highlighted. These benefits can be summarized as making the processes as "sustainably smaller, cleaner, safer and efficient" as possible.

Engineering and efficiency consideration early on in the development stage of processes can lead to a better understanding of investment risks. Cost is also associated with ecological ramifications. "Green" technologies and processes are needed to reduce industry's environmental impact and increase long term sustainability. Nearly all steps in

the industrial process are subject to intensification. Some of these steps include; energy generation/storage/use, resources (sources and feed stocks), transport, waste and recycling. Several challenges and factors limiting the implementation of more efficient and beneficial technologies are addressed [1].

The diversity of the modern global marketplace requires flexible processes that can be adapted to the specific needs of consumers. With such a diverse consumer base, production and supply flexibility offers more efficient fulfillment of localized demands. It was also suggested that many smaller productions facilities can be more beneficial than one large "world scale" facility, with long supply routes and limited local resources. This approach is to address the appropriate "scale" for unique processes and optimizing the scale of production to limit waste and maximize return on investment. Modular approaches were also suggested achieve agile production. Process management is also criticized. Concerns over product testing led many manufacturing processes to use a "batch" production method to ensure product quality. It is suggested a more efficient and effective method is "continuous productions" which can provide many economic and ecological benefits. Quality by (process) design is a technique developed to help transition to the continuous production methods. Although these factors are well known, to claims implementation of innovations is slow moving, regardless of their demonstrated value and benefit [8].

Quickly transitioning advances made in research and development to sustainable industrial processes is a crucial component of this "intensification" and its success will require interdisciplinary teams with diverse knowledge bases. Several suggestions are made for different aspects of production, manufacturing and supply. Novel approaches affecting the nano-, mirco- and macro scales of these chemical and pharmaceutical processes could help overall performance of the industry [4,5]. Ultimately, it is useful to emphasize that the chemical and pharmaceutical industries need to be looking at more than just upfront cost when considering how to design processes. Supply and long term operational efficiencies are needed to guarantee sustainable business practices in the future [7].

Towards Green and higher efficiency many studies emphasizes the need for increased efficiency

in industrial processes, specifically addressing chemical and pharmaceutical manufacturing. It employs the term "intensification" to describe the detailed analysis and improvement in efficiency of all steps in production, manufacturing and supply through several technical approaches and knowledge bases. The economic benefits offered by higher efficiencies are highlighted. These benefits can be summarized as making the processes as "sustainably smaller, cleaner, safer and efficient" as possible. The Engineering and efficiency consideration early on in the development stage of processes can lead to a better understanding of investment risks. Cost is also associated with ecological ramifications. "Green" technologies and processes are needed to reduce industry's environmental impact and increase long term sustainability [8].

3. New manufacturing concepts

Nearly all steps in the industrial process are subject to intensification. Some of these steps include; energy generation/storage/use, resources (sources and feed stocks), transport, waste and recycling. Furthermore, the diversity of the modern global marketplace requires flexible processes that can be adapted to the specific needs of consumers [1-3]. With such a diverse consumer base, production and supply flexibility offers more efficient fulfillment of localized demands.

Several process inefficiencies key to intensification are addressed. These inefficiencies are often artifacts of earlier process development; however, they can lead to unsustainable overall practices. Considerations in areas of manufacturing such as; equipment cost and availability, process development and design, infrastructure and supply, are key to a successful optimization of efficiency and productivity [5].

It was suggested that many smaller productions facilities can be more beneficial than one large "world scale" facility, with long supply routes and limited local resources. This approach is to address the appropriate "scale" for unique processes and optimizing the scale of production to limit waste, while maximizing return on investment. Modular approaches were also suggested to achieve such agile production [3-5].

Figure(3) shows the relationship between years and investment as billion US Dollar globally and it was found that the rate is linear to follow equation 19*(years since 1980) -37463. This relation suggests that R square is almost perfect to reach 0.9816. Process management is also criticized. testing led Concerns over product many manufacturing processes to use a "batch" production method to ensure product quality. Researchers in the field suggest a more efficient and effective method is "continuous productions" which can provide many economic and ecological benefits. "Quality by (process) design" is a technique developed to help transition to the continuous production methods [7].

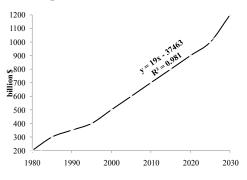


Figure (3) Global Investment in the pharmaceutical industries since 1980 as billion Dollar

Several suggestions are made for improving efficiency in different aspects of production, manufacturing and supply. Novel approaches affecting the nano-, mirco- and macro scales of these chemical and pharmaceutical processes could help overall performance of the industry. It is stressed that interdisciplinary cooperation is crucial to intensification of these processes. Citing specific projects, examples of recently implemented improvements to a number of industrial processes were reported. These "examples illustrate how academia, industry and equipment suppliers work together on the development of these novel processes, manufacturing concepts and their industrial implementation."

Work done on a project funded by the European Commission called "Impulse" focused on improving synthetic efficiencies in consumer goods, ionic fluids and pharmaceutical intermediates through implementation of micro-reactors, compact heat exchangers, and thin-film devices. This project was reported to achieve "radical performance enhancements." To overcome equipment specificity challenges, the "Copiride" consortium, also funded by the European Commission, aims to modularize reactor technology by offering a "cell-based" approach that can suit a wide variety of consumer needs. Other successes of the modular approach include the "F3 Factory" (Flexible, Fast and

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Future), which aims to improved infrastructure by offering a flexible modular manufacturing platform. Modularization of processes allows for quick adjustment in processing loads and scaling. The F3 Factory is currently in joint efforts with Bayer Technology Service and TU Dortmund University to assess and demonstrate the capabilities of the modular approach [1-3].

Supplementing modular approaches, improvements to traditional "batch" manufacturing processes are currently being studied in the four year, industry-academia cooperative; project "Blue Sky Vision" overseen by Novartis and MIT. This project looks to stream line manufacturing through integrating quality by design, new product development processes, and facility lay-out to improve overall system efficiencies [3-6].

Although these factors are well known, many studies did claim implementation of innovation is slow moving, regardless of demonstrated value and benefit. Quickly transitioning advances made in research and development to sustainable industrial processes is a crucial component of this "intensification." Success will require interdisciplinary teams, with diverse knowledge bases, working together to move developing technology to where its value can be fully utilized. Ultimately, the researchers in the field emphasizes that the chemical and pharmaceutical industries need to be looking at more than just upfront cost when considering how to design processes. Supply and long term operational efficiencies are needed to guarantee sustainable business practices in the future [5].

Although many studies push towards new and provides several useful considerations any industrial process should be aware of, it fails to present anything substantially "new." It seems like "intensification" and improvements of all aspects of a business should always be considered. The examples presented are applicable, however, any business wanting to survive in the quickly evolving world economy must always be looking to improve efficiencies, lower cost, decrease waste and optimize productivity [1].

Recent progress in the intensification process has proven the validity of the approach and its future successful possibilities in large scale application process. However, in order to move the process into production phase, join efforts of chemical engineers, equipment developers and suppliers, and supply chain coordinators is required.

Joint efforts of multidisciplinary team of specialists would pave a route to successful implementation of the developed intensified chemical processes which would potentially advance both chemical and pharmaceutical industries [1,5]. The examples given above within the European program illustrates how joint efforts of multidisciplinary team of specialist collaborating across different disciplines and across borders of the countries involved in the project can successfully achieve the goals of the program.

4. Impediments

One should notice several hurdles and many impediments which slow down the implementation of the intensified chemical processes. Specifically designed intensified processes have somewhat special scaling cost reflection. For usual chemical processes the scaling cost is well known as being about 0.7 power of the equipment size. With intensified chemical processes however, the scaling factor can raise up to 1 resulting in the scaling issues when the cost of equipment becomes more important than the cost of materials. However, more research is needed to completely understand and correctly estimate the scaling manufacturing cost issue [5-7].

A second issue is the process development and design. On the development and design phase of the intensified chemical process, more traditional and widely accepted processes are usually used. More optimized and "state-of-the-art" processes are usually introduced later during manufacturing phase. The most optimized and developed processes are most of the time applied during the manufacturing phase of the whole development process [3].

A third issue relates to the fabrication and development infrastructure which is available in Europe. The production capacities in Europe are well developed and established for the traditional chemical processes. Recently, many fabrications facilities has been moved into developing countries. In order for new intensified manufacturing capacities to be developed and established in Europe, they must fulfill both strict economic and ecological criteria [3-5].

Finally, the supply logistic network has to be firmly established in order to satisfy quickly changing demand factors across the Globe. The final product needs to be shipped quickly and economically efficiently. The logistic network has to be developed to optimize the delivering process



and eliminate possible losses associated with logistics [6-8].

5. Conclusion

However, the final implementation of the developed intensified chemical processes will eventually be determined by their economic validity and ecological footprint. Finally, different regional policies within the Europe might pose some additional hurdles for the final implementation phase. Additional standardization of the developed intensification processes is required before the final implementation.

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