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Process Modification of Pharmaceutical Tablet Manufacturing Operations: An Eco-Efficiency Approach

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Abstract: A process improvement in a tablet manufacturing process within a pharmaceutical industry was carried out based on an eco-efficiency approach. As it is one of the most energy consuming processes in the production line, the tablet manufacturing process was considered. It has the highest production volume with a complicated and long manufacturing product life cycle. Data were collected on energy inputs and emissions data for the stages of powder direct mixing, particle size reduction, and tableting. A straightforward approach was then used to analyze environmental impacts in terms of GHG emissions. Non- added value steps were removed from the product life cycle process, which has led to significant time and cost savings, as well as to a reduction in the emission. Annual economic savings have been achieved, a time reduction of approximately 71% was attained, and the reduction in GHG emissions and energy cost were 73.2%. The g CO_2eq per tablet reduction has been calculated within the process improvement to be 2.06 g CO_2eq per tablet instead of 7.71 g CO_2eq per tablet.

Keywords: process improvement; pharmaceutical industry; tableting; eco-efficiency; carbon emission

1. Introduction

Tablets are currently among the most common oral solid dosage forms for drugs [1]. The active pharmaceutical ingredient (API) molecule is the limiting factor in the development of an appropriate formulation; hence, the manufacturing process for solid dosage forms varies from compound to compound.

In the competitive environment of business, it is necessary for the compression operation to be efficient in terms of production cost [2–4]. Pharmaceutical manufacturing operations are inefficient and costly due to "self-imposed" constraints in the system that lead to low efficiency processes [4–6].

Moreover, variability in product quality is caused through insufficient process control; hence, advanced control strategies can be employed to ensure consistent product quality [5,7–9].

"Eco-efficiency" is a term that does not yet appear in dictionaries but has already gained considerable force in shaping the environmental policies and practices of leading corporations. Pharmaceutical industries should find the eco-efficiency assessment instrumental to systematically identifying opportunities to increase energy efficiency and decrease waste generation. Consequently, this leads to positive change in sustainable production and consumption [10–13]. It is a well-used and proven approach to identify cost saving energy conservation and pollution prevention technologies that enhance a facility's performance.

The tableting process, through which a small quantity of powder is processed to form a tablet, is quite common in pharmaceutical industries. It includes direct compression, dry granulation, and wet granulation. Dry granulation may be used if the materials have sufficient inherent binding or cohesive properties to form granules without the use of liquids. Direct compression is defined as the process by which tablets are compressed directly from a powder mixture of API and suitable excipients.

Direct compression is considered the most efficient process as compared to other processes, since it involves only dry blending and compaction of API with necessary excipients, reduces processing time, reduces labour costs, and includes fewer manufacturing steps, a smaller amount of equipment, and less process validation. It also reduces power consumption and eliminates heat and moisture, thus increasing not only the stability, but also the suitability for moisture-sensitive API's particle size uniformity [14].

The tablet direct compression and tableting operations require the use of significant amounts of both energy and time and, most importantly, release greenhouse gas (GHG) emissions into the environment. In order to reduce the emissions into the atmosphere, pharmaceutical manufacturing processes can be changed and improved by eliminating the use of a variety of organic solvents [15,16].

Process modification and technological changes to improve production efficiency and reduce the impact on the environment are of significant importance in many industries, as well as in pharmaceutical manufacturing. This has been investigated using different tools and concepts: waste reduction (WAR) algorithm [17], the product Life Cycle Assessment tool [18], cleaner production concept [15,19,20], and ISO14001 [21].

The influx of refugees into in Jordan, coupled with the increasing demand for energy, while the energy supply in Jordan depends on about 96% on imports of oil, oil products, natural gas, and electricity, have caused a significantly increased economic burden in Jordan [22–30]. The industrial sector consumes 17% of the final energy demand (5.38 Mtoe), and 24% of the electricity demand in Jordan [22]. Eco-efficiency and cleaner production measures in the industrial sector are therefore very critical for energy efficiency and pollution reduction in Jordan [22].

In the present study, the direct compression process was selected to be thoroughly investigated using the eco-efficiency approach due to its high volume production rate in the chosen pharmaceutical tablet manufacturing process, to achieve more energy efficiency and, consequently, to release fewer emissions into the environment.

2. Materials and Methods

The assessment has been carried out following the Guide to Industrial Assessment for Pollution Prevention and Energy Efficiency to facilitate the assessment [31–33]. Several detailed visits were carried out to collect necessary data and to establish the material and energy flow analyses. Moreover, the study assessment covers all the production steps with main focus on the energy consumption and materials flow analysis of the processes. The greenhouse gas emissions were calculated using IPCC Guidelines for national greenhouse gas inventories [34].

2.1. Overview of the Manufacturing Process

A pharmaceutical company located in Amman, Jordan, was selected for undertaking the present study. The company has a multinational business, developing, manufacturing, and marketing generic, branded, and injectable pharmaceuticals on a global scale.

The pharmaceutical tablet processes in the company were the focus of the present study, in which the tablet direct compression and tableting operations require the use of significant amounts of both energy and time and, most importantly, the GHG emissions into the environment. In order to achieve our objectives to reduce the emissions and energy consumption in a pharmaceutical manufacturing process, there are several techniques and practices that are possible to implement, such as processes improving methods, raw material change, equipment modification, better process control, good housekeeping, and technology change.

The tableting process involves the compaction of powder blends to form a hard compact.

As shown in Figure 1, the pharmaceutical tablet process originally includes many complicated steps, namely size reductions steps for the raw materials (API and excipients) using the oscillator and Fitz miller, and blending the powder mixture every time the excipients are be added. The final blend is directly compressed to form tablets by single punch compression machine. However, material properties can significantly affect tableting performance. For instance, broad particle size distributions or density variability can result in segregation causing non-uniform tablet composition during die filling [5]. Furthermore, tablet weight variability and insufficient tablet hardness might result due to low bulk density, poor compressibility, or flow properties, which affect die filling and the pressure profile during compaction [5,35,36].

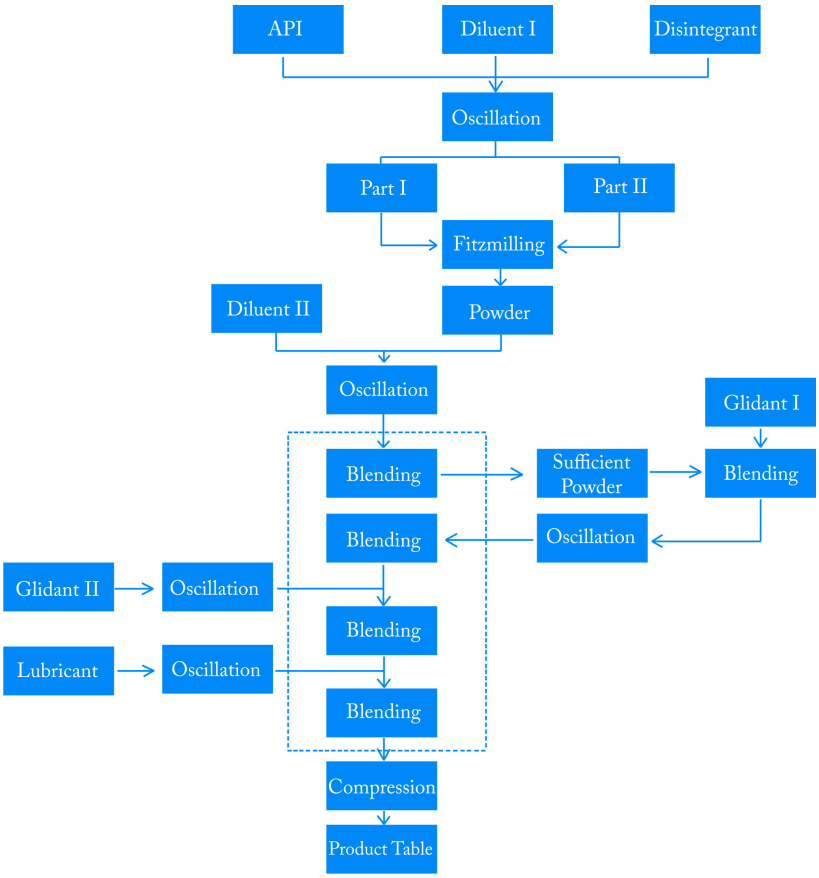

Figure 1. Baseline pharmaceutical tablet processes block diagram.

2.2. Consumption

According to the steps of eco-efficiency assessment steps, each process unit was surveyed in terms of energy consumption and operating time. The primary investigated data, which provide important information for the process analysis, are shown in Table 1. The blending (including oscillation and fitzmilling) and tableting (direct compression) steps consumed most of the energy and time required. The baseline pharmaceutical tablet processes require 170 h and consume 5600 kWh for one tables' manufacturing batch.

Table 1. Summary of baseline pharmaceutical tablet process units' data per batch.

Process Unit	Power (kW)	Operating Time (h)	Energy Consumption (kWh)
Oscillation Fitzmilling Sifter Blending	2 3 0 35	130	5200
Tableting	10	40	400
Total	50	170	5600

3. Results and Discussion

Process was changed to include fewer steps and more simple steps. It is found that the oscillator and Fitz miller have a mesh size of around 600 µm, while the particle size diameter of the product powder equals or is less than 100 µm; therefore, there is no need in this case study process to use them, because the homogeneity of the powder is not affected and the sifter is used instead of them. The size reduction steps were removed, with no effects on the product quality. However, as stated before, the particle size distribution has significant impact on tableting performance.

The blending steps are reduced. The compression machine is changed from single punch to triple punch, leading to a threefold increase in efficiency, as it is shown in Figure 2. This process requires 50 h and consumption of 1499 kWh to manufacture one batch. (See Table 2).

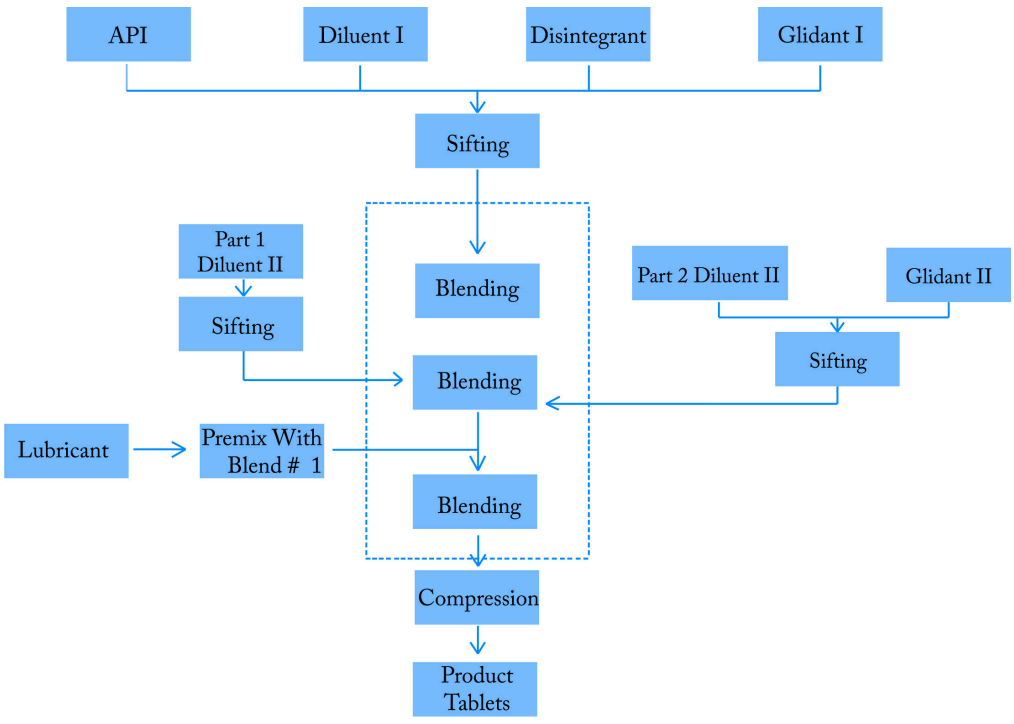

Figure 2. Manufacturing process flow chart after improvement.

Table 2. Summary of manufacturing process units of the product per batch after improvement based on 2013 data.

Process Unit	The Power (kW)	The Operating Time (h)	The Energy Consumption (kWh)
Oscilaation Fitzmilling Sifter Blending	0 0 2 35	37	1369
Tableting	10	13	130
Total	47	50	1499

The effects of changing the process: It was found that the operating time of the manufacturing process units (blending (in addition to oscillation and sifter units) and tableting) per batch was reduced from 170 h to 50 h with a 70.6% reduction. Moreover, the energy consumption was reduced from 5600 kWh per batch to 1499 kWh per batch with a 73.2% reduction. The amount of emissions was calculated to be 1032 kg CO_2eq per batch instead of 3855 kg CO_2eq per batch, knowing that the company produces 100 batches of this product per year, resulting in savings of 34,858 JOD in 2013, as shown in Table 3 and Figure 3.

Table 3. The energy consumed and emissions comparison in old process and new process.

Process	The Operating Time (h)/Batch	The Energy Consumption (kWh)/Batch	The Amount of Emissions * (kg CO_2eq)/Batch	Energy Cost (JD)/Batch
Old Process	170	5600	3855	476
New Process	50	1499	1032	127

* calculated by multiplying the energy consumed with the emission factor (688.453 kg CO_2eq/MWh) that calculated by dividing GHG emissions of electricity sector (kg CO_2eq) on the generated energy (MWh). Data taken from Jordan's Third National Communications on Climate Change for year 2013.

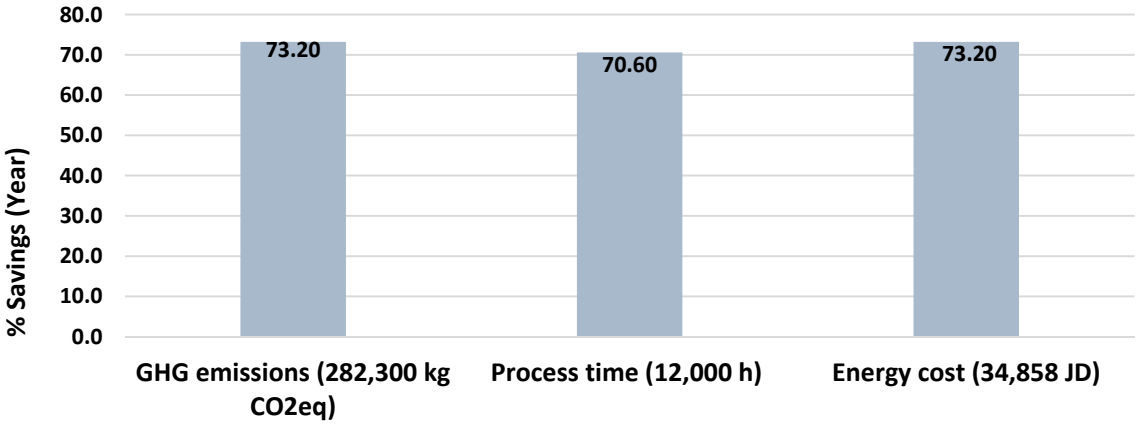

Figure 3. Percentual savings in process time, energy cost, and GHG emissions due to process improvement.

Figure 4 demonstrates the g CO_2eq per tablet reduction that has been calculated within the process improvement to be 2.06 g CO_2eq per tablet instead of 7.71 g CO_2eq per tablet.

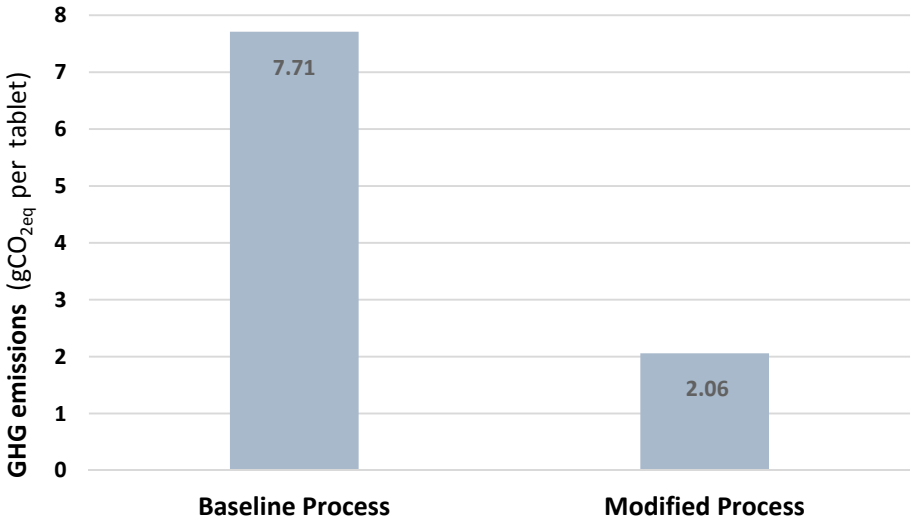

Figure 4. GHG emissions comparison in old process and new process for one tablet produced.

4. Conclusions

Pharmaceutical manufacturing industries need to employ innovation, cutting edge scientific and engineering knowledge, and the best principles of quality management to respond to the challenges of new discoveries.

Although tablet manufacturing is a well-established technology, its improvements, however, in some cases, have come with more stringent requirements for material and process control. This study resulted in the improvement of the environmental and economic performance in terms of energy consumption, GHG emissions reduction, and time consuming processes. The influence of process improvement on minimizing process time, cost, and GHG emissions on pharmaceutical tablet manufacturing processes has resulted in a significant improvement in the energy consumption, process time, and cost reduction performance. Moreover, a true comparison between the old process and the new process has demonstrated a major reduction in GHG emissions, which shows that applying simple tools and strategies accordingly leads to a large business impact.

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