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APPLICATION OF LIFE-CYCLE ASSESSMENT FOR A PHARMACEUTICAL PRODUCT

K. HERNER, J. RÉDEI, L. TAMASKA, SZ. VIZI and Á. RÉDEY

(Department of Environment Engineering and Chemical Technology, University of Veszprém, Egyetem st. 10., Veszprém, H-8200, HUNGARY)

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In this paper the object is a life-cycle assessment (LCA) of a pharmaceutical product. The target of the analysis is to compare different packaging alternatives from environmental aspect. The product is an antidepressive produced by one of the leading Hungarian pharmaceutical factories. In the market the product appears as injection and as a pill packaged in two different ways, in glass bottle and in blister (aluminium and plastic foils laminated together). These three systems: injection, glass and blister are compared in this paper using LCA.

Keywords: pharmaceutical product, life-cycle assessment (LCA), packaging alternatives

Introduction

Pharmaceutical products as well as other products have certain affects on the environment during their entire life-cycle. The life-cycle of a product means the steps from the excursion of the raw materials, the production, the usage of the product to the waste management. The affect depends on the raw material of the product, the technology, and the waste management as well as the function of the product.

LCA [6] is a method used for analysing the environmental effects connected to a given product and it gives an overview of the contribution to the environmental problems during the life-cycle stages of the product. It deals with data of the material and energy usage, the emissions and waste output, connecting them to the following environmental effects:

- Greenhouse effect
- Ozone depletion
- Acidification
- Eutrophizaton
- Heavy metal
- Carcinogenic
- Winter smog
- Summer smog
- Pesticide

In this way the environmental performance of the product can be clarified so the priority for the improvements can be done. By using the method the differentiation between products, raw materials or energy sources is becoming possible by environmental aspect. Thus LCA is a tool of the continuing environmental development and a tool for the environmental performance improvement of the product or firm [5].

Environmental analysis method

LCA is an internationally accepted and applied environmental management tool for improving the environmental performance of a product or for comparing alternative products. The ISO 14040-49 [4] international standards contain the basic principles of the analysis but the method can differ as they are under development in several parts of the world.

The method used for this analysis is the Eco-Indicator 95 method, developed by PréConsultants B.V. in the Netherlands and an LCA software called SimaPro 4.0 developed by the same firm. The principles of the method are explained by Goedkoep et al. (1996) [2].

The software uses the same method, Eco-Indicator 95, but it simplifies the calculations, the results are histograms and tables. The histograms can give the following information: the relative contribution to the environmental effects of the materials and processes during the product life-cycle (characterization), which environmental effects are bigger (normalization), the relative importance of the effects (valuation), besides these the life-cycle stages of the product become comparable (indicator) [2].

The reliability of data is important for the analysis. A part of data is based on the software database while other data originate from the pharmaceutical firm [1]. Data missing from both sources was developed by our own publications and handbooks mentioned in the references [7-10].

Life-cycle stages of the product

The first step is the production of the elementary substance and the production of the effective substance of it. Then a part of the effective substance is granulated and pearled, the result is dragee, while injection is made from the other part of the effective substance. The next step of the technological process is packaging: injections in 2 ml glass ampoules, dragees in 15 g glass bottles with PE bottle caps and cotton-wool damper or PVC and aluminium blisters. Life-cycle stages of the product continue through the distribution to the waste management.

All the stages of the process involve material and energy input, emissions to water and air and waste output. Waste treatment in this case means landfill or incineration.

Packaging processes

Dragee packaging

A part of the pharmaceutical products are packed in 15 g glass bottles with written tickets and collected in loose cards.
The following materials are used for dragee packaging:

- Pill
- Glass material
- Cotton-wool
- Paper products (tickets, loose-cards, consignment note)
- Others (PE bottle-cap, adhesive tape)

Blistering

The other part of the pills packed in blister, which is a cut and signed PVC-aluminium packaging form.
Materials used for the packaging:

- Pill
- Primary packaging materials: PVC, PVC/PVDC foil, aluminium foil
- Secondary packaging materials: tickets, boxes, loose-cards.
- Packaging with complement information: consignment note, tickets.
- Auxiliary materials: paints, reducer, PE tape for bundle (60 mm wide, 40-50 μm thick PE foil), sticking tickets (50 mm in diameter), plastic adhesive tape.

Blister is made of PVC and PVC/PVDC foil and printed aluminium foil closed with welding.

Packaging of injection:

The 5 pieces of 2 ml injections are placed in one hard, covered, white PVC foil. Two of these PVC foils are placed in one loose-card provided with a consignment note. This means there are 10 injections of 2 ml in one package.

Distribution

Pharmaceutical end-products are going to the next step of the distribution chain: from the factory to the wholesalers and from these through the pharmacies and hospitals to the consumers.

Waste management

It was assumed that the packaging of the pharmaceutical product becomes waste at the consumer and treated as household waste. As household waste most of it is deposited in landfills. Waste generated through the processing is incinerated as industrial waste.

Life-Cycle Assessment for the pharmaceutical product

Analysis is made for the following steps of the products life-cycle:

- Elementary substance
- Effective substance
- Production and packaging of the injection
- Production and packaging in glass bottles of the dragee
- Production and packaging of the dragee in blisters

Since the object of this analysis does not extend to the effects of the elementary and effective substances and to the changes of these effects, and since these effects are included in the analysis of packaging forms, this paper only deals with the analysis of the three packaging forms.

For the analysis, SimaPro 4.0 software was used, the results are presented in histograms below [2]. There are four types of histograms, showing the different aspects of the environmental loads connected to the materials and processes of the life-cycle steps [3].

Characterization: The histogram shows the contribution of the technological steps to each environmental problem in percentages.

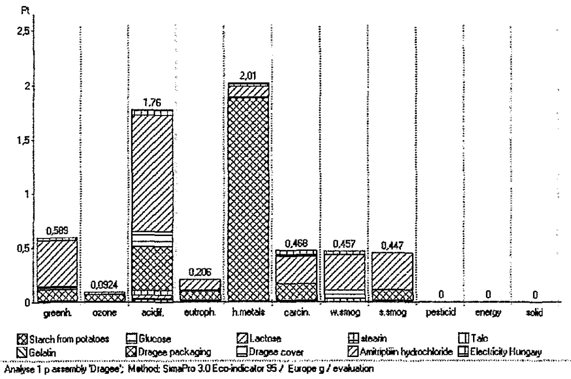

Fig.1 Evaluation histogram for dragee production

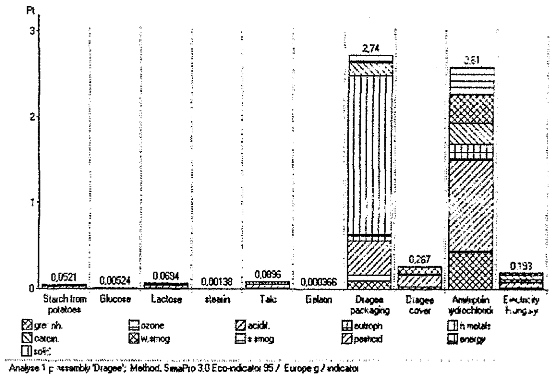

Fig.2 Indicator histogram for dragee production

Normalisation: The absolute volume of the environmental problems connected to the product.

*Evaluation: It s*hows the relative importance of the environmental problems caused by the life-cycle steps of the product expressed in ecoindicator points (Pt), which show the contribution of the process or material to the environmental problems. The higher point means bigger environmental load. The most significant environmental loads and technological steps are signed by this histogram.

*Indicator: It s*ummarizes the environmental loads of each technological process stages to make them comparable. In this way it assigns the life-cycle step of the product with the most significant environmental load.

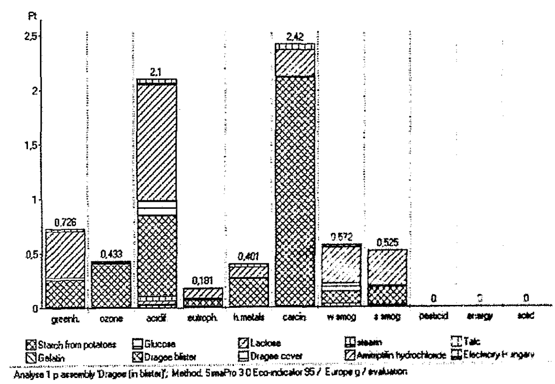

Fig.3 Evaluation histogram for dragee blister

Results

Dragee form packaged in glass bottles

Environmental effects of the dragee production are connected to the production of the effective substance and the packaging. The effects of the production are significant for all the environmental problems except the ozone and heavy metals, in which case the effects of the packaging (the glass production) are more significant. Other life-cycle steps as effective substance production, dragee cover and electricity generation Hungary (Electricity Hungary) have significantly lower effects. By the evaluation, the highest value can be found at the environmental problem of heavy metals with 2.01 ecopoint. This is partly caused by the glass production connected to the dragee packaging. Glass production can cause Pb, Ba, Cr, Ni, As, Cd, Hg, Cu emission to air and water. A heavy metal, mercury also originates from the production of hydrochloride acid used for the effective substance. Besides these, the electricity generation, the production of the effective substance, the transportation and the usage of TiO_2 for the covering involve heavy metal emission.

Acidification is the next environmental problem occurring through the life-cycle of the product with 1.76 ecopoints. Acidification is the result of the elementary substance production, the packaging in 30% and the covering in 8%. It is caused by the SO_2 emission from the covering and the effective substance, the NO_x emission from the dragee packaging, the NH_4 emission of the elementary emission, and the HCl emission from the effective substance.

Other problems have smaller ecopoints but the elementary production is the main cause in these, too. Besides these, the CO_2 and the methane emission from the dragee packaging play a role in the greenhouse effect and the dust by the covering have an influence on the winter smog.

By comparing the environmental problems connected to the life-cycle stages of the dragee production the result is that the packaging has the greatest environmental contribution with 2.74 ecopoints. This is mostly due to the heavy metal emission of the glass production mentioned before. The next is the effective substance production with 2.61 ecopoints caused by acidification. Environmental effects caused by the dragee covering are the acidification and dust from the transportation and have 0.267 ecopoints.

Elementary sustances do not have significant effects because the analysis only counted data of transportation. Data on production of elementary substances is missing.

Dragee form packaged in blister

The histogram *Fig.3* differs from the glass forms *Fig.1* in the following aspects: the results of the packaging are

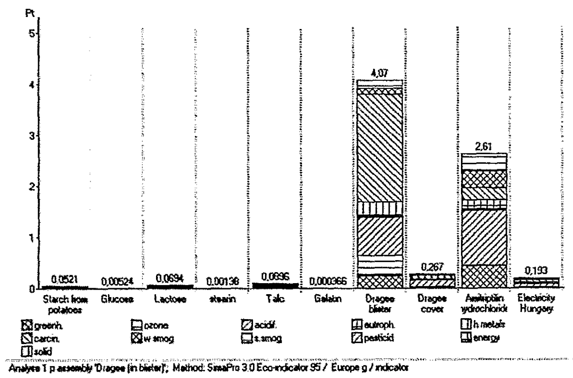

Fig.4 Indicator histogram for dragee blister

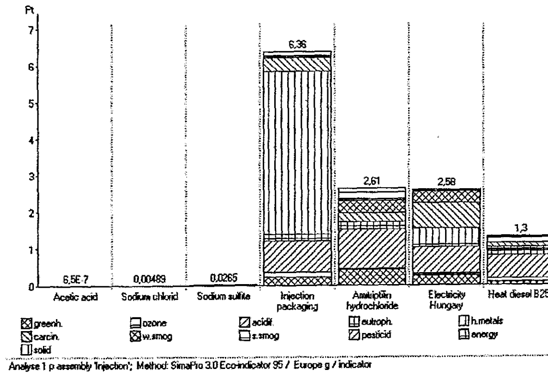

Fig.5 Indicator histogram for injection production

more significant in all environmental problems, but mostly the ozone, carcinogenic effect and the summer smog. The histogram shows that the biggest environmental problem is the carcinogenic with 2.42 ecopoint, caused by the packaging in blisters. Poliaromatic-hidrocarbons occur in the aluminium foil production and cause carcinogenic problems. The next more important environmental effect is acidification with 2.1 ecopoint, caused by NO_x and SO_2 emissions occur in plastics production. Besides the effect of the packaging, the production of elementary substance also generates acidification. At the covering the SO_2 emission occurs at the transportation causing acidification.

Greenhouse effect has 0.726 ecopoint. The contribution of the effective substance production is 60% while 30% proceeds from packaging. In both cases the greenhouse gases cause the problem emitted by the energy generation. Summer and winter smog are caused by the production of effective substance. Heavy metals such as Pb, Ni, Cr, Ba, As are emitted by the aluminium foil production used for blister packaging.

As the histogram shows, among the life-cycle stages the packaging, the blister production has the most significant contribution to the environmental problems. It has 4.07 ecopoints, 30% of it is carcinogenic effect caused by the poliaromatic-hydrocarbons and Ni emission of the aluminium production. Acidification and ozone depletion are also important effects, caused by the poliaromatic-hydrocarbons and the SO_2.

After the packaging, the production of the effective substance has important effects, mainly in the acidification.

Dragee covering has lower influence, but it contributes to the acidification and winter smog caused by the transportation and production.

Elementary substance has very low effects on the histogram because only the effects of the transportation were counted as mentioned before.

Life-cycle assessment for the injection form:

The other form of the pharmaceutical product is injection packed in 2 ml colourless ampoules. This form is mostly used in hospitals and surgeries. Assessed injection form contains the same amount, 50 mg effective substance, as the dragee form to make them comparable.

Summarising the environmental effects connected to the injection form, in the following the indicator histogram shows that packaging has bigger influence on environmental effects. Injection packaging has 6.36 ecopoints, the heavy metal contribution to it is 80%, caused by the heavy metal emission of the glass production.

Environmental load connected to the generation and usage of energy is equal to 2.58 ecopoints, two thirds of it is caused by acidification and carcinogenic effects.

Carcinogenic are benzene, benzpyrene, poliaromatic-hydrocarbons, chrome and nickel. These occur from the energy generation. Gas burning causes the third part of the emitted benzpyren and poliaromatic-hydrocarbons.

Effective substance production also has an influence (2.61 Pt) on the acidification, greenhouse effect, summer and winter smog.

Heat diesel used for disinfecting has low influence on environmental effects.

Elementary substance2 also has very low influence because the program only counted the data of the transportation. There are no data on the production of these substances.

The contribution of the generation and usage of energy and heat energy are significant. Electricity has a contribution to winter smog and carcinogenic effect in 50%.

Comparison of the three packaging forms by their indicator histograms

With the same effective substance containment (1p) the potential environmental load of the different forms become comparable.

The histogram *Fig.6* shows the scale of the packaging forms from environmental aspect. The most significant environmental load is connected to the injection form. It should be noticed that the function of the injection form is not the same as the dragee form, so they can not be compared as alternatives. Injection form is needed in hospitals and surgeries and can not be discharged with the dragee form.

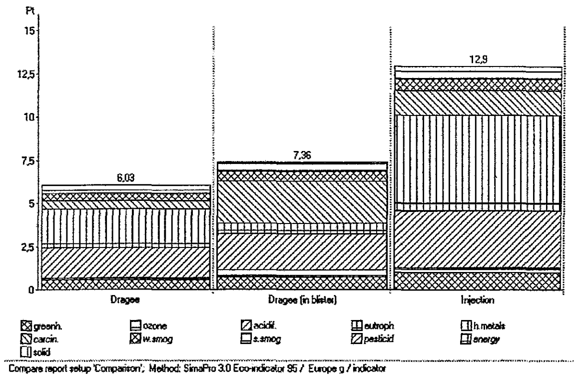

Fig.6 Indicator histograms of dragee in glass, dragee blister and injection forms.

Between the two packaging alternatives for the dragee form the glass packaging seems to be better from environmental aspect, the differences is almost 20%. This alternative is better in the following environmental problems: carcinogenic, ozone depletion, acidification, while it is worth in heavy metals as the blister packaging.

Summarising the dragee form packed in glass is the best solution from environmental aspect. The injection form of the pharmaceutical product has the biggest effect on the environment, but its function is differs so it cannot be changed.

Conclusions

By the assessment of the product life-cycle we got a view on the potential environmental load. The most important environmental problems, which occur through the entire life-cycle of the pharmaceutical product are acidification, carcinogenic and heavy metals.

The acidification is mainly caused by the elementary substance production, and extracting solvents in it. Through the effective substance production the contribution of the organic acids is important. Besides these, the SO_2 and NO_x emissions from the PVC plastic production also generate acidification. This occurs at the dragee blister form of the pharmaceutical product. In addition, at dragee covering SO_2, at dragee packaging NO_x and at the elementary substancel ammonium is emitted.

Carcinogenic effect is mainly caused by the poliaromatic-hydrocarbons and nickel emitted by aluminium foil production used for the dragee blister. Besides these the contribution of the emissions occurred at the energy generation and the diesel oil used for transportation at the elementary substance production is significant. By the dragee production the acid extraction and the diesel oil usage is responsible for the carcinogenic effect. Carcinogen effects by the injection form are caused by the benzene, benzpyrene, poliaromatic-hidrocarbons, chrome and nickel occurred at the energy generation and the poliaromatic-hidrocarbons and benzpyrene generated at the gas burning.

Heavy metal emissions of the pharmaceutical products are caused by the glass production, needed at the injection and dragee glass packaging forms. During the glass production the next heavy metals can occur and are emitted to air or water: Pb, Ba, Cr, Ni, As Cd, Hg, Cu. Besides these the antimonies, arsenic, cadmium and barium emission also cause heavy metal effect, which occurs in the fly ash originated from the energy generation. Some of the elementary substances also have a contribution to the heavy metal problem because of the energy generation. Mercury emission occurs at mercury-pool cathode acid production used in the elementary and effective substance production.

Pb, Ni, Cr, Ba, As emission can occur during the aluminium production for dragee blister packaging form. Dragee covering also has a contribution to these effects.

The previous shows that the main part of the potential environmental effects are originated from the packaging, so the conclusion is that it is worth paying attention to the alternative solutions and choose the right and most environmentally friendly one. This harmonizes the interests of the pharmaceutical factory, the interests of the environment and the interests of the environmentally conscious customers in order to satisfy the environmental demands which are an important part of the competitive position.

Figure 6, which compares the packaging alternatives with the same effective containment, shows that the dragee form packed in glass bottle is the best from environmental aspect. The next is the dragee blister form and the injection form seemed to have the most environmental loads. Inspite of these facts the injection form is needed in hospitals and surgeries.

Finally, the result of the analysis is that besides the effects of the packaging, the production of the pharmaceutical product causes the most potential environmental effects. The reduction of the environmental load connected to the product can be probable and effective in these two stages of the life-cycle. By choosing the right packaging alternative some of the environmental effects connected to the product can be reduced or avoided.

The analysis also reflects the "weak" points of the production, in which cleaner production changes can be used to improve the environmental performance of the analysed product.

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