AMERICAN UNIVERSITY OF BEIRUT

DRUG PRODUCT IMMOBILIZATION IN POLYETHYLENE/POLYPROPYLENE MATRICES FOR THE TREATMENT OF PHARMACEUTICAL WASTES

by
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A dissertation
submitted in partial fulfillment of the requirements
for the degree of Doctor of Philosophy
to the Department of Mechanical Engineering
of the Maroun Semaan Faculty of Engineering and Architecture
at the American University of Beirut

Beirut, Lebanon
August 2019

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ACKNOWLEDGMENTS

During the past couple years, I had been trying to manage my time between my family, work at the army and research projects. The least that I can say, after sleepless nights, and literally “blood, sweat, and tears”, it was never an easy task.

I am grateful to all the help and support I received from the University, the professors, my advisor, my colleagues and it is a pleasure to acknowledge their roles to the completion of my PHD research.

It would have been impossible to achieve this without the support of my friends and family members. My deepest appreciation belongs to you all since without your support this work wouldn’t have been made possible.

” Sleeping is no mean art: for its sake one must stay awake all day”
Friedrich Nietzsche

AN ABSTRACT OF THE DISSERTATION OF

Zara Fouad Mawla for Doctor of Philosophy
Major: Mechanical Engineering

Title: Drug Product Immobilization in Polyethylene/Polypropylene Matrices for the Treatment of Pharmaceutical Wastes

Plastic products and pharmaceuticals are both problematic when it comes to the end of their lifecycle, non-recyclable plastic wastes presents serious environmental risks when improperly disposed into the environment; while, active pharmaceutical ingredients have raised a major concern in last two decades, particularly after being detected in surface and ground water at trace concentrations in several parts of the world, triggering potential ecological damage. Combining both elements in one package by transforming plastic and pharmaceutical wastes into a potentially useful material is desirable, and follows a cradle-to-cradle circular economy approach, thus reducing the environmental risks while providing a useful function. This study explores the potential of using recycled plastic material reclaimed from municipal solid waste as a method for immobilizing expired pharmaceutical waste. Mechanical properties and leaching tests were conducted on the reclaimed plastic material containing expired medication. The material properties were comparable to expanded poly(vinyl chloride), which highlights its potential usage in similar applications. Tests were conducted following ASTM guidelines. Pharmaceuticals leaching tests were conducted to identify the leaching mechanism, and a Kalman filter model used to predict the leaching behavior over a period of five years under weather conditions typical for Beirut, Lebanon. The material proved to have limited leaching over a prolonged period. Based on the data obtained, active pharmaceutical ingredient leaching occurs by diffusion from the plastic matrix. Finally, in addition to the containment of the pharmaceuticals in their solid form, their elimination from solution was also assessed. A novel approach of combining advanced oxidation processes and flash NanoPrecipitation (FNP), a recently developed micromixing technique, was compared against common batch techniques. Carbamazepine and Sulfamethoxazole degradation was evaluated using a chemically activated persulfate system through static mixing and FNP. The results indicate FNP did not provide any advantage over batch mixing, suggesting the process is reaction limited.

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INTRODUCTION

B. Overview on the Pharmaceutical Waste Management

1. Pharmaceutical Waste Disposal

The occurrence of pharmaceuticals in the environment as a result of human use and consumption has now been well established [1,2]. With over 200 pharmaceuticals detected in rivers worldwide, they constitute a class of environmental contaminants of growing concern that are yet to be regulated [3]. Pharmaceuticals can be introduced into the environment by several sources, such as the disposal of unused or expired household medicines, pharmacies, healthcare facilities, drug distributors, and manufacturers Fig 1.1.

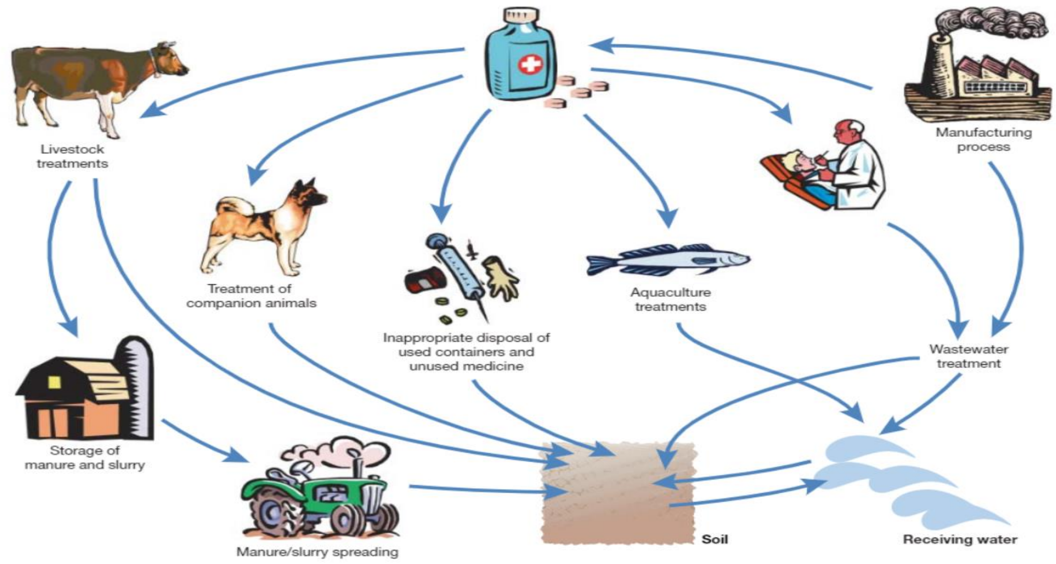

Figure 1.1. Routes of Pharmaceuticals Entry into the Environment [4].

The improper disposal of pharmaceutical waste leads to its presence and detection in wastewater discharges [4]. Frequently used options for disposal include landfilling, incineration, and toilet flushing [4–6].

2. Waste Management Crisis in Lebanon

In Lebanon, waste management remains a challenge. Recently, a municipal solid waste (MSW) management crisis and a shortage in landfills and other waste treatment technologies have left municipal waste on the streets and in random sites for months [7]. A vast portion of the estimated 3,000 to 4,500 tons/year of hazardous solid waste produced in Lebanon [8] is mixed with MSW [9]. For instance, a recent study reveals that the fate of most waste produced in Lebanese dental clinics is landfilling in MSW landfills [10]. Currently, there are no operational, built, under construction, or planned hazardous waste landfills [9]. As a result, about 55% to 60% of generated healthcare waste is treated by a local NGO, while few establishments export their hazardous waste following the Basel convention [8]. Remaining healthcare waste is disposed with MSW, or through uncontrolled and unauthorized incineration [8]. In particular, pharmaceutical waste, which belongs to the special waste category of healthcare waste [8], is accumulating in pharmaceutical distributors' warehouses with no proper disposal option available. The lack of wastewater treatment which could remove a portion of pharmaceutical contaminants and the random hazardous waste disposal practices exacerbate the environmental impact of pharmaceutical waste disposal in Lebanon.

In order to address this issue, this study explores the immobilization of pharmaceutical solid waste using matrix materials composed of recycled polyethylene/polypropylene mixture reclaimed from MSW. In this approach, the pharmaceutical drug products are embedded in mixed recycled plastic material, which immobilizes the active pharmaceutical ingredient (API) in a solid matrix, and limits the extent of its exposure to the environment. The plastic sheets, termed Ecoboard (EB), have been developed by Cedar Environmental, a local company specializing in MSW treatment through a proprietary process. EB are molded into 2 m × 1 m × 13 mm panel boards composed of polyethylene/polypropylene obtained from about 3700 plastic shopping bags and plastic waste material, all of which are reclaimed from MSW. EB finds its uses in construction applications, including green walls and recycling bins.

3. Merits of the Approach

The approach has several advantages on policy and implementation levels;

a. Avoiding Incineration

Cook et al. used the life cycle assessment approach to determine the environmental impact through monitoring API and non-API emissions into air and water. Three pharmaceutical disposal options were considered: incineration after collection, disposal into wastewater and disposal into landfills. Results showed that relative to a disposal baseline of 40% toilet flushing and 60% trash disposal, incineration increases non-API emissions by 200%, ozone depleting agents, global warming, and smog forming compounds by over 1700%, and non-carcinogens, carcinogens, and substances with eutrophication potential by over 700%, thus toilet flushing and incineration will lead to higher environmental impact than trash disposal and landfilling [11]. On the other hand, Gerassimidou and Komilis studied the leaching of hazardous metals from raw expired drugs and from drug ashes following a simulated incineration test. Eight selected hazardous metals were assessed during the leaching potential test using a standardized leaching test (EN 14429). The total release for a liquid to solid ratio of 10/l exceed the limit values for non-hazardous waste, hence creating the need for a hazardous waste landfill according to the established criteria and procedures for the acceptance of waste at landfills published in decision 2003/33/EC. The leaching tests were performed on solid drugs, packaging, ashed drugs, and ashed packaging. After collecting expired drugs and packaging shells, dating over three years, and including the aforementioned categories of hazardous waste, the samples were dried to ensure a constant weight at 70 °C. After drying and measuring the loss on ignition, the samples were grinded and incinerated at 900 °C. After incineration, the ashes obtained were also tested. The initial properties and equilibrium pHs of the samples were identified and leaching tests was performed under various pH values. Acid or base solutions were added to the sample solution to ensure the target pH is met while agitation was performed over 48 hours. The analysis in the flame atomic absorption spectrophotometer (FLAAS) required previous filtration using a vacuum based filtering device (0.45 µm) followed by an acid digestion. Blank tests were performed in order to subtract the obtained metal concentrations from the samples results. Using the method 4-12B provided by the US department of agriculture, the measurement results for eight metals were obtained: Cd, Cr, Cu, Fe, Mn, Ni, Pb, and Zn. As a conclusion for this experiment, the ashed drugs resulted in the highest amount of metals where the concentrations of Cd, Ni, and Pb implied the need for disposing the ashed drugs in a hazardous waste landfill by either building a hazardous waste landfill or upgrading a non-hazardous one. While all other substrates do not require an upgrade to a hazardous waste landfill, the interest lays in the ashed drugs, resulting from the oxidation process in incineration. In Lebanon, the institutional and legal framework of industrial and hazardous waste management remains weakly implemented. Despite the classification of waste based on the Basel convention and the enacting of two major decrees (No. 8471/2012 and No. 8633/2012), the initiation of a well-studied strategy and planning lacks the enforcing of the implementation [9]. Based on these inputs, one can explore the possibilities of avoiding the use of incinerators in pharmaceutical waste.

b. Immobilization of the Waste

Pharmaceutical waste immobilized in a solid matrix result in reduced API entry into the environment through landfilling. In the US patent #5,732,364 invented by Kalb et al., the innovative method of encapsulating the waste using polyethylene is developed [12]. The matrix assembled by combining thermoplastic anhydrous additive, dry waste powder, and non-biodegradable thermoplastic polymer, will form a barrier for waste to leak into the surrounding environment [12]. The process flow of polyethylene encapsulation is based on an extrusion mechanism where waste, binder, and additives pass through a single screw extruder into a heated container with a polyethylene liner.

The cooled down molten homogenous matrix coupled with the anhydrous additives present an advantage over hydraulic cement by allowing a broader variety of waste types and a bigger loading efficiency, where a polyethylene capsule can handle a loading of 60% by weight and maintain a leachability of toxic materials below EPA limits while a percentage of 16% is observed in using a conventional Portland cement [12]. The limitations of conventional cement polymer process, in addition to its low efficiency, extend to the necessity of treating the matrix chemical and thermal curing, which leads to higher operational costs. Both low density polyethylene (LDPE), manufactured at high temperatures, and high density polyethylene (HDPE), manufactured at low temperatures, provide important characteristics for the capsule. HDPE is usually harder to process, present a better advantage concerning the mechanical stress and resistance to external stresses the capsule is subject to. However, the same favorable characteristics can be obtained through LDPE via an easier fabrication process, rendering it a desirable encapsulating agent. Through the use of polyethylene, environmental stresses such as chemical attacks, microbial degradation, photodegradation, cracking are resisted [12]. With such a well-developed patent, encapsulation using recycled materials such as Polyethylene, and especially in Lebanon, stands strongly from a strategic and scientific implementation point of view.

c. An Integrated Solution for Plastic and Pharmaceutical Waste

This approach reduces the environmental impact of plastic and pharmaceutical waste through recycling plastic reclaimed from MSW and immobilizing pharmaceutical waste to limit its entry to the environment. An integrated approach for plastic and pharmaceuticals waste treatment has recently been called for to provide solutions for sustainable environmental management [13].

Both microplastics and macroplastics form an eminent threat to the surrounding ecosystem where the disposal is taking place [14]. Degradation from unmanaged disposal extends beyond the aesthetical features of the habitat and leads to serious threats to fauna via smothering, entanglement and the facilitation of alien species invasion coupled with the absorption of serious toxins [14]. Facing such threat remains a standing challenge, given the current situation of plastics where minimal recycling is observed, since most of the plastics ends up in landfills or incinerators. A sustainable and participatory approach is called for, in order to achieve a closed loop system and an effective strategy concerning the life cycle of plastic [14]. This participatory approach can be achieved through the integrated solution of using the plastic waste to contain pharmaceutical waste.

The creation of such synergy can be optimized through financial enticements or legislative forms and through systems that achieve the required objective. The EB approach can form a viable solution and system that falls into this participatory approach by immobilization of the drug product in the plastic composite board. A functioning example on how such approach can be implemented, through a planned strategy and frame, can be portrayed in China regarding the e-waste strategy. The extended producer responsibility (EPR) system applied imposes regulatory and compulsory laws addressing the complete life cycle of a product. Hence, the manufacturer is not only entailed to produce an output or a product, but to also address its collection, dismantling, and reuse and the end-of-life stage. In five year, china was able to increase the amount of recycled e-waste by a staggering 67 million units per year [14]. The effectiveness of such policy, with relation to the application of EB in Lebanon, sets in the needs assessment implemented by the Chinese government, the analysis of implementation methods, and eventually the operation management through a carefully studied EPR policy. This seemingly top down approach, with an integration of a participatory approach, would provide a baseline from the implementation of an integrated and synergetic solutions for both waste and pharmaceutical waste in Lebanon.

d. Solutions on the National Level

The proposed method addresses an unmet need and provides a potential disposal solution for pharmaceutical waste, which reduces the API's entry into the Lebanese environment, and creates potentially valuable product. Solid waste recycling and treatment for the production of secondary materials is being explored as a novel approach for sustainable development and carbon footprint reduction [15]. Following the zero waste principle, Komnitsas et al. studied the application of a geopolymer technology in relation to green buildings and sustainable cities [15].

The use of waste and by-products to produce geopolymer concrete and construction components falls mainly under the pillar of environmental protection and also addresses the economic and social pillars of sustainable development. Recyclable materials falls under several criteria within the leadership in energy and environmental design (LEED), and especially under the "waste", "productivity and Health", and "emissions" tools [15]. The municipal and construction waste produced can be used in the production of the geopolymeric materials. A very common application of a geopolymeric material is concrete where silicates and aluminate can be identified. Another application of the geopolymer is its use as stabilizer for hazardous waste and capping of waste dumps. Compared to Portland cement, the recipe of a geopolymers, obtained by mixing raw material with alkaline and silicate solutions, leads to a higher 28-day compressive strength of 100 MPa or more [15,16].

In Addition, porosity is minimal, a characteristic common in materials with desirable mechanical properties. Such process and analytical chemistry in geopolymerization address major trends in cement and concrete production. Given that the building sector is the third largest sector emitting CO2 worldwide, and that 85% of these emissions originate from the provision of cement, geopolymerization possess the potential of obtaining a “greener” concrete with estimations ranging between 20% and 80% [16,17]. Through a concept of life cycle assessment and by studying the inputs of raw materials and energy vs. the outputs of emissions to air and water in addition to the solid waste, standard types of geopolymers were found to be less impactful than Portland cement concrete [16]. In the study provided by Weil et al, two geopolymer mix-designs were not only assessed on the basis of CO2 emissions, but also following a life cycle assessment [18]. Three phases were studied: production, utilization, and after use. The phases were linked to use of resources and emissions into air, water, and earth.

Based on the available data and inventory, two geopolymers (MI and SI) were chosen to for their global warming potential and the Abiotic resources depletion. Respectively for the aforementioned indicators, the GWP is obtained as kg CO2 equivalent and ADP as antimony equivalent. By measuring the process scheme and boundary system for the means of production of both geopolymers, both indicators were obtained and found to be less than the emissions induced by the Portland cement concrete. Such results and finding establish a scientific backup for the above mentioned policy and legal framework, enforcing even further its implementation [18].

e. Applicability of the Approach on Other Systems

The use of plastic in immobilization of hazardous waste has been mainly investigated for leftover radioactive materials [12]. Reclaimed plastic waste mixed with radioactive material, hazardous waste, and anhydrous material were extruded together into a monolithic material, preventing environmental damage [12]. Such approach investigates the use of reclaimed plastic, and thus solves the extra problem of plastic waste.

Toledo et.al investigated the use of reclaimed waste material such as rubber from tires, woodchips, and biochar to successfully adsorb high concentrations of highly toxic organic compounds such as VOCs, plasticizers, and PAIs from simulated wastewater [19]. The adsorbent was added simultaneously with bacteria such as *Phanerochaete chrysosporium*, *Acinetobacter sp*, and *Phanerochaete chrysosporium,* in order to eliminate the immobilized hazardous compounds from the wastewater matrix [19].

Hacioglu et.al explored the use of wasted bisphenol-a polycarbonate BPAPC for the embedding of low and intermediate level radioactive waste [20]. BPAPC has an aromatic ring facilitating the embedding process. Mechanical stability of the plastic after exposure to irradiation was examined where a significant decrease in elongation at break and tensile strength was observed [20]. Atomic force microscopy AFM and Scanning Electon Microscopy SEM also showed a significant increase in surface roughness of the polymer upon exposure to irradiation and thus the susceptibility to degradation [20]. Thus, BPAPC waste alone, is a poor candidate for embedding radioactive hazardous waste. Such shortcomings were addressed in a study by Tonguc Ozdemir in which bismuth-III oxide filler is to be added into the radioactive waste drums, converting nuclear radiation into photoelectric effect and protecting bisphenol- a polycarbonate [21]. Monte Carlo simulations showed that the polymer lifespan was enhanced in terms of retention of mechanical properties by the addition of bismuth-III oxide [21].

Two other studies investigated the use of LDPE and Epoxy resins for the containment of evaporator concentrator waste and low-medium level radioactive waste respectively. The LDPE method used extrusion in the same procedure described by Kalb et.al while the epoxy resin method used the polymer as a seal to prevent leaching from the storage drums [12]. The two studies showed the possibility of using new and recycled plastics in the containment of radioactive hazardous waste [22,23].

Pacheco et.al performed the only study available on using recycled Polyethylene Terephthalate (PET) polymer to immobilize incinerator ash. However, the immobilization method used was through extrusion, leading to 1% leaching from the immobilized matrix over a period of 18 hours using the ABNT NBR 10005:2004 standard method [24].

f. Studies on Hazardous Waste Leaching from Concrete

Leaching behavior and mechanism are essential to understand, in order to ensure a predictability of the stabilized waste behavior, whether in a landfill or experimentally [25]. The process of leaching from the stabilized matrix must be assessed before applying modelling and simulation tools. Leaching is the process of the release of soluble waste, through the binding membrane, into the surrounding environment [25]. While dry locations represent the most favorable conditions, groundwater and flow conditions are very prominent in many landfills. Based on these scenarios, Glasser et. al identified two system behaviors: Open system and closed system [26]. The two systems result concurrently in cement of the matrix reacting with cations in groundwater and with materials (organic/inorganic). The reactions induced leading to hydrolysis, oxidizing reactions and decrease of pH (carbonation of cement) amplify the leaching of the matrix [26]. Carbonation and low pH conditions are the major inducer of leaching and porosity conditions in cement [27]. According to Van gerven et.al, carbonation, leaching and porosity are affected interchangeably. By testing two samples of modified cement, one with integrated bottom ash, the other with modified gas cleaning fluids, Van gerven et.al showed that carbonation induced a decrease in pH , leading to leaching, and similarly decrease porosity, inhibiting leaching [27].

Three pores are identified in the cement matrix: gel pores, capillary pores and macropores [28,29]. These pores will form an interface with the waste mixture where the reactions leading to diffusion will occur. Such complexity in reactions require modeling and experimental knowledge to properly assess and predict the behavior. Creep, microcracking and other structural integrity issues form a threat to the permeability of a concrete matrix [30]

In general, leaching is understood and assessed through experimental data since the reactions happening lead to conflicting effects [31]. Leaching tests are classified based on diameter, where powder and granular materials are classified for diameters less than 40 mm, and stabilized waste products for diameters more than 40 mm. Such leach tests can form a baseline for predicting long term behavior of leaching [31].

Muberra et al addressed this concept by performing a modified leach test for municipal solid waste stabilized in Portland cement [32]. Using the Dutch tank leaching method with a bubbled CO_2 to maintain a constant pH, the results of leaching vs time suggested that Fick’s Law for diffusion, normally descriptive of the initial behavior, is not applicable for long term behavior. This supports the complexity of leaching modeling, which suggests going on a case by case application depending on the input factor and time [32].

Sanchez et.al performed such modelling and study for the case of three metals: Arsenic, Cadmium and lead [33]. A dynamic leaching test was performed on cement cubes with continuous and intermittent wetting cycles. These cycles replicate the conditions of saturation and unsaturation found on field. As a result, Sanchez et. al identified the differences in behavior of three metals for pH, and for carbonation. Solubility, release and flux were found to be different for three metals and for the surrounding conditions. Based on these results, Sanchez et.al argued against the use of a simple correction factor for modelling and replicating field behavior of leaching and called for further methodologies [33].

g. Modelling of Leaching of Waste Containment in Literature

The modelling of leaching is required to assess the long-term behavior of a waste repository or capsule. While leaching tests provide insightful behavior data for a relatively limited period of one to two years, the target duration of studying the waste encapsulation system is expected to be projected for over than 1,000 years. According to Yokozeki et.al, the durability of cementitious materials used in waste containment ranges from 1,000 to 10,000 years, depending on the type of solid handled [34].

According to Seveque et.al, the basis of any modeling of leaching should look at migration processes taking place [35]. Elements are transported through diffusion, advection, and as moving colloids. A set of differential equations will establish the interaction with elements and surfaces in the system creates reaction with dissolved systems, precipitation/dissolution reactions and surface reactions. Based on this, the modelling will simulate: Bulk diffusion, solubility limits, and chemical reactions [35]. Through this process, many models can be constructed, then validated through experimental data.

An application of such modelling is presented in the study done by Van der sloot et. al on a waste landfill, in order to form an efficient disposal behavior to reduce emissions. In order to establish such model, Van der sloot et. al used the principle of chemical speciation with the use of speciation reactions integrated with the modelling of ion adsorption on organic matter and aluminum oxide [36]. The adsorption modelling used two established mathematical models, NICA-Donnan model and Dzombak and Morel model. Over a wide pH range (3 to 11), the NICA model allows to obtain the binding of metal to organic matter, while Dzombala and Morel model is used for the case of hydrous ferric oxide HFO [37]. The obtained leached model simulates the leaching of several metals like Al, Fe, Mg, Ca and Pb with respect to the pH. The results, validated by experimental leaching tests, allows for deciding on sound and safe care measures for the waste of the landfill [36].

Seveque et.al explored a similar modelling approach in embedded radioactive waste [35]. The modeling techniques studied the variations of concentration with respect to time, and integrated to obtain eventually a release equation.

$$M(t) = 2\,C_0\sqrt{\frac{De\ \in R\,t}{\pi}}$$

Where C_0 is the initial concentration in mg/l, De is the apparent diffusion coefficient in m^2/s, R is the retardation factor, ε is the porosity, and t is the time in seconds.

Another release equation is obtained for the waste immobilized, with consideration to the chemical reactions undertaken. From these release equations, the waste composition for three types of matrices was obtained and studied for agreement with experimental results.

$$M(t) = 2\,\frac{C_{sol}}{erf\lambda}\sqrt{\frac{De\ \in R\,t}{\pi}}$$

Where C_{sol} is the solubility limit (Ci/m^3 pores), λ is obtained following ERF model.

Though several modelling systems do not show full agreement with experimental results, the use of mathematical techniques remains essential and an area of study to be developed [35].

4. Treatment of Leached Pharmaceuticals: Applying AOPs

The immobilization of pharmaceuticals in a mixed plastic waste composite tackles the problem from the solid waste management perspective; however, leaching will eventually occur due to weathering and other environmental factors [38]. These factors will transfer the APIs into a stream of wastewater that might necessitate treatment [39]. API are, most of the time, organic compounds designed to have high stability and persistence [40]. The high stability poses a challenge to conventional wastewater treatment that relies heavily on biological metabolization by microorganisms [41]. Solutions to concentrate or filtrate the infinitely small molecules such as reverse osmosis and nanofiltration are not recommended due to their high costs and low performance [40]. Advanced oxidation processes (AOPs) are the common practices nowadays to eliminate hazardous organic compounds from an aqueous matrix [42]. AOPs rely on the formation of the highly reactive hydroxyl radical in the medium for the breakdown and possibly mineralization of APIs and thus detoxification of the medium [43]. Persulfate oxidation is an AOP that have been highly studied and reported recently [44]. Persulfate salts are more stable and affordable than other AOP reagents and safer to work with [45]. Ghauch et al. conducted several studies on persulfate oxidation of APIs in which the process was optimized for each API [46–48]. The common laboratory procedure for testing AOP is through mixing the oxidant into a batch reactor containing the polluted wastewater. Such a process is different from reality in which a flow of wastewater is continuously dosed with the oxidant [49].

In this project, we aim to provide enhanced kinetics and conversion through intense mixing using a bench-scale multi inlet vortex mixer MIVM.

5. Model Organic Pharmaceutical Compound

The model pharmaceutical used in this study is diclofenac (DF), a widely used anti-inflammatory drug [53,54]. Its occurrence in the environment has been well established [55,56]. The European Commission currently lists DF as a priority hazardous substance [3], and is among the pharmaceuticals placed on a watch list for monitoring and risk assessment purposes [57]. In addition to its relevance as a major environmental contaminant, DF has a relatively high decomposition temperature [58,59], and a degradation profile following first-order kinetics [60], which makes it a suitable candidate for the leaching studies explored in this work.

6. Research Objectives

This project focuses primarily on limiting the introduction of pharmaceuticals in the solid form into the environment. Additionally, the project explores potential methods for the treatment of pharmaceuticals in water through AOPs. The work presented in this thesis provides proof of concept for assessing matrix materials' ability to immobilize solid hazardous waste. In this study, a model pharmaceutical is immobilized in plastic material reclaimed from MSW, and the leaching of the pharmaceutical from the plastic matrix is assessed experimentally and through simulation, which is conducted in collaboration with Dr. George Saad and Mr. Wael Slika, Civil and Environmental Engineering department, American University of Beirut, Lebanon. This approach can be used and expanded to other pharmaceuticals and other matrix materials. Based on reviewing the literature, no studies have explored such an approach as an alternative to incineration or other techniques from treating pharmaceutical waste.

The recommended method by WHO for the treatment of expired pharmaceuticals is high temperature incineration on which no recent cost estimation is present in the literature and the main reference is a document published by who in 1999 stating:

”*The cost of waste pharmaceutical high temperature incineration: Pharmaceuticals are ideally disposed of by high temperature (i.e. above 1,200ºC) incineration. Such incineration facilities, equipped with adequate emission control, are mainly to be found in the industrialized world. Quotations for disposing of the pharmaceutical waste in Croatia and Bosnia and Herzegovina in this way range from US$2.2/kg to US$4.1/kg. To incinerate the current stockpile of waste pharmaceuticals in Croatia would therefore cost between US$4.4 million and US$8.2 million. Quoted weights of pharmaceutical waste. The gross weights mentioned previously include packaging. Actual pharmaceutical contents may be half, or less than half, of the gross weight.*” [61,62]

Such costs are subjected to inflation and increased oil prices over the years. In Lebanon no proper pharmaceuticals waste management plan exists, with expired pharmaceuticals stockpiling in distributers warehouses or disposed by citizens to landfills and open dumps through the municipal solid waste streams. Based on the above, the research objectives are:

- Experimentally determine the leaching behavior of diclofenac, a model pharmaceutical compound, from a matrix of polyethylene/polypropylene reclaimed from MSW, and identify the mechanism of leaching.
- Determine the effect of immobilizing pharmaceutical drug products on the reclaimed plastic material’s mechanical properties.
- Identify and conduct simulation work to predict the behavior of diclofenac leaching from the plastic matrix under environmental conditions typical of Beirut, Lebanon.
- Explore the treatment of pharmaceuticals in water using Flash NanoPrecipitation (FNP), a fast mixing technique to afford degradation of the pharmaceuticals using AOPs.

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CHAPTER II

MECHANICAL PROPERTIES OF RECYCLED POLYETHYLENE/POLYPROPYLENE MATERIAL WITH EMBEDDED PHARMACEUTICAL WASTE

Investigating several approaches and practices that optimize the life cycle of any material under study, is an increasing trend in the solid waste management context and falls under the notion of sustainable material usage. The optimization of the life cycle of a waste material is studied in this chapter where recycled polyethylene/polypropylene, contains and immobilizes a common pharmaceutical waste found in Lebanon, Diclofenac. The mechanical properties of the obtained material, combined with the leaching behavior, will guide its final use. As a result, determining the mechanical properties of the material, is the first step to assess the suitability of this approach. Such identification is essential in justifying the applicability, suitability, and safety of the material obtained. The engineering properties identified are tensile, compressive, and flexural strength, along with the water absorption properties. The performance of these tests, and following the American Society for testing and materials (ASTM) international standard tests, allows to characterize the material using experimental setups and to compare the properties with benchmark materials currently in use in construction

A. Introduction

In a developing world context, solid waste management has been a challenge, particularly in a country like Lebanon where the absence of an integrated sustainable waste management approach has led to an ongoing waste crisis. Unsustainable controlled dumping has become the dominant emergency approach in such conditions. Lebanon generates around 0.95 kg/capita/day of municipal solid waste, which includes 50% organic waste and 40% recyclables [1]. However, the recycling rate is estimated at a mere 8% [2], which are comparable to some nearby developing countries such as Jordan and Morocco at 10%, and higher than others such as Palestine, Egypt and Syria at 2%, 2.5% and 3% respectively [3].

Within the multitude of recyclable components in municipal solid waste, plastic is one of the most versatile materials commonly used in the manufacturing of a wide variety of products. However, plastic waste management is a challenging issue, since the disposal methods adopted for organic waste are undesirable for plastic due to its low degradability rate [4,5].

Accordingly, recycling discarded plastics and turning them into durable materials not only decreases their impact on the natural environment but also provides a variety of secondary use products [6]. In this context, recycled sheets, termed Ecoboard (EB), made out of HDPE and LDPE plastic, are an interesting alternative to natural wood sheets in construction and industrial activities. Such material has the potential of adding an extra value to the final stage of the life cycle of plastics, by reducing the overall carbon and environmental footprint in the plastic's life cycle assessment (LCA) and shifting towards a cradle-to-cradle, rather than a cradle-to-grave, approach in theory [6,7].

Ecoboard are highly resistant compressed panels made of recycled plastic waste (Primarily HDPE, LDPE and other plastic material reclaimed from municipal waste), and their value is two-fold: reducing the extent of the waste crisis by diverting the aforementioned plastic recyclables away from landfills/dumps, as well as decreasing the use of wood, a resource with a high ecological footprint, in domestic and industrial applications [8,9].

Therefore, this paper aims to assess the mechanical properties of Ecoboard (tension, compression, bending, and absorption) in order to evaluate their potential suitability in construction application and compare them to those of existing construction materials.

B. Materials and Methods

Mechanical properties including tension, compression, and bending, as well as water absorption were tested according to ASTM standards, providing an international framework for certification and trading [10]. This section details the materials and methods utilized to achieve the study’s objectives.

Raw Materials

Ecoboard material (Figure 2.1) was obtained from CedarEnvironmental SARL and made using their proprietary technique as compressed recycled plastic waste panels, composed mainly of Low- and High-Density Polyethylene (LDPE and HDPE), in addition to other mixed plastics including Polyvinyl chloride (PVC), Polyethylene terephthalate (PET) and Polystyrene (PS). The plastic mixture is pressed under high temperature to form two different versions of the Ecoboard with the composition shown in Table 2.1 below:

Table 2.1. EcoBoard Composition.

Eco-Board version	**%LDPE**	**%HDPE**	**%Mixed plastics**	**Thickness (mm)**
Light board	65	10	25	12.5~15
Heavy board	75	20	5	8~10

Figure 2.1. EcoBoard.

2. Equipment

The equipment used in this study include a Computer Numerical Control router (Haas VF-6) to cut the boards in to the desired dimensions, a universal testing machine (Hounsfield H100KS) to conduct the mechanical properties assessment (tensile, compressive and flexural), as well as a universal drying oven (Labtech LDO-060E), a water bath (Daihan WSB-30) and an analytical balance (Radwag AS 220.R2) to measure the Eco-Board specimens’ weight during the absorption test.

3. Methods

To assess the mechanical properties of the EB, ASTM international standard test methods for plastics were adopted, as detailed in Table 2.2.

Table 2.2. Standard Test Method Adopted to Assess the Mechanical Properties.

Mechanical Property	Standard	Description
Tensile strength	ASTM D638	Standard Test Method for Tensile Properties of Plastics
Compressive strength	ASTM D695	Standard Test Method for Compressive Properties of Rigid Plastics
Flexural strength	ASTM D790	Standard Test Methods for Flexural Properties of Unreinforced and Reinforced Plastics and Electrical Insulating Materials
Water absorption*	ASTM D570	Standard Test Method for Water Absorption of Plastics
*Physical property: conducted using distilled water at room temperature and at 50°C		

The Eco-Boards were first cut into the desired dimensions (table 2.3), depending on the mechanical property being tested and the Ecoboard type (light vs heavy). The tensile strength test was conducted on four samples while the compressive and flexural strength tests used 5 samples. On the other hand, three samples were used in the water absorption test. The dimensions of the specimens according to the type of test are detailed in the table below.

Table 2.3. Eco-Board Specimen Dimensions for Each Test.

Test type	Eco-Board version	Length (mm)	Width (mm)	Thickness (mm)
Tensile strength	Light	246	12.7	12.7
	Heavy	246	8	8
Compressive strength	Light	50.8	12.7	12.7
	Heavy	33	8	8
Flexural strength	Light	200	50	12.5
	Heavy	136	13.5	8.5
Water absorption	Light	76.2	25.4	12.7
	Heavy	76.2	25.4	8

D. Results

The results of the tests to determine the mechanical properties (tension, compression, flexural) and water absorption characteristics of the Eco-Boards are detailed below. Overall, the heavy version of the Eco-Board displayed superior mechanical properties and water absorption characteristics as compared to the light version.

1. Tension

The tensile strength [11] (figure 2.2) result values of the Eco-Board specimens are detailed in Table 2.4. It could be observed that the heavy version of the boards performs better than the light version in terms of Mean tensile strength, by around 70% increase

Figure 2.2. Tensile Strength.

Table 2.4. Results of the Tension Tests Based on ASTM D638.

Specimen Identification	Light Plastic	Heavy Plastic
Mean Tensile Strength, MPa	2.90±0.23	4.92±2.20
Mean Offset Yield Strength, MPa	2.33±0.09	4.19±1.22
Mean Percent Elongation at Yield (%)	0.51±0.04	1.11±0.78
Mean Percent Elongation at Break (%)	1.45±0.08	5.71±2.68
Mean Nominal Strain at Break	1.45±0.08	5.71±2.68
Mean Modulus of Elasticity, MPa	175±10	103±37
Mean Secant Modulus, MPa	94.2±7.60	75±19

2. Compression

The compressive strength [12] (Figure 2.3) result values of the EB specimens are detailed in Table 2.5. Similar to the tensile strength results, the heavy Eco-Boards had a 71% higher mean compressive strength value.

Figure 2.3. Compression Test.

Table 2.5. Results of the Compression Tests Based on ASTM D695.

Specimen Identification	Light Plastic	Heavy Plastic
Mean Compressive Strength, MPa	4.55±1.24	7.78±0.81
Mean Compressive Yield Strength, MPa	3.29±1.06	5.18±0.67
Mean Offset Yield Strength, MPa	4.54±1.24	7.07±0.94
Mean Modulus of Elasticity, MPa	208±21.4	200±42.4

3. Flexural

The flexural strength [13] result (figure 2.4) values of the Eco-Board specimens are detailed Table 2.6. In terms of flexural strength, the Heavy Eco-board had a higher strength than the light version, compared to the other properties, with a 243% increase in value.

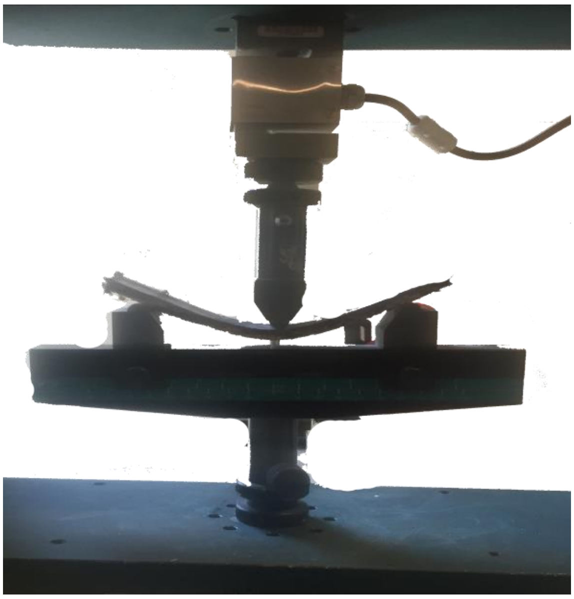

Figure 2.4. Flexural Strength.

Table 2.6. Results of the Flexural Tests Based on ASTM D695.

Specimen Identification	Light Plastic	Heavy Plastic
Mean Flexural Strength, MPa	6.64±0.64	22.8±8.31
Mean Flexural Stress at Break, MPa	5.35±0.90	21.1±6.67
Mean Flexural Offset Yield Strength, MPa	6.61±0.66	22.76±8.36
Mean Flexural Strength at Max Def.	0.05±0.01	0.08±0.00
Mean Modulus of Elasticity, MPa	517±114.1	1068±494.1
Mean Secant Modulus of Elasticity, MPa	215±56.9	475±224.9
Mean Chord Modulus of Elasticity, MPa	152±46.2	321±124.2

4. Water absorption

The water absorption [14] result values of the Eco-Board specimens are detailed in Table 2.7. The test was stopped after 5 weeks of immersion, as the average weight increase in a 2-week period became less than 1%. In this test, the heavy version of the Eco-Board absorbed less water, at varying percentages depending on the immersion period. Overall during the water absorption test, the light version increased by around 9.83% while the heavy version increased by 5.83%.

Table 2.7. Results of the Water Absorption Tests Based on ASTM D570.

Time	**Average weight, g**	
	Light Plastic	**Heavy Plastic**
Initial, before conditioning	21.98	15.61
Initial, after conditioning 24h-50°C	21.76	15.43
After immersion, 24h-23°C	23.30	15.92
Increase in weight, %	7.100	3.132
After immersion, 1 week-23°C	24.57	16.07
Increase in weight, %	12.93	4.105
After immersion, 3 week-23°C	25.45	16.25
Increase in weight*, %	3.590	1.150
After immersion, 5 week-23°C	25.62	16.33
Increase in weight*, %	0.660	0.492
Overall weight increase**, %	9.835	5.833
*Weight increase in the last 2 weeks ** Weight increase compared to initial state, after conditioning		

5. Discussion of Results

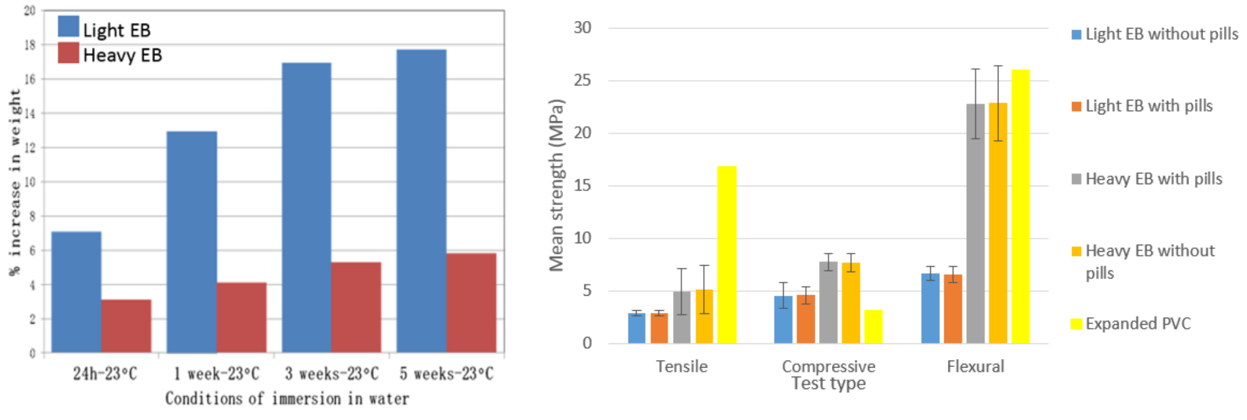

Figure 2.5. Summary of test results for light and heavy EB vs expanded PVC [15]

The obtained results presented in figure 2.5 show that the heavy EB has superior water absorption resistance to that of the light EB. After 5 weeks of immersion at t= 23 °C the heavy EB had a maximum weight gain of approximately 6% while the Light EB had triple that value at approximately 18%. This shows that only heavy EB is suitable for usage in locations partially exposed to water. On the other hand, both light and heavy EB presented superior compressive strength to that of expanded PVC, this is possibly due to the stratification of plastic inside the EB. However, this was not the case for tensile strength: expanded PVC showed improved performance. As for flexural strength, only heavy EB exhibited properties that are comparable to that of expanded PVC with the light EB falling behind. It is worth noting that the addition of diclofenac pills at a load of 2.4 mg/cm^3 didn't affect the mechanical properties of the EB as it is shown if figure 2.5. It is recommended to install the heavy EB in situations with high physical stress and vice versa. Examples of calculations of the obtained values from metadata are found in Annex I.

E. Conclusion

Ecoboard, a highly resistant compressed panels made of recycled plastic waste (Primarily HDPE, LDPE and other plastic material reclaimed from municipal waste), has good mechanical properties (tension, compression, bending, and water absorption) which are not affected significantly when expired pharmaceutical products are embedded in the Ecoboard matrix.

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G. Annex I

This annex provides sample calculations and analysis of the data obtained from the aforementioned ASTM tests performed on the EcoBoad.

Compression Test: ASTM D695

Table 2.8. Compression Test Specimen Data.

Test	Compression
Tested According to	ASTM D695
Specimen No.	5- Heavy Plastic
Specimen Dimensions	
Breadth (mm)	8
Width (mm)	8
Length (mm)	33
Area of Specimen (mm^2)	64.0

Table 2.9. Excerpt from Recorded Data During Test.

L, mm	Force, N	Stress, MPa	Strain	Corrected Strain
0	0	0.000	0.00000	-0.03600
0.004	0	0.000	0.00012	-0.03588
0.008	0	0.000	0.00024	-0.03576
0.012	0	0.000	0.00036	-0.03564
0.016	0	0.000	0.00048	-0.03552
0.02	0	0.000	0.00061	-0.03539
0.024	0.5	0.008	0.00073	-0.03527
0.028	0.5	0.008	0.00085	-0.03515
0.032	0.5	0.008	0.00097	-0.03503
0.036	0.5	0.008	0.00109	-0.03491
0.04	0.5	0.008	0.00121	-0.03479
0.044	0.5	0.008	0.00133	-0.03467
0.048	0.5	0.008	0.00145	-0.03455
0.052	0.5	0.008	0.00158	-0.03442
0.056	0.5	0.008	0.00170	-0.03430
0.06	0.5	0.008	0.00182	-0.03418
0.064	0.5	0.008	0.00194	-0.03406
0.068	0.5	0.008	0.00206	-0.03394

Based on the recorded data, the stress vs strain curve is plotted, allowing the extraction of the parameters presented in our study. The analysis of the stress-strain curve results in the parameters of the compressive strength, compressive Yield strength, offset stress and offset strain, and modulus of Elasticity.

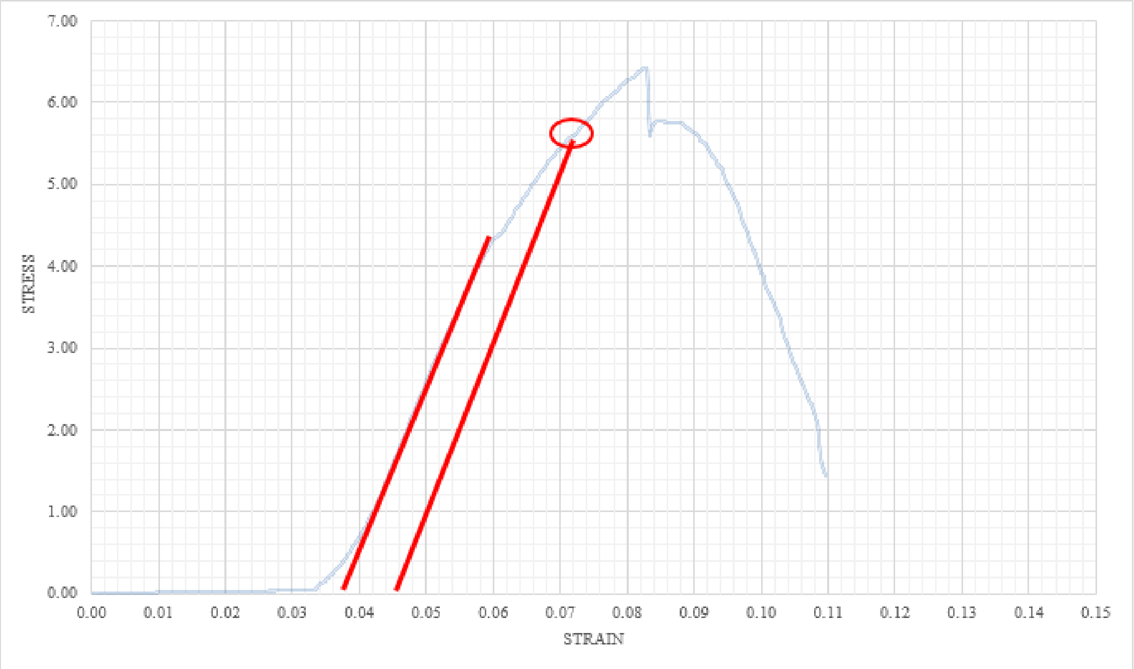

Figure 2.6. Stress-Strain Curve for Compressive Test.

Table 2.10. Obtained Parameters from the Stress-Strain Curve.

Max Load, N	411.5	(Maximum Force in Newton)
Compressive Strength (MPa)	6.43	(Maximum Force / Area)
Compressive Yield Strength (MPa)	4.36	(Stress at Elastic Limit)
Offset Strain, mm	0.007	0.02% of Lo = (0.02 x Lo / 100)
Offset Yield Strength (MPa)	5.59	(Stress: intersection between offset tangent and stress-strain curve)
Modulus of Elasticity (MPa)	190	(Slope of tangent to stress-strain curve at elastic zone)

Flexural Strength Test: ASTM D790

Table 2.11. Flexural Test Specimen Data.

Test	Flexural
Tested According to	ASTM D790
Specimen No.	5- Heavy Plastic
Specimen Dimensions	
Thickness (mm)	8.5
Width (mm)	13.5
Length (mm)	136

Table 2.12. Excerpt of Data from Flexural Test.

Elongation (mm)	**Force (N)**	**Flexural Stress (MPa)**	**Flexural Strain**	**Strain after Toe Compensation (mm)**
0	0.4	0.084	0.000	0.000000
0.04	0.8	0.167	0.000	0.000110
0.08	2.8	0.586	0.000	0.000221
0.12	3.6	0.753	0.000	0.000331
0.16	4.8	1.004	0.000	0.000441
0.2	5.2	1.088	0.001	0.000551
0.24	6.8	1.422	0.001	0.000662
0.28	7.2	1.506	0.001	0.000772
0.32	8.8	1.841	0.001	0.000882
0.36	9.2	1.924	0.001	0.000993
0.4	10.4	2.175	0.001	0.001103
0.44	10.8	2.259	0.001	0.001213
0.48	12	2.510	0.001	0.001324
0.52	12.4	2.593	0.001	0.001434
0.56	13.2	2.761	0.002	0.001544
0.6	14	2.928	0.002	0.001654
0.64	14.8	3.095	0.002	0.001765
0.68	15.2	3.179	0.002	0.001875
0.72	16	3.346	0.002	0.001985
0.76	16.4	3.430	0.002	0.002096
0.8	17.2	3.597	0.002	0.002206
0.84	18	3.765	0.002	0.002316
0.88	19.2	4.016	0.002	0.002426

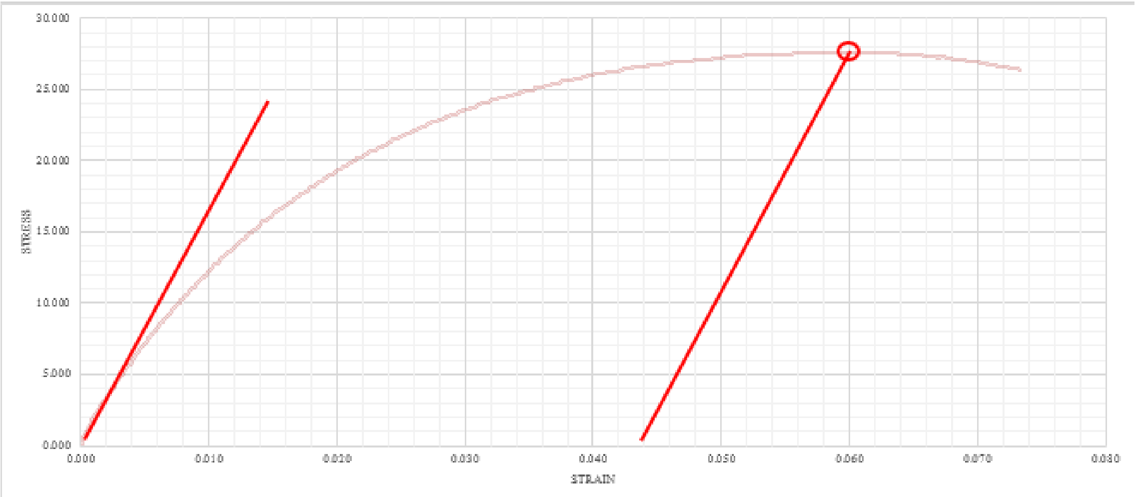

Figure 2.7. Stress-Strain Curve.

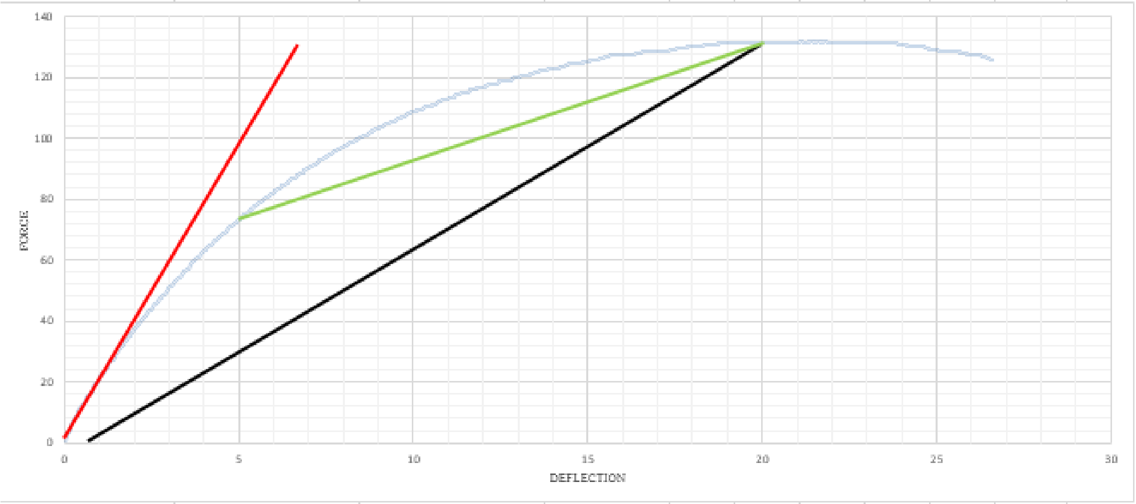

Figure 2.8. Force-Deflection Curve.

Based on the analysis of the graphs, the following parameters and engineering properties can be deduced:

Table 2.13. Engineering Properties Obtained from the Flexural Test.

Toe Compensation	0	(Stress-Strain Curve)
Offset Strain (mm)	0.0440	Line parallel to the tangent to stress-strain curve at elastic zone
Flexural Strength (MPa)	27.61	Max Flexural Strength
Flexural Offset Yield Strength (MPa)	27.6	Intersection between the parallel to the tangent to stress-strain curve and the graph
Flexural Stress at Break (MPa)	26.35	Flexural stress at break
Flexural Strain at max. deflection	0.073	
Modulus of Elasticity (MPa)	1517	(Slope of Tangent to stress-strain curve at elastic zone)
Secant Modulus (MPa)	493	(Slope of line connecting zero stress to any specific point on stress-strain curve)
Chord Modulus (MPa)	293	Stress/strain for two random points

Tension Test: ASTM D638

Table 2.14. Tension Test Specimen Data Sheet.

Test	Tension
Tested According to	ASTM D638
Specimen No.	4- Heavy Plastic
Specimen Dimensions	
Thickness (mm)	7.5
Width (mm)	20
Specimen Length, L (mm)	246
Gage Length, G (mm)	50
Gage Length, G% (%)	20%
Grip Separation Length, D (mm)	115
Grip Separation Length, D% (%)	47%
Area of Specimen (mm2)	150

Table 2.15. Excerpt from Tension Test Data.

Elongation (mm)	Force (N)	Stress (Pa)	Strain	Strain after Toe Compensation (mm)	Percent Elongation	Nominal Strain%
0.01	2	13333	0.000	0.000200	0.004%	0.004%
0.02	6	40000	0.0004	0.000400	0.008%	0.008%
0.03	10	66667	0.0006	0.000600	0.012%	0.012%
0.04	15	100000	0.0008	0.000800	0.016%	0.016%
0.05	19	126667	0.0010	0.001000	0.020%	0.020%
0.06	24	160000	0.0012	0.001200	0.024%	0.024%
0.07	28	186667	0.0014	0.001400	0.028%	0.028%
0.08	33	220000	0.002	0.001600	0.033%	0.033%
0.09	37	246667	0.002	0.001800	0.037%	0.037%
0.1	41	273333	0.002	0.002000	0.041%	0.041%
0.11	45	300000	0.002	0.002200	0.045%	0.045%
0.12	49	326667	0.002	0.002400	0.049%	0.049%
0.13	53	353333	0.003	0.002600	0.053%	0.053%
0.14	57	380000	0.003	0.002800	0.057%	0.057%
0.15	60	400000	0.003	0.003000	0.061%	0.061%

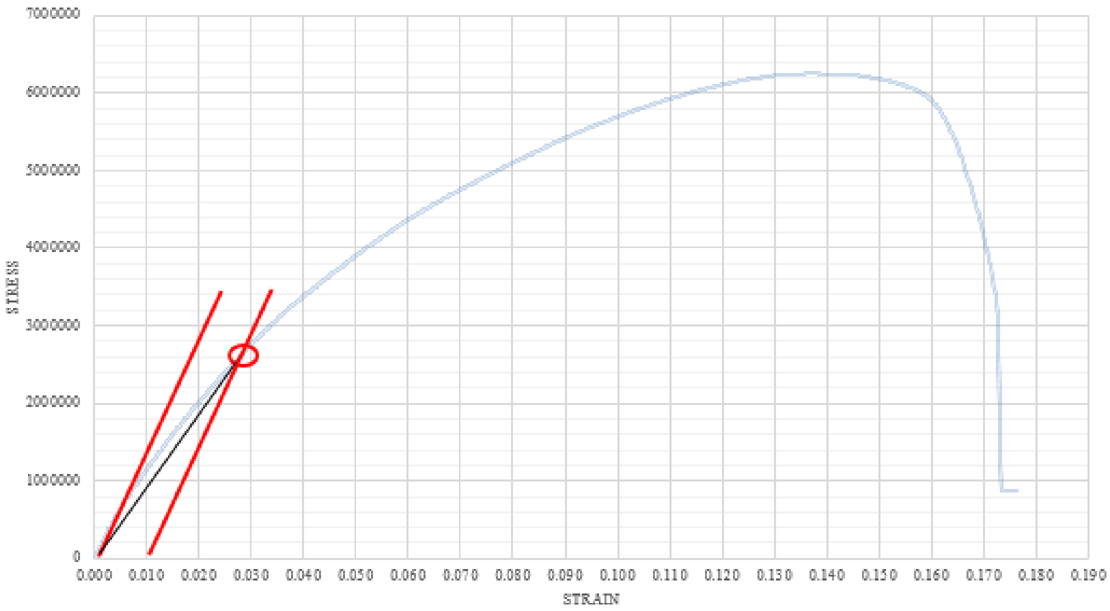

Figure 2.9. Stress Strain Curve Obtained from Tension Test.

Table 2.16. Calculations Based Tensile Test Data.

Toe Compensation	0	(Stress-Strain Curve)
Offset Strain (mm)	0.01	0.02% Gage Length = (0.02 x G /100)
Offset Yield Strength (Pa)	4906667	(Stress at Elastic Limit)
Tensile Strength (Pa)	6253333	(Max Stress / Area)
Percent Elongation at Yield (%)		1.51%
Percent Elongation break (%)		3.59%
Nominal Strain at Break (%)	3.59%	
Modulus of Elasticity (Pa)	140000000	(Slope of Tangent to stress-strain curve at elastic zone)
Secant Modulus (Pa)	92643678	(Slope of line connecting zero stress to any specific point on stress-strain curve)

CHAPTER III

LEACHING MODEL

The in-depth assessment of the created matrix requires, in addition to the characterization of the mechanical properties, a study of the leaching behavior presented by the stabilized waste. This analysis will establish, following an experimental setup, the suitability of the leaching behavior with respect to the intended use of the EcoBoard. Based on this, a leaching model shall be established to estimate and analyze the studied behavior. Following the mathematical theories of diffusion and the empirical data presented, the leach test shall present the amount of organic pharmaceutical compound leached following several experimental conditions. The compound shall be studied in two cases; in form of powder and in form of pills. Looking into factors like shape, temperature, and initial distribution of the stabilized compound, will help furthermore in characterizing optimal conditions for the waste matrix created. The studied conditions can be related to the conditions present in the intended use of the EcoBoard and will furthermore present a potential data reference for justifying the use of the EcoBoard stabilizing pharmaceutical waste.

A. Introduction

Recently, there has been a growing interest in identifying suitable routes for the disposal of pharmaceutical waste [1,2]. This study investigates the potential of matrix materials composed of recycled polyethylene/polypropylene reclaimed from municipal solid waste at immobilizing pharmaceutical solid waste. Diclofenac (DF) drug product was embedded in boards of recycled plastic material and leaching in water was assessed at various temperatures.

B. Model Organic Pharmaceutical Compound

The model pharmaceutical used in this study is diclofenac (DF), a widely used anti-inflammatory drug [3]. Its occurrence in the environment has been well established [1,4]. The European Commission currently lists DF as a priority hazardous substance, [5] and is among the pharmaceuticals placed on a watch list for monitoring and risk assessment purposes [6]. In addition to its relevance as a major environmental contaminant, DF has a relatively high decomposition temperature [7,8], and a degradation profile following first-order kinetics [9], which makes it a suitable candidate for the leaching studies conditions explored in this work.

Additionally, DF has been identified as a priority contaminant in an environmental risk analysis of pharmaceuticals used in Lebanon [10]. The objective of this study is to quantify the amounts of DF leaching from a monolithic material form in water at various temperatures and determine the value of the diffusion coefficient by means of sequential data assimilation using experimentally acquired data. Short-term data is used to validate/calibrate the numerical model that will be used for predicting the DF leaching behavior.

C. Materials and Methods

1. Sample Preparation

DF drug product pills (Rofenac 100 mg diclofenac sodium, Spimaco, Saudi Arabia) were crushed using a pestle in a mortar and the powder dispersed into raw plastic material consisting of 85% PE, 15% PP waste material by weight reclaimed from municipal waste, which is molded into ~1.3 cm thick sheets termed Ecoboard (EB) using a proprietary process developed by Cedar Environmental, Lebanon. The product is a monolithic material composed of the processed plastic in which the drug product powder pharmaceutical waste is embedded at a DF loading of 2.4 mg/cm^3. Additionally, DF drug product pills were dispersed without prior crushing into EB raw materials and processed identically to the powder samples. Samples were cut into 6 cm × 6 cm and the transversal sides taped using aluminum tape. This ensures leaching occurs only through the top and bottom square faces and allows for the process to be modeled as one-dimensional leaching from a solid. The produced EB specimens containing DF in the powder or pill form were used for the leaching test.

2. Leach Test

Leaching of DF from EB specimens was assessed via a static leach test. Samples were contacted with de-ionized water at a leachant volume to specimen exposed surface area (L/S) of 5 cm. A low L/S ratio (5 cm) was selected to increase the DF concentration in solution for enhanced detection with negligible chemical gradient changes between the solid and solution. At the beginning of a testing interval, each EB specimen is introduced into a beaker with water at an L/S of 5 cm. The beaker size was selected to ensure complete water contact of the specimen leaching area and was closed using aluminum foil to prevent water evaporation during testing. For accelerated temperature conditions, the water and beaker are preheated to the test condition before introducing the test sample. Temperature was maintained by placing samples in an oven. In initial leaching tests, samples were exposed at 20 °C, 50 °C, and 70 °C for a duration of 10 days for powder material and 11 days for embedded pills.

Additionally, extended testing periods at 20 °C and 70 °C were conducted to gain insight into the extent of leaching over prolonged periods. Samples of 1 mL were collected at the specified time interval and the equivalent amount of water was added to the test solution to maintain the identical leachant volume. Collected samples were stored under refrigerated conditions until analyzed. The results represent an average of three tests. Leaching under various pH conditions was not evaluated since the stability profile of the organic compound tested is sensitive to pH and will prevent monitoring of DF leached over time due to degradation.

Based on initial experimental findings from a semi-dynamic leach test, the DF release was minimal compared with the total mass in the waste form. As a result, the leachant solution in subsequent testing was not replenished at regular intervals as in semi-dynamic leach tests conducted to evaluate leaching of inorganic contaminants from solidified waste [11].

The leaching levels were significantly lower than the solubility limit of DF at the temperature and pH conditions of the test [12,13]. For instance, at a pH value of 6.2 and room temperature, DF solubility was >1400 ppm, while the amount leached was <2 ppm. Therefore, the low accumulated levels of DF in the leachant have a minimal effect on the concentration gradient and subsequently the diffusion process.

3. Sample Analysis

The concentration of DF in solution was determined using HPLC (Agilent 1100 Series), equipped with a quaternary pump, ALS auto sampler, diode array detector (DAD) and supported by an analytical work station (LC solutions chromatographic software) (Agilent Technologies, California USA). The chromatographic separation method was based on the method by Ghauch et al.[14] and was achieved on an reversed phase column (Discovery C18, 5 µm, 25 cm × 4.6 mm ID) connected to a security guard column (Discovery HS C18, 5 µm, 2 cm × 4.0 mm ID),both sourced from Supelco, Bellefonte, Pennsylvania, USA. The HPLC method consists of an isocratic elution using methanol (Riedel de Haen, Germany)/0.1% formic acid in water (80/20, v/v), at a flow rate of 0.9 mL/min. The injection volume was 25 µl, the column temperature was set to 30°C, and DF (Sigma, USA) was detected at a wavelength of 276 nm with a retention time of 8.0 min. The limit of detection (LOD) defined as a signal to noise ratio of three was 0.5 ppm, and the limit of quantification (LOQ) defined as a signal to noise ratio of 10 was 2 ppm.

4. Diffusion Leaching

Leaching of solid species in saturated media is usually attributed to three processes: Diffusion, dissolution and wash-off. Depending on the binding medium, the characteristics of the species and their location with respect to the surface one or more mechanism might govern the mass transport of the species. In theory, the governing mechanism could be assessed experimentally by monitoring the cumulative mass released per surface area B_t (mg/m^2) versus contact time t (s). In the case of leaching by diffusion, the following equation holds [15]:

$$\log \mathrm{B_t} = \frac{1}{2}\log(\mathrm{t}) + \log(\mathrm{U_{max}}\, \mathrm{d}\left(\sqrt{\frac{\mathrm{D_e}}{\pi}}\right)) \qquad (1)$$

Where De (m^2/s) is the effective diffusion coefficient, U_{max} (mg/kg) is the maximum leachable quantity, and d (kg/m^3) is the bulk density of the product.

The dominant mechanism is determined by the slope of B_t versus t, which determines the primary leaching mechanism [16]. A slope value close to one indicates dissolution, a value close to 0.5 indicates diffusion, and a value near zero indicates leaching through wash-off. Therefore, an experimental slope value close to 0.5 is needed for accurate modeling of the leaching process by diffusion.

Diffusion is typically simulated using Fick's second law. In the performed experiment, the species can be transported only in one direction, thus the 1-D Fick's second law is adequate to represent the experimental setup:

$$\frac{\partial \mathrm{C}(\mathrm{x},\mathrm{t})}{\partial \mathrm{t}} = \mathrm{D_e} \frac{\partial}{\partial \mathrm{x}} \left(\frac{\partial \mathrm{C}(\mathrm{x},\mathrm{t})}{\partial \mathrm{x}} \right) \tag{2}$$

Where $C(x, t)$ (kg/cm^3) is the concentration of DF at location x (cm) for the period t (s). D_e (cm^2/s) is the effective diffusion coefficient at time t and is assumed constant.

Effective diffusion coefficient is used due to DF mass transfer limitations in the drug product powder dispersed in the solid matrix leading to a decrease in the fraction of DF available for diffusion through the porous medium. Both analytical and numerical solutions for the diffusion equation are found in the literature. The simplest analytical solution is referred to as the Crank solution [17]. It is based on a semi-infinite dimension assumption with constant diffusivity and a constant solute concentration at the surface:

$$\frac{\mathrm{C}(\mathrm{x},\mathrm{t}) - \mathrm{C_1}}{\mathrm{C_0} - \mathrm{C_1}} = \mathrm{erf}\left(\frac{\mathrm{x}}{2\sqrt{\mathrm{D_e t}}} \right) \tag{3}$$

Where C_0 (mg⁄cm3) and C_1 (mg⁄cm3) are the surface constant concentration and initial concentration respectively, and x (cm) is the distance away from the surface.

The above solution loses its accuracy when the cumulative fraction leached is greater than 0.2 [15]. Moreover, it lacks the capability of accounting for initial spatial variability inside the solid matrix. Therefore, for robust and accurate representation of the leaching mechanism, the general differential equation is used to simulate the solution using a finite elements/ finite difference (central difference) numerical discretization scheme. Therefore, to simulate the forward problem several modeling assumptions were adopted: First, the boundary nodes are set to zero after each time integration, to simulate the leaching of the material to the external solution, and without violating the conservation of total mass in the system.

Secondly, the available leachable DF, which is determined using extended testing, is assumed to be uniformly distributed along a certain length of the sample's depth.

Third, based on sensitivity analysis for an efficient and accurate numerical solution of the general diffusion equation, the mesh size was set to be 0.5 mm in space and 0.01 days in time. Moreover, quadratic shape functions were employed for the interpolation of DF concentrations between nodes. The leaching mass transport, in the adopted scheme, is based on differential concentration gradient in an assumed fully saturated medium.

Using this approach, the diffusion coefficient is calculated based on experimentally acquired measurements, which requires the solution of an inverse problem. Such solution is not readily available as the forward one, especially with the presence of several sources of uncertainties and noises. However, by the incorporation of experimental measurements with sequential data filtering techniques the solution of the inverse problem can be accurately approximated by iterative solutions of the forward problem. Therefore, *De* is estimated to minimize the mismatch between the forward simulated model and the measured quantities in a probabilistic framework.

5. Uncertainty and Inverse Problem

In the experimental setup, the diffusion rate is determined using indirect monitoring of the leached quantity. Consequently, several uncertainties should be quantified and incorporated in the inverse modeling to find an optimal and representative solution of De. Such uncertainties include spatial variability in the depth of the board, uncertainty in the fraction of available initial concentration for leaching due to DF internal diffusional resistances, uncertainty in the DF distribution across the board due to the manufacturing process, and simplification errors in model formulation and measurement errors in estimating the amount of DF in solution. In this setting, the Bayesian approach to inverse problems has become popular for inference and identification of system parameters when uncertain measurements are available. However, in practice, the posterior behavior, based on prior knowledge and measurements is challenging to compute and convergence is not guaranteed.

Consequently, a close form robust solution, with relatively easy implementation, was derived for linear systems with Gaussian errors using the Bayesian inverse approach with a minimum variance, named Kalman filter [18]. The Kalman filter is an identification filter with an attractive sequential structure to find posterior measures from arriving data. The Kalman filter is an optimal sequential data assimilation method for linear dynamics and measurement processes with Gaussian error statistics. It provides a linear, unbiased, minimum variance algorithm to optimally estimate the state of the system from noisy measurements. The Kalman filter loses its optimality for nonlinear dynamical systems and for non-Gaussian sources of uncertainty. As such many extensions of the Kalman Filter have been developed to tackle the different challenges associated with the problem of sequential data assimilation. In this study the Ensemble Kalman Filter (EnKF) will be used to estimate the diffusion rates of DF based on measurement data.

6. Ensemble Kalman Filter

EnKF was proposed by Evensen in 1994 [19] and has gained popularity in several engineering fields [20,21]. It employs Monte Carlo sampling to forecast the error statistics in the system. These Monte Carlo samples are propagated forward in time using the dynamic model, which is the general diffusion equation, and is updated based on experimental measurements once available. In this application, the state vector U consisting of dynamic state variables and model parameters is expressed as:

$$\mathrm{U} = [\mathrm{V}.\mathrm{De}.\mathrm{M}]^{\mathrm{T}} \tag{4}$$

Where *V* consists of the DF concentrations at mesh nodes in the numerical solution scheme, D_e represents the effective diffusion rate and *M* is the cumulative mass leached.

The initial ensemble is chosen so that it properly represents the error statistics of the initial guess of the model states. The initial ensemble is typically created by adding perturbations to a best-guess estimate, and then the ensemble is integrated over a time interval covering a few characteristic time scales of the dynamical system. Due to the process of the manufacturing of the board, the initial concentration is best represented by uniform distribution across a certain length only. The initial guess of De is calculated using a suggested ASTM approximation model [11].

In the update step, the observation matrix is used to relate an ensemble of observed leached mass to the forecasted leached mass and to update the state vector accordingly, as to decrease the mismatch between these two estimates. The ensemble of observations is generated by adding perturbations with zero mean and variance equal to 5% of the observed measurement value. The latter measurement error is estimated based on repeated measurements for control quantities using HPLC.

A summary of the forward model elements and quantification of uncertainty is shown in Table 3.1 and Table 3.2.

Table 3.1. Forward Model Summary.

Forward model	1-D general diffusion equation
Solution	Finite element/Finite difference scheme
Mesh size / time step	0.5 mm / 0.01 days
Shape function for FEM	Quadratic elements
Sequential assimilating technique	EnKF

Table 3.2. Uncertainty Quantification Summary.

Uncertainty	Error estimation	Comments
Initial concentration dispersion	Uniform distribution across certain length of board	Due to non-homogenous manufacturing process. Determined by sensitivity analysis (Figure 3.4)
Initial concentration available for leaching	Lognormal distribution	Mean and std were determined experimentally using availability test for similar samples
Initial D_e	Lognormal distribution with mean calculated using ASTM standard [24] and 10% std	Approximation for initial guess using infinite medium approximation for small leached quantities
Model error: Numerical solution	Normal noise with zero mean and 0.2% std	Due to problem formulation, numerical integration and shape function interpolation
Model error: Diffusion only process	Normal noise with zero mean and std which depends on how representative the diffusion only approximation eq.(1). The estimated range of std error is 4%- 7.5%	Refer to model description section
Measurement error	Gaussian distribution with zero mean and 5% std	Estimated using repeated measurements for control samples

D. Results

1. Leaching of DF Pills Embedded in EB

DF pills embedded in EB were subjected to a static as well as semi-dynamic leach tests over 11 days at 20 °C, 50 °C, and 70 °C. DF was below LOD in all of the tested solutions over 11 days at all temperature conditions tested. Mass transfer limitations inhibit DF leaching from an intact pill and result in minimal diffusion into the matrix material and subsequently into the water solution.

2. Leaching of DF Powder Embedded in EB

In order to promote leaching and allow for the assessment of the leaching rates, and gain insight into the leaching mechanism, DF was introduced to EB in the form of powder dispersed in the EB matrix. Initial leaching tests results conducted in triplicate at 20 °C, 50 °C, and 70 °C are shown in Figure 3.1.

DF leaching increases with increasing temperature. The DF concentration levels over 10 days for samples tested at 20 °C were between LOD and LOQ. Samples tested at 50 °C reveal an initial increase in DF leached, which plateaus after about five days, with a corresponding maximum cumulative fraction leached of 1% of the total initial DF content. The fraction released is even lower for samples tested at 20 °C, where concentration levels are below LOQ. The maximum fraction released at 20 °C is less than 0.3%, which is the corresponding value at LOQ. Therefore, the leachability of DF from recycled polyethylene/polypropylene matrix at room temperature is considered low. Samples tested at 70 °C show an increasing trend of DF leached over the test period of ten days. Based on these results, long term testing was conducted for samples at 70 °C in order to quantify the maximum leachable amount at that temperature. Additionally, long term testing was conducted at 20 °C in order to identify any increasing trend of DF leaching leading to quantifiable DF concentrations levels. The results are shown in Figure 3.2.

The extended period testing provides information on the quantity that can be leached on the long term. For samples exposed at 70 °C, the amount leached reaches a plateau equivalent to 4% of the total DF content. This value is used in the forward model to estimate the effective diffusion coefficient. The results obtained under accelerated temperature conditions are used to assess the validity of the forward model in predicting DF leaching and establish the leaching mechanism for this system. The increased leaching of DF with increasing temperature could be due to changes in DF desorption from the plastic mixture, or increased water absorption into the polymer matrix with increasing temperature. Our experimental data reveal that the maximum leached quantities increase with temperature (4% at 70 °C, 1% at 50 °C, and less than 0.3% at 20 °C), which correlates with increased desorption of initially adsorbed DF with increasing temperature. In order to check on the effect of water permeability affecting leaching, we evaluated the water absorption capacity of the material at 20 °C and 50 °C to assess the effect of temperature. Our results reveal similar absorption profiles at both temperature conditions. For instance, the % weight increase for a board immersed in water following one week at 20 °C is 4.1±1.3%, and 4.0±0.7% at 50 °C. Therefore, we do not expect temperature to affect the EB water absorption and subsequently the leaching behavior.

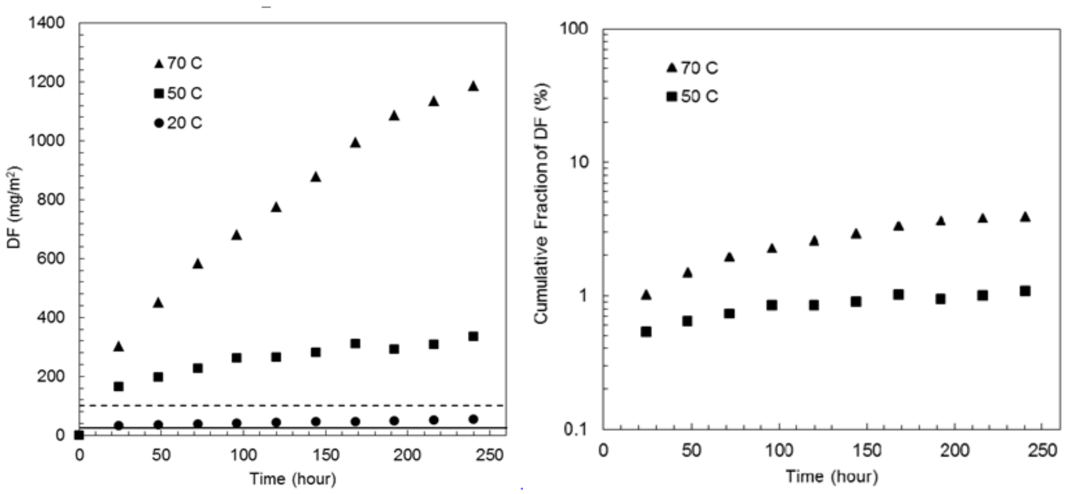

Figure 3.1. Left Graph: Leaching Behavior for DF Powder Dispersed in EB Over Ten Days at 20°C, 50°C, and 70°C Expressed As DF (mg/m2). Note that the 20°C data is between LOD (solid line) and LOQ (dashed line) and cannot be used quantitatively. Right graph: DF cumulative fraction for samples at 50°C and 70°C. Results are an average of 3 runs.

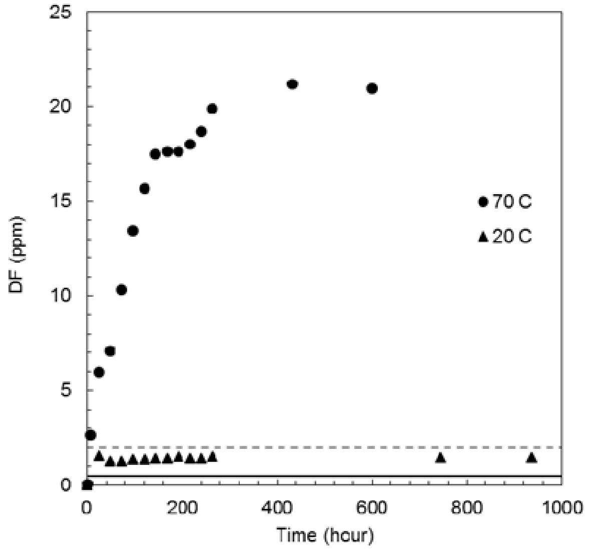

Figure 3.2. Leaching Profile for DF Powder Dispersed in EB at 20°C and at 70°C. Note that the 20°C data is between LOD (solid line) and LOQ (dashed line) and cannot be used quantitatively. It is included to show no increasing trend over a 39 days period.

3. Ensemble Model Prediction for DF Powder Leaching from EB

Model prediction for De estimated using the forward model based on the experimental data for short term leaching under accelerated conditions (Figure 3.1) is shown in Table 3.3.

Table 3.3. Mean Value and std for the Effective Diffusion Coefficient Determined Using the Forward Model.

Temperature	D_e (cm^2/s)	Std (cm^2/s)
70 °C	11×10^{-08}	1×10^{-08}
50 °C	71×10^{-09}	9×10^{-09}

The ability of the estimated D_e to predict the experimental results was evaluated using forward propagation of the general diffusion equation, simulated using 10,000 Monte Carlo samples. The estimated uncertainty in the forward model is as listed in table 3.2, except for effective diffusion, where the calculated values listed in Table 3.3 were used. Figure 3.3 shows the comparison between the mean leached mass predictions using the estimated De versus the mass determined from measured DF concentrations in the leachate at 50 °C and 70 °C. The figure also includes error bars representing the range for one standard deviation away from the mean predicted values.

The results show accurate predictions at 70 °C with almost all the measured points falling within one std from the mean prediction, and good prediction at 50 °C with almost all the measured points falling within two std from the mean prediction. The results confirm that the leaching mechanism is primarily through diffusion.

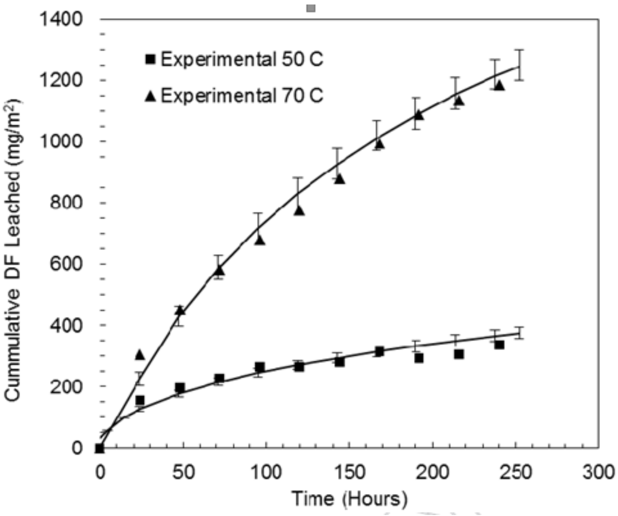

Figure 3.3. Measured and Predicted DF Leached from EB at 50°C and 70°C. The predicted values (solid lines) were obtained using the forward model. Error bars represent one standard deviation from the mean predicted values

4. Initial DF Powder Distribution in EB

The effect of DF distribution across EB is critical for accurate simulation of the leached mass over time. For instance, DF powder concentrated at the center of EB and DF powder distributed across the whole cross section in EB in the direction of diffusion will result in different leaching profiles. Using the current EB manufacturing process, the powder distribution within EB cannot be controlled. Different scenarios were assumed for the initial distribution fraction of DF to investigate the best representative scenario. The distribution fraction is defined as the portion of the EB cross sectional width containing DF at the initial time point. The distribution fraction originates at the center of the cross-sectional width. Figure 4 shows the results of various distribution fractions at 70 °C, with initial distribution fraction values between 0.7 and 1, where a fraction of 1 indicates a uniform distribution across the entire thickness of EB while 0.7 indicates that DF is uniformly scattered in the middle 70% portion of the EB. Using least square error between the estimated mean and the measured values, a distribution fraction of 0.9 was found to best fit the data. The same analysis was performed for all the boards to determine the best estimate of the initial distribution of DF and its corresponding D_e.

5. Room Temperature DF Diffusion Model Prediction

The temperature dependence on the diffusion coefficient is typically described by an Arrhenius relationship [11]. Assuming the leaching mechanism and structural controls such as tortuosity, porosity remain unchanged, the effective diffusion coefficient De as a function of temperature is estimated using Monte Carlo analysis (100,000 samples). The results are summarized in Figure 3.5. At 20 °C, the predicted value for De is 3.3 ± 1.3 × 10-08 cm^2/s.

The accuracy of values reported in Figure 3.5 is expected to be low, especially for temperatures outside the range experimentally tested, due to the assumption of identical leaching mechanism and structural controls at all temperatures reported. The experimental determination of De at a wider temperature range is constrained by LOQ at lower temperatures, and the risk of structural integrity of EB over prolonged exposure at high temperatures (above 70 °C). Leached amounts calculated using the estimated room temperature value for De are of the same order as the amounts experimentally detected and shown in Figure 3.1.

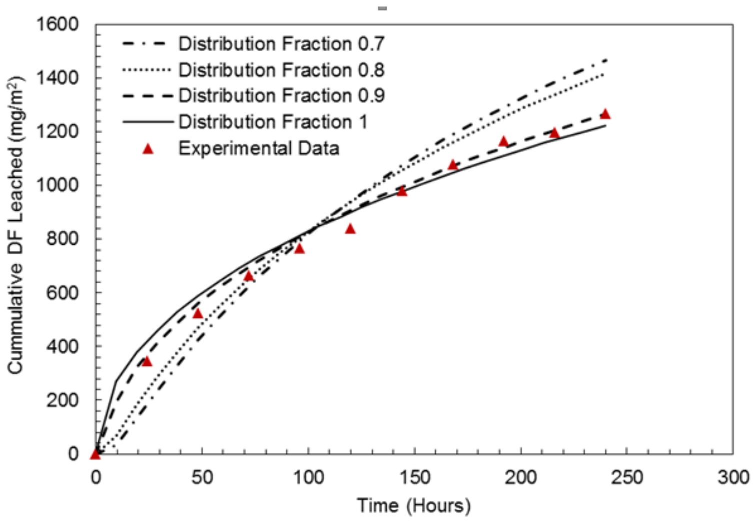

Figure 3.4. Sensitivity Analysis for the DF Distribution Fraction Within EB at the Initial Time Point.

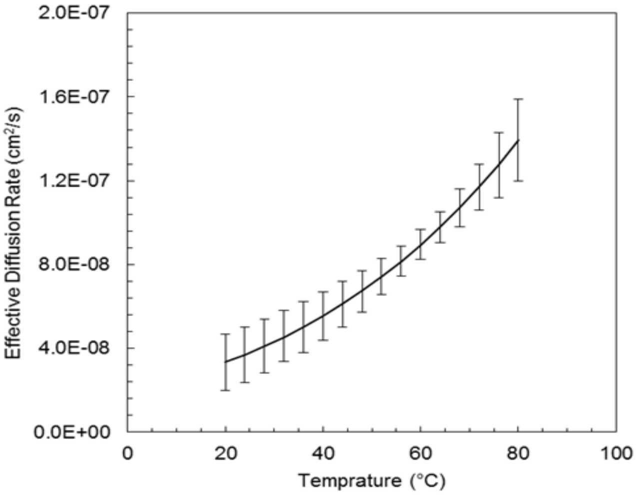

Figure 3.5. Model Predictions for De As a Function of Temperature Assuming the Leaching Mechanism and Structural Controls Remain Unaffected by Temperature Change and Follow an Arrhenius Relationship.

6. The potential of EB at Immobilizing Drug Product API

The results shown in the present study reveal EB is efficient at immobilizing DF and presents internal diffusional resistance to leaching, with less than 0.3% of the total amount leaching at room temperature for DF in the powder form. For DF drug product embedded in EB as pills, the amount leached was below LOD. The smaller surface area of DF in pills compared with the powder form, and the pill surface characteristics limiting DF diffusion results in significantly lower leaching levels for pills embedded in DF.

The forward model was used to illustrate DF leaching under conditions similar to exposure conditions during utilization. Leaching of DF was computed using the forward model at DF powder loading of 2.4 mg/cm^3 and a leachable amount of 0.3%, which corresponds to the value at LOQ. The loading and leachable amount values were selected to represent an extreme case which results in higher DF leaching levels. In a practical application, loading is less than 2 mg/cm^3, and leaching is less than 0.3%. The model incorporates the number of wet days and temperature in Beirut, Lebanon. The leaching profiles for three EB board thicknesses are shown in Figure 3.6.

In this scenario, leaching is assumed to occur on wet days only since DF and most pharmaceuticals have completely negligible volatility, as evident from the low values of Henry’s constant [22]. Since July and August are dry months in Beirut, no leaching occurs during this period and the result is a flat cumulative DF fraction during this interval. Based on these data, 0.3% of the DF leaches in about two years for a 10 mm thick board, three years for a 13 mm thick board, and four years for a 15 mm thick board. For DF embedded as pills, leaching is expected to be significantly lower based on the observed lab results.

Therefore, EB material has potential for use as a barrier for pharmaceutical leaching from expired drug products.

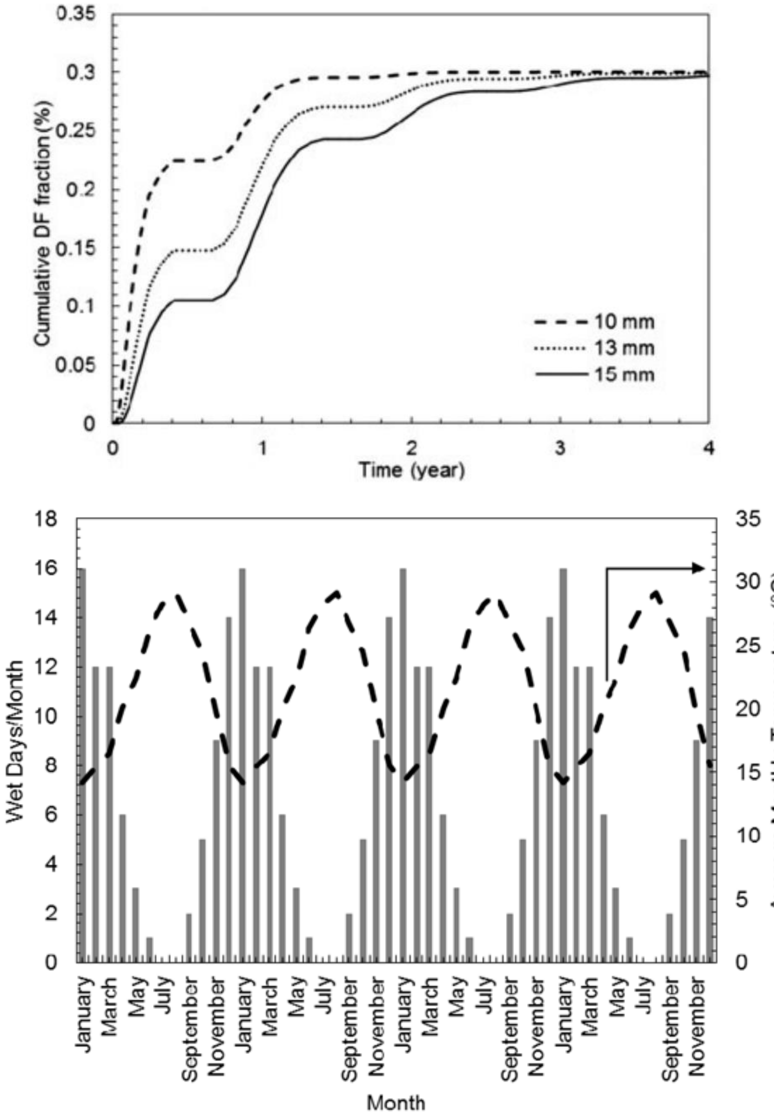

Figure 3.6. DF Leaching Profile Estimated Using the Forward Model for DF Powder in EB of Various Board Thicknesses (top). Leaching occurs during wet days in Beirut, Lebanon (bottom, data obtained from http://www.beirut.climatemps.com/precipitation.php)

E. Conclusions

EB composed of PE/PP reclaimed from municipal waste was effective at immobilizing DF and reducing its leachability. For DF pills embedded in EB, leaching was below LOD at all temperature conditions tested over 11 days. For DF powder immobilized in EB, the maximum leachable amount was 4% under accelerated conditions of 70 °C, and less than 0.3% following 39 days at 20 °C. The forward model with EnKF reveals leaching of DF occurs through diffusion. The model was successful at predicting the leaching behavior of DF at 50 °C and 70 °C.

The results obtained for DF present a proof of concept for the approach used to characterize the leaching of pharmaceuticals from immobilizing matrix materials. The model can be applied for other API/matrix systems. Using limited amount of experimental data, the leaching profile of drug product API can be predicted, provided the drug is stable at the conditions tested.

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H. Annex I

The following annex contains data for HPLC tests performed for the following three temperatures: room temperature, 50 ^{0}C, and 70 ^{0}C.

At T-room: 96 mg DF in 6*6 EcoBoard

Table 3.4. Specimens Data Sheet for DF (96mg) at Troom.

Size	V.EB (ml)	M.EB (g)	V water (ml)	A (cm^2)	V/S	length (cm)	Width (cm)	height (cm)
A	45	38	160	32	5	6	6	1.1
B	43	35	160	32	5	6	6	1
C	49	41	160	32	5	6	6	1.15

Table 3.5. Leaching Data for DF96mg @Troom.

Days	**Area**			**ppm**		
	A	**B**	**C**	**A**	**B**	**C**
1	9.2	13.5	0	0.54762	0.7738	0.0637
2	9.6	13.6	0	0.56866	0.77906	0.0637
3	10.1	14.6	0	0.59496	0.83166	0.0637
4	11.4	15.6	0	0.66334	0.88426	0.0637
5	12.8	16.7	0	0.73698	0.94212	0.0637
6	13.6	17.8	5	0.77906	0.99998	0.3267
7	14.3	18.5	5.6	0.81588	1.0368	0.35826
8	14.5	19.1	6.6	0.8264	1.06836	0.41086
9	15.3	19.3	7.2	0.86848	1.07888	0.44242
10	16.1	20.4	10	0.91056	1.13674	0.5897
11	16.3	22.8	11.6	0.92108	1.26298	0.67386

Table 3.6. pH Measurements for EB A

days	pH of EB(A)
3	6
5	5.94
7	6.42
9	6.7
11	6.8
12	6.8

Table 3. 7-Standard curve data for 96mg @Troom

ppm	**Area**
0.975	17.88
1.953	35.08
3.906	73.26

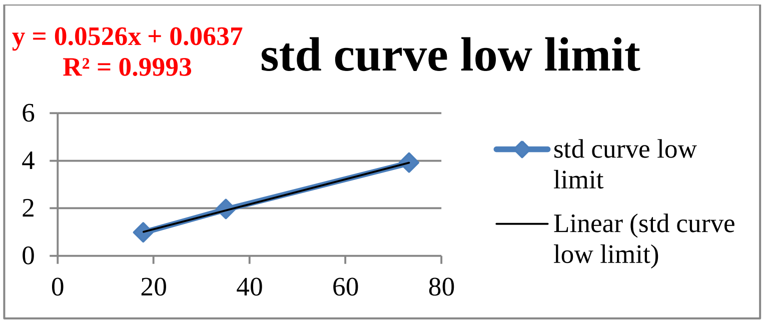


Figure 3.7. Standard Curve Low Limit Used for Under LOD.

Table 3.8. Availability Test Data for DF (96mg) at Troom.

Days	Area	ppm
1	19.56	1.528376
2	13.6	1.24766
3	14.3	1.28063
4	15.8	1.35128
5	15.6	1.34186
6	17.1	1.41251
7	16.7	1.39367
8	18.8	1.49258
9	17.2	1.41722
10	17.1	1.41251
11	19.1	1.50671
31	17.8	1.44548
39	18.1	1.45961

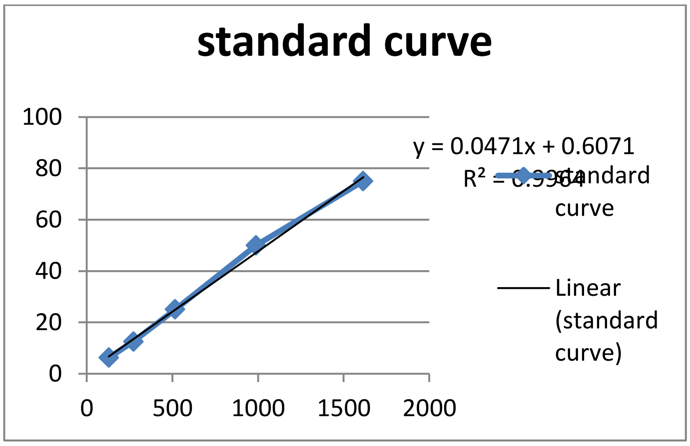


Figure 3.8. Standard Curve Data for DF (96 mg) at Troom.

Table 3.9. Standard Curve Data.

ppm	Area(m^2)
6.25	128.5
12.5	272.9
25	516.7
50	989.1
75	1614.6

At T-70^{0}C:96mg DF in 6*6 EcoBoard

Table 3.10. Specimen Data Sheet for DF (96mg) at T70.

Size	V. EB (ml)	M. EB (g)	V water (ml)	A.Contact (cm2)	V/S	Length (cm)	Width (cm)	Height (cm)
K	45	37	160	32	5	6	6	1
L	49	42	160	32	5	6	6	1.15
M	46	39	160	32	5	6	6	1.1

Table 3.11. Leaching Data for DF (96mg) at T70.

Days	**Area**			**ppm**		
	K	**L**	**M**	**K**	**L**	**M**
1	81	11.3	55.8	10.1566	1.26288	6.94108
2	124.4	23.5	83.7	15.69444	2.8196	10.50112
3	155.2	28.9	105.6	19.62452	3.50864	13.29556
4	173.5	31	121.6	21.9596	3.7766	15.33716
5	203.2	32.6	133.2	25.74932	3.98076	16.81732
6	229	34.6	154.9	29.0414	4.23596	19.58624
7	273.6	46.7	170.4	34.73236	5.77992	21.56404
8	315.2	48.8	184.3	40.04052	6.04788	23.33768
9	325.1	61.2	189.3	41.30376	7.63012	23.97568
10	336.7	65.1	200	42.78392	8.12776	25.341

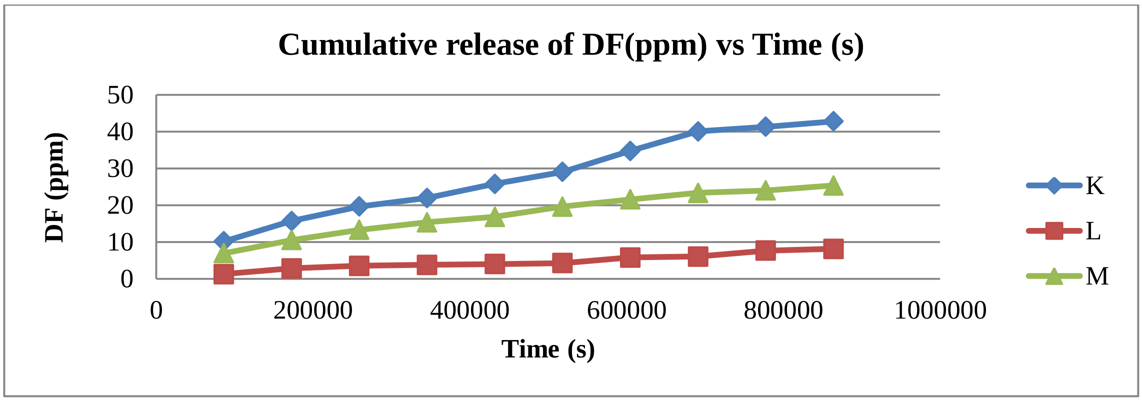


Figure 3.9. Cumulative Release of DF (96mg) at T70.

Table 3.12. Release of DF/EB Area.

Release of DF(mg)/EB area(m^2)			
	K	**L**	**M**
1	507.83	63.144	347.054
2	784.722	140.98	525.056
3	981.226	175.432	664.778
4	1097.98	188.83	766.858
5	1287.466	199.038	840.866
6	1452.07	211.798	979.312
7	1736.618	288.996	1078.202
8	2002.026	302.394	1166.884
9	2065.188	381.506	1198.784
10	2139.196	406.388	1267.05

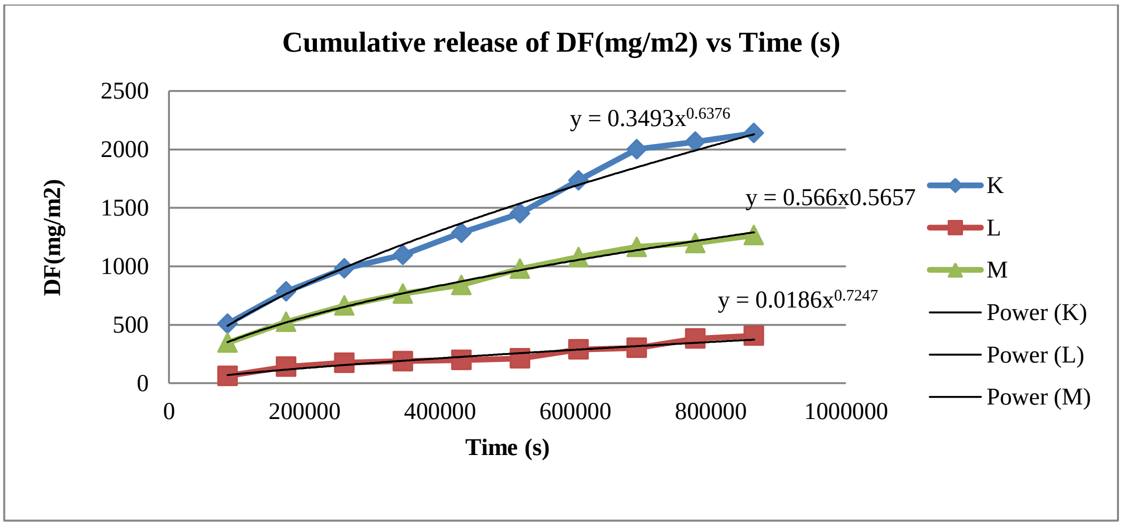


Figure 3.10. Cumulative Release of DF/EB.

At T-50^{0}C: 32 mg DF in 6*6 EB

Table 3.13. Specimen Data Sheet for DF (32mg) at T-50.

Size	V. EB (ml)	M. EB (g)	Vwater (ml)	A.Contact (cm2)	V/S	Length (cm)	Width (cm)	Height (cm)
X1	75	65	325	65	5	10.3	6.3	1
X2	80	76	320	64	5	10.2	6.2	1.3

Table 3.14. Leaching data for DF (32mg) at T50.

Days	**Area**		**ppm**		
	X1	**X2**	**X1**	**X2**	**Average**
1	25.23	130.23	1.08	5.57	3.32
2	58.36	127.85	2.45	5.46	3.96
3	78.45	137.74	3.28	5.89	4.58
4	95.51	153.65	3.98	6.57	5.27
5	106.90	144.19	4.45	6.16	5.31
6	114.69	151.50	4.78	6.47	5.62
7	119.88	176.89	4.99	7.56	6.27
8	116.54	160.00	4.85	6.84	5.84
9	96.34	192.96	4.02	8.25	6.13
10	117.32	201.15	4.88	8.60	6.74

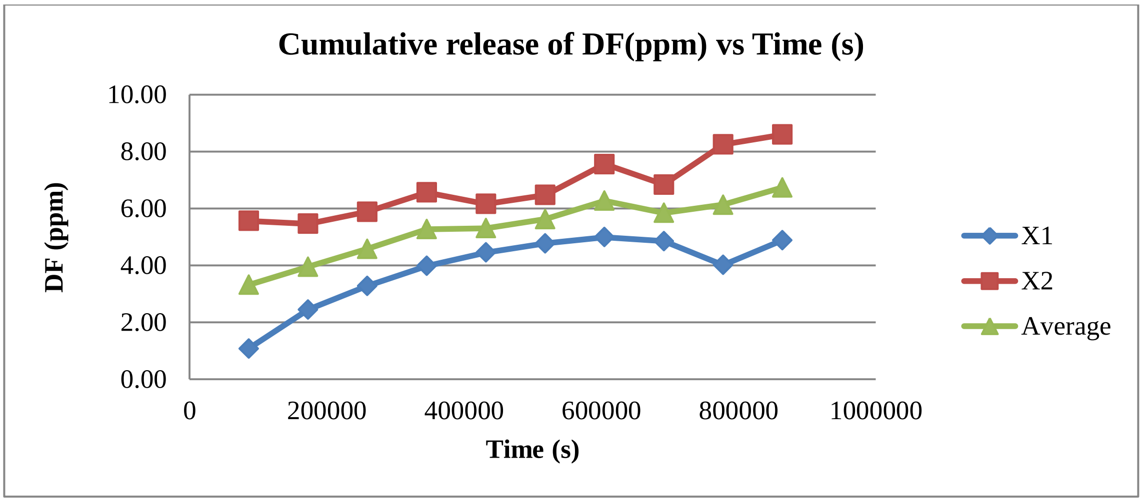


Figure 3.11. Cumulative Release of DF (32mg) at T50.

Table 3.15. Cumulative Release of DF (32mg)/EB Area.

	Release of DF(mg)/EB area(m2)		
Days	**X1**	**X2**	**Average**
1	53.9	278.3	166.1
2	122.4	273.2	197.8
3	163.9	294.3	229.1
4	199.1	328.3	263.7
5	222.7	308.1	265.4
6	238.8	323.7	281.2
7	249.5	378.0	313.7
8	242.6	341.9	292.2
9	200.8	412.3	306.6
10	244.2	429.8	337.0

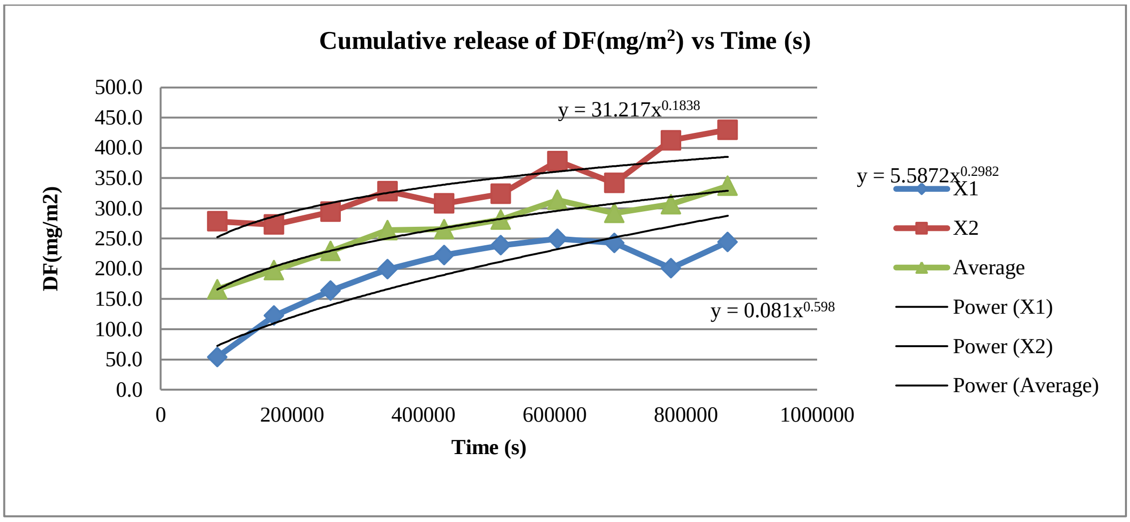
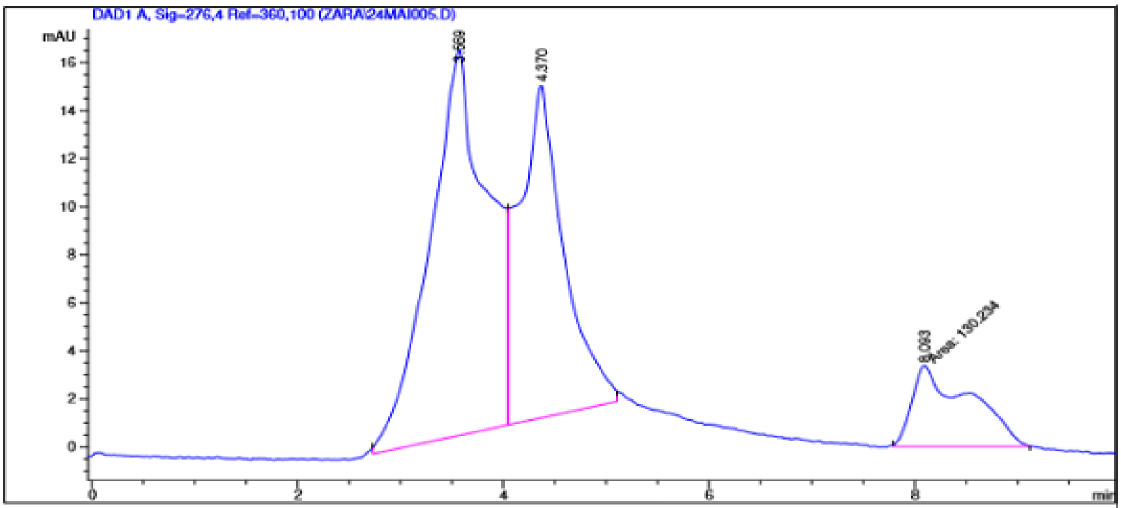


Figure 3.12. Cumulative Release of DF (32mg) at T50.



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=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=276,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   3.569 BV    0.4822  624.61884   16.04544  53.2402
   2   4.370 VB    0.3769  418.35696   13.83249  35.6592
   3   8.093 MM    0.6484  130.23413    3.34781  11.1007
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Figure 3.13. EB Sample X2 Data on Day 1.

3D model of leaching setup

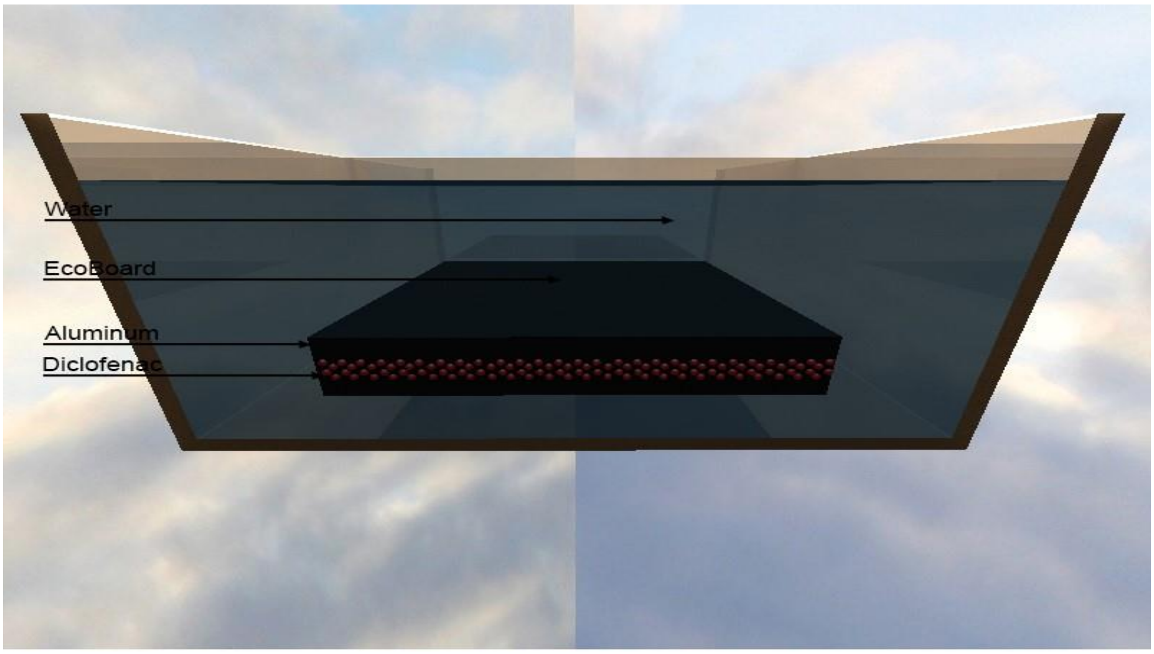

Figure 3. 14- Leaching model section layout

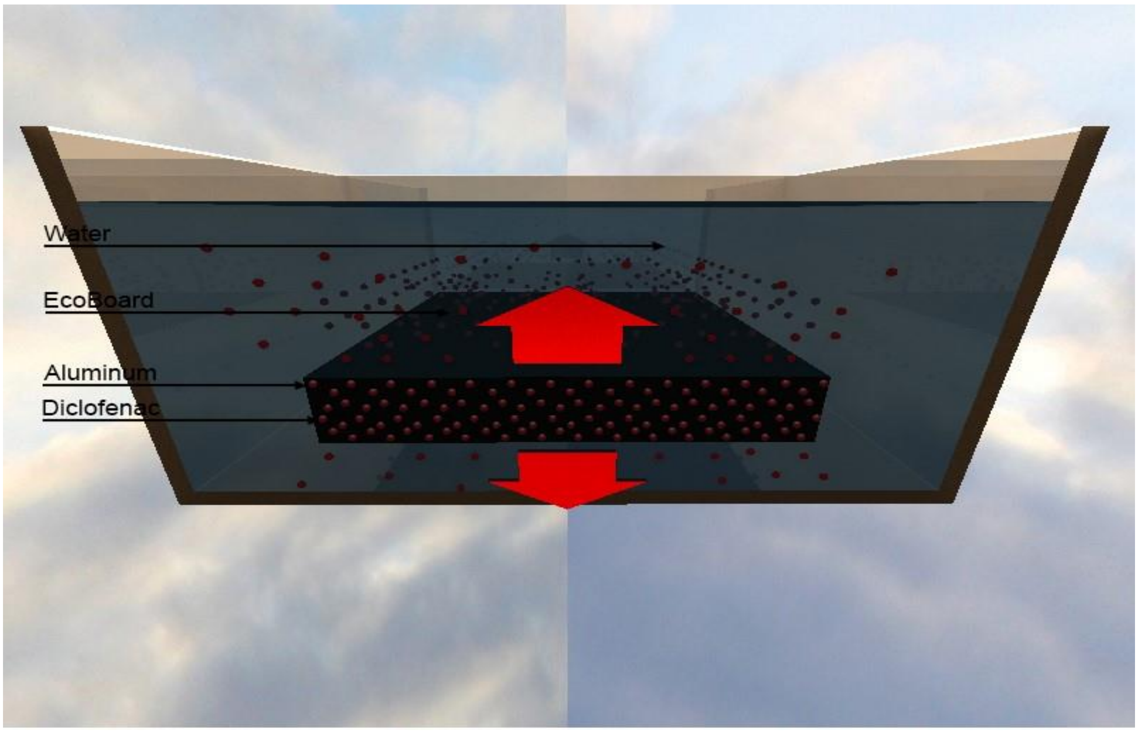

Figure 3.15. Diffusion 3D Model.

CHAPTER IV

ADVANCED OXIDATION PROCESS (AOP)

A. AOP

Previous parts addressed waste pharmaceutical containment in the solid form. In this chapter, we explore a treatment method of pharmaceutical waste in the solution form. As mentioned earlier, the problem of hazardous organic contaminants and more specifically pharmaceuticals and personal care products (PPCPs) that are persistent in nature, resistant to degradation by conventional wastewater treatment techniques and hazardous to aquatic and wildlife is an urgent global issue [1–3]. Advanced Oxidation Processes (AOPs) is the technology on the frontline to degrade such contaminants [4]. AOPs involve the use of an oxidant and a mean of activation to create very strong radicals that will target the PPCPs molecules till they are biodegradable, less toxic and in some cases till complete mineralization [5]. Oxidants such as permanganate, persulfate, monosulfate and hydrogen peroxide are the most commonly used [6]. Upon activation, the oxidants produce, directly and indirectly, radicals such as hydroxyl, sulfate, oxygen, and superoxide [7]. The oxidants can be activated by physical means such as UV-254nm radiation, ultrasound, heating or by the mean of a chemical catalyst. The chemical catalysts used can be heterogeneous and in a different physical state (solid) than the solution (liquid) such as titanium dioxide, zero-valent iron, magnetite, and hematite or it can be homogeneous and in the same liquid state such as ferrous, copper, cobalt, nickel and hydroxide ions [8–11].

AOPs studies are usually done in batch reactors that are stirred using a magnetic stirrer; however, in real-case scenarios a dosing pump is used which injects a high concentration oxidant solution into a continuous flow of the polluted water, a mixer compartment ensure proper mixing and another dosing pump injects the chemical activator. A four-port multiple inlet vortex mixer (MIVM) equipped with Harvard apparatus PHD2000 syringe pumps to control the injection flow rates was used, such apparatus is adopted for the Flash Nano Precipitation (FNP) application in which the intensity of mixing affects nanoparticle formation rate and structure. The four inlet MIVM reactor has a confined space in which an environment of turbulence with high energy dissipation rate [12] is present, facilitating the proper activation of the oxidant molecule supposedly enhancing degradation, and thus providing better yields than that of the batch mode. Two target pharmaceuticals: Carbamazepine (CBZ) and Sulfamethoxazole (SMX) were selected since previous research was conducted on their degradation using a chemically activated persulfate (PS) system. For the batch experiments, 180 mL of pharmaceutical solutions, CBZ and SMX, were spiked with 10 mL PS and 10 mL $FeCl_2$. The final concentrations were as following: [CBZ] = 40 µM, [SMX] = 40 µM, [PS] = 1 mM, $[Fe^{2+}]$ = 1 mM. The same volumes and concentrations were used for the MIVM-vortex experiment, however the solutions were filled into syringes and mixed inside the chamber and into a beaker at a total flow rate of 59 L min^{-1} simulating an online dosing system. Total reaction time was 60 minutes commenced by the addition of $FeCl_2$. 0.6 mL samples were collected at t = 0, 5, 10, 20, 40 and 60 minutes, samples were filled into HPLC vials containing 0.6 mL of MeOH solution to quench the remaining radicals. The samples were quantified using the same HPLC system used for Diclofenac. Experiments were conducted in duplicates and each pharmaceutical was tested alone.

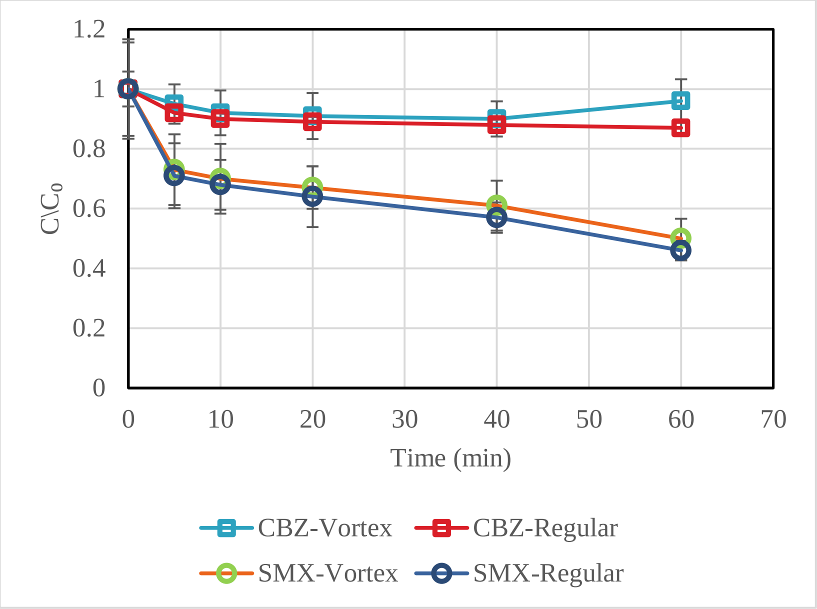

Figure 4.1. C/C0 Versus Time for MIVM (vortex) and Control Experiments.

Results in figure 4.1 show no significant difference for degradation using the FNP process vs. the batch process. This suggests that the process is reaction controlled and the centrifugal mixing found in the batch process does not affect the process efficiency. Hence, the use of FNP in AOP for CBZ and SMX removal does not provide an advantage.

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CHAPTER V

CONCLUSION

This research work tackled two problems that are of national and international concern, the problem of proper disposal of expired pharmaceuticals in the solid form, and the domestic solid waste management issue especially plastics. The recommended method by WHO for the treatment of expired pharmaceuticals is high temperature incineration which has high capital and operational costs that are subjected to inflation and increased oil prices over the years. In Lebanon no proper pharmaceuticals waste management plan exists, with expired pharmaceuticals stockpiling in distributers warehouses or disposed to landfills and open dumps through the municipal solid wastes streams.

This could be attributed to the high cost and lack of proper management policy. On the other hand the plastic portion of the municipal solid waste is a major player in the Lebanese solid waste crisis and around the world. Cedar Environmental SARL, an industrial engineering company in Lebanon, found a proprietary solution for this issue by mixing the non-reclaimable and recyclable plastics into a board the can be used in construction (Ecoboard). The components of the board represent the plastics of highest percentage inside the wastes (Polyethylene, Polypropylene mainly and other plastic material). This paper is a study on a proof of concept for using recycled plastic material as an immobilizing matrix for pharmaceuticals and other wastes: Ecoboard + drug.

Such a product doesn’t have current alternatives in the Lebanese market or around the world. The solution also studied one of the most common pharmaceuticals (Diclofenc) as a model for embedding other drugs later and the most common plastic compounds in the fabrication of the Ecoboard. The limit of loading of pharmaceuticals into the Ecoboard was defined by the manufacturing process. The product was tested for mechanical properties using ASTM methods and results were compared to other construction material showing acceptable properties.

As for the possibility of pharmaceuticals leaching from the product, leaching tests were performed at various temperatures of which the data obtained were used to predict leaching at extended periods of time using an appropriate validated model. Data reveals leaching occurs, by diffusion, and the proposed model reveals limited leaching over a prolonged period of time. As an alternative, using FNP to enhance AOPs had limited success. Data show that the process is limited by the reaction rather than mixing.

The present study demonstrates the effectiveness of recycled plastic material sourced from municipal solid waste at immobilizing an API. The leaching study experiments show leaching of the API occurs by diffusion, and modeling of the system reveals minor leaching relative to the immobilized material over a prolonged period of time. Additionally, the mechanical properties data show that incorporating the pharmaceutical waste into the matrix does not affect the mechanical properties of the recycled PE/PP material. As such, the results show the potential of this approach at treating pharmaceutical waste.

Moving forward, several aspects will require further analyses to optimize the product design. First, the effect of modifying the composition and nature of the matrix material on the leaching process should be assessed. This includes incorporating various types of plastic material at different compositions to optimize the immobilization and stabilization of the waste material. In addition, mapping of defects due to incorporating DF should be assessed using several analytical and imaging techniques, including Raman spectroscopy, scanning electron microscopy, and transmission electron microscopy. This will provide further insight beyond the mechanical properties characterization on the effect of modifying the matrix material with pharmaceutical products. For the case of DF, it would be interesting to investigate the intermolecular effects of the molecule, including π- π stacking and H-bonding leading to quasi-Fickian behavior.

In order to further develop the concept explored in this work into a working solution for pharmaceutical waste, further understanding on the environmental impact of pharmaceuticals needs to be elucidated. In particular, the environmental acceptable limit for DF and other pharmaceuticals needs to be set before the approach for immobilizing pharmaceutical waste in recycled material could be applied. Regulation concerning these compounds can only be set once the environmental assessment and toxicity profile for these molecules is further understood. Such regulation can be used to develop an acceptable solution for treating pharmaceutical waste. Economic analysis and life cycle assessment will also need to be conducted in order to benchmark this approach against traditional treatment methods such as landfilling and incineration.

In the case of AOP, varying the pH to optimize drug degradation could be explored to identify conditions favorable for the treatment of pharmaceutical wastes in water.