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A review on characterization and recyclability of pharmaceutical blisters

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ABSTRACT

Packaging is one of the biggest sectors in the world and the use of aluminium is widespread in the packaging industry. Pharmaceutical blister packages generate a significant amount of solid waste, typically containing plastics and aluminium as thin layers. Since these packages have a complex structure with multiple layers, they are hard to recycle. A separation process of the plastic and aluminium is needed prior to recycling. Hydrometallurgical or thermal processes can be used for the separation. This work reviews the characterization of different types of blisters and the different reagents used in the separation process of the blister layers. Parameters and results of separation processes by using hydrochloric acid, formic acid, acetic acid, organic solvents, and phosphoric acid were discussed as well as the thermal degradation.

1. Introduction

Pharmaceutical blister packages are inexpensive, have good protection against moisture, and are easier to use than other drug packages. Blister packages provide information about the usage of the relevant drugs and are used as an advertising tool in addition to protecting drugs (Agarwal et al., 2020). Blister packages are more suitable for solid drugs than bottles in daily life. The solid drugs in the bottle show rapid deterioration as they contact with air often during usage. Contrary, solid drugs are stored separately from each other in blister packages, they are airtight and safer for use (Pilchick, 2000).

The value of the pharmaceutical blister packaging market is estimated to be US$149.3 billion by 2026 at a compound annual growth rate (CAGR) of 6% between 2019 and 2029 (Brooks, 2019). The use of blister packaging for pharmaceuticals has increased recently, generating a significant amount of waste, accounting for 4% by weight of the total packaging waste generated daily (Pilchick, 2000).

Pharmaceutical blister packages are typically produced by thermoforming or cold-forming. Blisters consist of four basic components: forming film, heat-seal coating, lidding material and printing ink (see Fig. 1) (Pilchick, 2000). Forming films are generally made of plastic such as polyvinyl chloride (PVC), polypropylene (PP), and polyethylene terephthalate (PET). The plastic used in blister packages is selected according to moisture resistance and product durability. The lidding material is usually aluminium because it can isolate drugs from the air and is mechanically stable. The cold-formed pharmaceutical blister packages contain aluminium in lidding and forming films. The cold-forming results in better resistance to light and moisture than thermoforming. However, cold-forming is more costly to produce (Nieminen et al., 2020).

There are three different types of pharmaceutical blisters (Nieminen et al., 2020):

1. thermoformed package with clear plastic forming film and aluminium lidding,
2. thermoformed package with white opaque forming film and aluminium lidding,
3. cold-formed package with aluminium forming film and lidding.

The first and second types are covered by forming films (plastic layer) and 10–15 wt% of a metal layer (typically aluminium layer). Polyvinyl chloride (PVC/PVDC) and polypropylene (PP) are generally used as plastic layers in the packages (Pilchick, 2000). The third type consists of aluminium, and plastic layers (PVC, and polyamide). The plastic types provide higher protection against external factors. In addition, the type 3 blister contains a double layer of aluminium which protects from the sunlight and moisture thus, avoids the deterioration of the drugs (Klejnowska et al., 2020). Foil/foil blister packages involve lamination of plastic film (PVC or PE), foil, adhesive and an outer plastic film. The outer film, which can be PET or PVC, acts as a heat-seal layer and supports the thin aluminium layer (Pilchick, 2000).

Plastic and aluminium value in blister packages should be recovered to decrease the environmental and economic impact (Nieminen et al., 2020). Currently, there are three possibilities for end-of-life blister packaging: landfilling, direct recycling and incineration depending on the policies and social behaviour. When landfilled, the plastic and aluminium components can cause soil acidification. In addition, the lack of recycling leads to an increase in primary aluminium production which is a highly energy-consuming process. The wastes that are not included in recycling processes adversely affect the environment and cause air and water pollution (Pikoń et al., 2021). Recently, blister packages tend to be considered as plastic waste, since the plastic content is high and are directed to facilities where the metal is not recovered (Czop et al., 2015; Klejnowska et al., 2020; Landrat, 2018). However, the aluminium content in the blisters should not be ignored. Furthermore,

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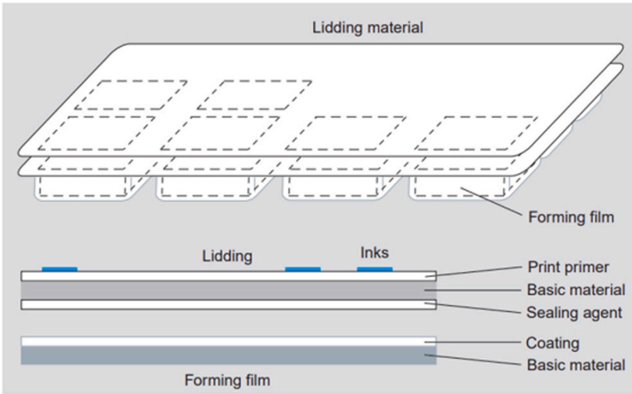

Fig. 1. Basic components of the pharmaceutical blister package (Pilchick, 2000).

recycling the waste of blister packages is complicated due to the layered structure (Nieminen et al., 2020). A dedicated facility is needed to recycle both the plastic and metal components of blisters efficiently (Klejnowska et al., 2020).

Separation (as aluminium and plastic) and recycling of waste pharmaceutical blister packages attract attention due to the cost and environmental impact of aluminium. The recycling efforts for the waste pharmaceutical blisters are increasing with the zero-waste strategy's aim (Zaman and Lehmann, 2013). This work reviews the characterization of different types of pharmaceutical blisters, the separation techniques of plastic and aluminium layers.

2. Characterization

The main components of pharmaceutical blisters (forming a film, lidding material, heat-seal coating and printing ink) are reported in this chapter including their chemical composition, thickness, toxicity and forming techniques (Pilchick, 2000).

2.1. Forming film

The forming film is the part of the package that holds the product in deep-drawn pockets. Selecting a suitable plastic film for the blisters in terms of type, grade, and thickness is crucial for the success of the packaging. The following parameters must be considered for the packaging quality: size and weight of the product, sharp or pointed edges of the packaging, impact resistance, ageing, migration, and cost. PVC, PP, PS, and PET are the plastic types utilized as forming films, and they can be thermoformed, while the support material, aluminium, is cold-formed (Pilchick, 2000).

PVC is the most used plastic type to form a film in blister packaging. Because it is almost devoid of softening ingredients, PVC-forming film is named rigid PVC. It has good thermoformability, flexural strength, chemical resistance, and low permeability to oils, and flavouring agents. Moreover, it is simple to print and inexpensive. The thickness of thermoformed PVC films is nearly 250 µm. PVDC plays a significant role in blister packaging as laminations or coatings on PVC, despite its tiny volume in blister packaging. PVDC is the most prevalent blister packaging material coating because it reduces gas and moisture permeability by a factor of 5–10 in comparison to PVC. The thickness of PVC films is 203,2–254 µm with a 25.4–50.8 µm of PVDC coating on one side of the PVC film (Liu, 1999; Montaudo, 1991; Pilchick, 2000).

PP as a blister package support material has become widespread recently. Uncoated PP has a lower water vapour permeability than PVC, but it has similar properties to PVDC-coated PVC. The thermoforming technique uses PP films with a thickness of 250–300 µm. PP has no toxic release after the cremation unlike PVC and has strong moisture-barrier qualities. However, PP cannot be processed as fast as PVC, is thermally unstable and sensitive to post-process shrinkage. That's why its use is limited in the United States and Europe (Pilchick, 2000).

PET is another material that can be used as a substitute for PVC, but its higher water vapour permeability than PVC limits its applicability. Although PVDC-coated PET has the same water vapour barrier function as PVC, it is not a good substitute for chlorinated plastics (Pilchick, 2000).

PS is another option for packaging. It is thermoformable and has high water vapour permeability which makes it unsuitable for using as a plastic layer in blister packaging (Pilchick, 2000).

The combination of different types of plastics and aluminium which are nylon/aluminium/PVC or oriented polyamide (OPA)/aluminium/PVC can be used as layers for the forming film. Laminates made of OPA, aluminium, and PVC are intriguing. It is possible to reduce the water vapour permeability using a laminate structure consisting of 25 µm OPA, 45 µm aluminium, and 60 µm PVC. Furthermore, because of the high proportion of aluminium in the laminate, it is recyclable. The OPA/aluminium/PVC laminate is cold-formed like other laminates incorporating aluminium. Cold forming needs more packaging material than thermoforming for the same packaging capacity (Allinson et al., 2001; Pilchick, 2000).

2.2. Lidding materials

The Lidding material serves as the foundation or primary structural component for the final blister package. It should be chosen based on the product's size, shape, and weight, as well as the style of the packaging that will be constructed. The thickness of the lidding materials varies from 0.36 to 0.76 mm, however, the most typical range is 0.46–0.61 mm. The lidding material is generally a plastic layer coated with a foil (for Snap-On blister types) or paper/foil or paper/PET/foil laminations (for a child-resistant peel). To improve the printing, clay coatings are applied to the cover material. Heat sealing and printability are critical factors, and the closure material should provide the best possible solution in the blister packaging. As with the forming films, the closing material should be suited for the type of opening accessible for the package (for example, push or peel). A cross-section of a peel-and-push closure material is shown in Fig. 2. Materials that are used as lidding materials are; aluminium, paper/aluminium, and paper/PET/aluminium (Pilchick, 2000).

Aluminium is the most used material for the push-through lidding process in Europe. The thickness of the foil is between 20 and 25 µm. The softness and thickness of this type of aluminium allow tablets to be easily pushed through the blister packages (Pedrosa de Oliveira et al., 2021; Pilchick, 2000). The aluminium layer is generally cold-pressed into a shape unlike all-plastic blisters. Paper/aluminium is utilized as a peel-off foil in the USA; hence the foil must be quite thick for an effective peeling. The thickness of the aluminium is 15.24–25.4 µm. Paper/PET/aluminium is a peel-off–push-through lidding material which is generally used in the USA. The idea is to peel off the paper/PET lamination off the aluminium first, then press the tablet through it (Pedrosa de Oliveira et al., 2021; Pilchick, 2000).

2.3. Heat sealing coatings

Heat-sealing coatings are the most important component of blister packages as they provide a bond between the plastic blister and the printed lidding material. Solvent-based types of vinyl and water-based products are

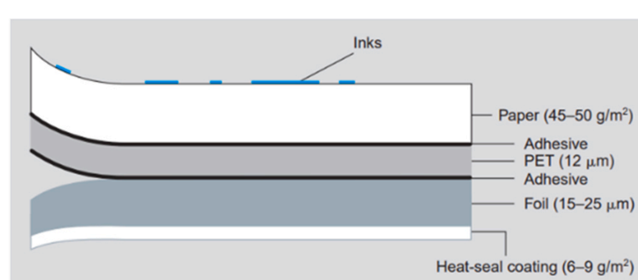

Fig. 2. Cross-section of a peel-off–push-through lidding material (Pilchick, 2000).

used for heat-sealing coating on blister packaging. A successful blister heat-seals coating must have good gloss, clarity, abrasion resistance, and hot adhesive, as well as be able to seal to a variety of blister films (Pilchick, 2000).

2.4. Print inks

Graphic and aesthetic appeal are provided by printing inks. Printing inks must be able to sustain fusing temperatures of up to 300 °C without changing colour form. It should have resistance against abrasion, bending, and fading as well as be safe to use with the intended product (Pilchick, 2000).

Fig. 3 presents the types of pharmaceutical blisters. Type 1 is the most used blister in general, type 3 is mostly preferred for drugs sensitive to moisture and light. Different types of blister packages have different proportions of components. The concentration of plastic and aluminium layers was measured as 85 wt% and 15 wt% respectively (Rimšaitė et al., 2019; Wang et al. 2015; Wang et al., 2015).

Thickness is critical for ensuring the film's barrier performance. Blisters might contain drugs of different shapes and sizes. Yousef et al. reported the variation in the thickness and surface area of different blisters which is shown in Table 1 (Yousef et al., 2018). Laasonen et al. and Shukla et al. measured the overall thickness of type 1 and type 2 ranged from 280 to 365 µm and also measured that containing two plastic layers in the range of 260–330 µm and an aluminium layer in the range of 25–30 µm (Laasonen et al., 2004; Shukla et al., 2022).

Shukla et al. presented the elemental composition (wt%) of the layers for types 2 and 3 as shown in Table 2. The elemental composition further reveals that the metallic layer of all samples following delamination is primarily aluminium. Furthermore, the presence of a significant amount of chlorine in the plastic layers indicates that they are made of PVC or PVDC (Shukla et al., 2022).

3. Environmental impact

Environmental effect is a significant factor in the pharmaceutical blister recycling process because reagents are required to separate aluminium from PVC. Reagents can be hazardous to the environment. Nieminen et al. indicated that DES and lactic acid are environmentally friendly (Nieminen et al., 2020).

Table 1
Mass and dimensions of different pharmaceutical blister types (Yousef et al., 2018).

blister type	Length x Width x Thickness (mm)	Mass (g)
1	40 × 92×0.26	1.821
1	38 × 85×0.225	1.252
1	50 × 128×0.128	2.834
1	66 × 100×0.236	2.945
2	53 × 105×0.25	2.969
3	50 × 90×0.137	1.212

However, Rimšaitė et al. stated the formic acid and acetic acid have negative effects on the human health, but the mixed organic solvents are acceptable for the environment (Rimšaitė et al., 2019).

Raju et al. compared type 1 and type 3 blister packages on the grounds of environmental sustainability. The analysis was based on four stages (Raju et al., 2016).

(i) manufacture of raw materials for packaging material, i.e., PVC and aluminium,
(ii) manufacturing process of packaging material, i.e., PVC sheet and aluminium foil,
(iii) transportation of packaging material to the drug plant, and
(iv) packaging of the tablets.

Raju et al. specified that environmental effects are estimated according to CML 2001 impact assessment method which contains midpoint impact categories such as climate change, acidification, and human toxicity. It was stated that type 1 packaging is more environmentally friendly than type 3. Considering the energy balance, it is stated that type 3 consumes 63% more energy than type 1. In addition, it was stated that the global warming potential of type 3 is 70% higher than PVC blister packages, and water depletion in type 3 is more than 80% compared to type 1 (Raju et al., 2016).

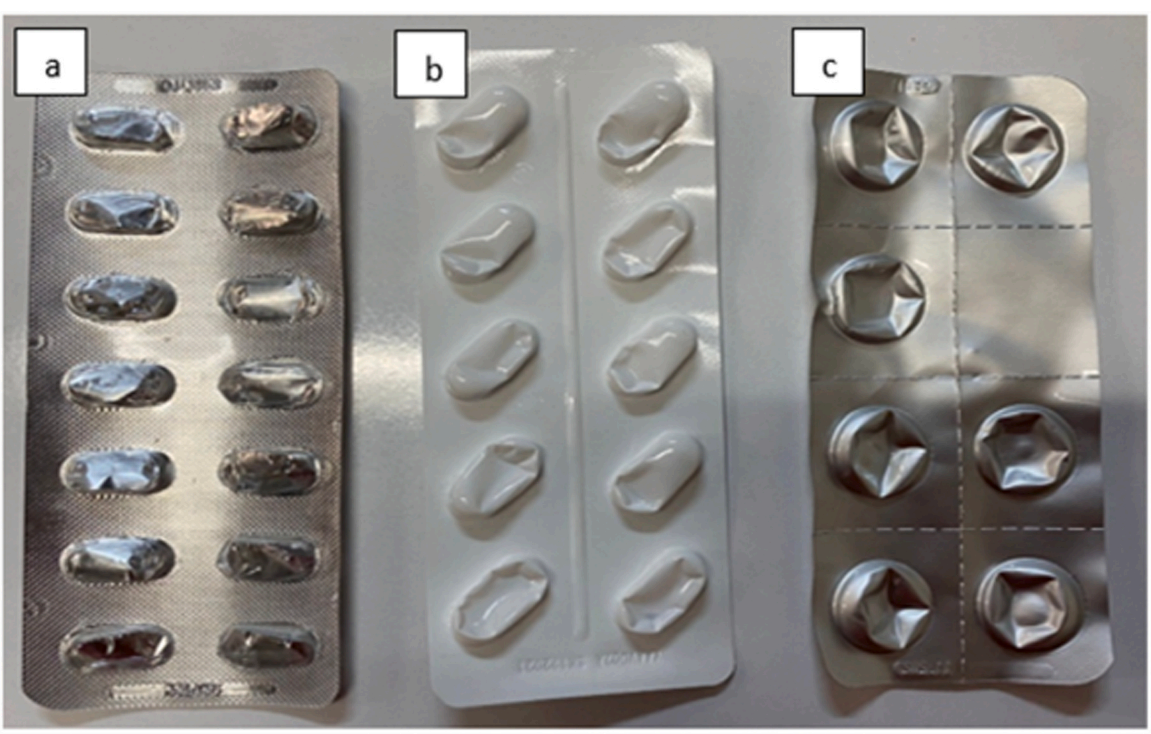

Fig. 3. Types of pharmaceutical blisters a) type 1, b) type 2, c) type 3.

Table 2
Elemental composition (wt.%) of the layers in type 2 and 3 blisters (Shukla et al., 2022).

Element	O	Na	Al	Si	P	S	Cl	Zn	Ca	Ti	Pd	Sn	Fe
Type 2													
P. layer 1	11.6	0.1	0.3	0.2	-	0.4	81.5	-	0.03	-	4.6	1.4	-
P. layer 2	16.1	1.3	0.3	0.1	0.4	0.8	76.6	0.2	-	-	4.3	-	-
Al layer	1.6	-	95.8	1.1	-	0.04	1.1	-	0.02	-	-	-	0.4
Type 3													
P. layer 1	15.8	-	0.5	0.2	-	0.4	73.0	-	0.1	4.6	4.6	0.9	-
P. layer 2	12.5	1.6	0.3	0.1	0.4	0.8	80.1	-	-	-	-	-	0.8
Al layer	1.8	-	97.3	-	0.1	-	0.1	-	-	-	-	-	0.8

4. Separation of the layers in pharmaceutical blisters

Since pharmaceutical blisters are multi-layered structures, it is necessary to separate these different layers before recovery. In the literature, 3 methods are mentioned as separation methods. These methods are the hydrometallurgical method, thermal degradation and electrohydraulic fragmentation (EHF). The hydrometallurgical method in which either one layer is targeted to take aluminium in solution or separate the layers by only dissolving the glue between the layers. Another method is thermal degradation which degrades the plastic part and separates it from the aluminium by forming corporate materials. The last method is electrohydraulic fragmentation which separates the aluminium from plastic by a new application of EHF and as well as decreases energy consumption.

4.1. Hydrometallurgical methods

Hydrometallurgical methods are commonly used for the separation of aluminium and plastic of WPBs. Hydrochloric acid (HCl) is one of the most preferred solvents for the separation. Some reagents such as sodium hydroxide (NaOH), formic acid (CH_2O_2), acetic acid ($C_2H_4O_2$), organic solvent (benzene-ethanol-water) (C_6H_6 + C_2H_6O +H_2O), deep eutectic solvent (DES) ([$(CH_3)_3NCH_2CH_2OH$] Cl+ $C_3H_6O_3$), lactic acid ($C_3H_6O_3$), N, N-Dimethyl cyclohexylamine (DMCHA) ($C_8H_{17}N$), ethanol (C_2H_6O), acetone (C_3H_6O) and isopropanol (C_3H_8O) are used for the separation trials in the literature.

4.1.1. Reagents that dissolve aluminium

Wang et al. used hydrochloric acid for the separation process. The pharmaceutical blister samples were prepared by cutting 1 cm × 1 cm or 1 cm × 2 cm for the experiments. It was observed that aluminium was completely dissolved in the solvent and plastic was separated. The separated plastic part was analysed with FTIR and the solution was analysed by spectrophotometric analysis. The effect of experimental factors (temperature, time, liquid/solid ratio, hydrochloric acid concentration and speed rate) was investigated on separating aluminium from plastic. It was observed that increasing temperature increases the separation of aluminium. In addition, it was shown that the dissolution rate of aluminium increased with increasing hydrochloric acid concentration, leaching time, and stirring rate. PVC from aluminium of 100% was separated in these conditions: 2.5 M HCl, 25 °C, 4 h, liquid/solid ratio 15:1 however, aluminium was not recovered since it dissolves in the solvent (Wang et al., 2015).

Chong-qing et al. studied the behaviour of pharmaceutical blisters in sodium hydroxide solutions. Type 1 blisters were used in the dimensions of 1 × 2 cm. Trials were conducted in a 1.25 M NaOH solution at 70 °C, for 20 mins with a solid/liquid mass ratio of 15:1. In addition, by using xylenol orange as an indicator and the EDTA (ethylene diamine tetra acetic acid) titration method determine the amount of Al^{3+} in the leaching solution. The aluminium leaching rate was up to 100% suggesting that aluminium and PVC are separated. It was reported that the most important factor was the sodium hydroxide concentration, followed by the leaching time and temperature. However, the recovery of aluminium from the solution is not possible similar to hydrochloric acid results (Wang et al. 2015).

4.1.2. Reagents that dissolve the glue

Rimšaitė et al. used formic acid, acetic acid, and organic solvents (mixed with benzene-ethanol-water) for the separation. Type 1 blister packages were used as a sample. Also, each reagent was prepared in 4 M (mol/L), and 200 ml volumes and blisters were prepared by cutting 1×1 cm samples. Experiments with all three reagents were carried out with stirring at 60–100 °C and 300 rpm (round per minute). Under suitable conditions, the reagents separated the metal and polymer layers, which allows recovery for both the metal and polymer. The solution was analysed by a UV spectrometer which showed that no aluminium was dissolved except in formic acid solutions. The mass loss was 0.02–0.08% in the use of formic acid (Rimšaitė et al., 2019) This may be due to the formation of aluminium formate which is aluminium salt of formic acid (Vargel, 2020). Furthermore, the organic solvent (benzene-ethanol-water) showed a better separation in comparison to the other two reagents (formic acid and acetic acid). It was reported that pharmaceutical blisters contained 17% aluminium.

Nieminen et al. used DES for the separation process. This study used all three types of blisters and experiments were performed with a 1 g sample. In addition, DES was prepared by mixing choline chloride and lactic acid (1:9) at 90 °C for about 60 min until being transparent. Lactic acid is not volatile and toxic, so it has a good option for the separation process. Also, all experiments were carried out with different parameters (80–120 °C, 50–100 wt% solvent concentration, 1:30–3:30 solid-liquid mass ratio and 0–200 rpm stirring speed). When temperature increases, the separation time decreases, and the separation time increases when solvent concentration and solid-liquid ratio decrease. Also, lactic acid is attacking the bond (glue) between plastic and aluminium, so it is an acceptable solvent for separation. Furthermore, Nieminen et al. analysed the polymeric layer using FTIR (Fourier-Transform Infrared Spectroscopy) and the metallic layer using SEM-EDS (Scanning Electron Microscope and Energy Dispersive X-ray Spectroscopy). They indicated that there are different polymer layers in pharmaceutical blisters by using Table 3 which represents the FTIR peaks and the relevant layer in the studies (Jung et al., 2018; Liang and Krimm, 1956; Zięba-Palus, 2017). It was observed that the polymer layer is PVC and there is an acrylic glue between the aluminium and PVC, matching the peaks for the three types. In addition, forming film that is the polymer layer closely specific peak that is PCTFE (polychlorotrifluoroethylene) and nylon for type 2 and type 3. The mass loss of aluminium was analysed by ICP analysis (Inductively Coupled Plasma) and the mass loss of aluminium content was calculated by ICP (Nieminen et al., 2020). Nieminen et al. indicated DES causes corrosion on the surface of the aluminium. Lactic acid was used both diluted and pure at different temperatures. It was concluded that the mass loss of aluminium was less than 5% when pure lactic acid was used. It has been reported that using pure lactic acid in future studies will be more efficient in terms of aluminium mass loss.

Additionally, it was observed that the surface of aluminium processed in lactic acid was smoother than the DES according to the EDS results. Finally, the main purpose of Nieminen et al. study is to evaluate the solvents' reusability. A total of six replicates were made for lactic acid and DES and it has been reported that the colour change in the solvent may prolong the separation time when reused. Therefore, it is necessary to purify solvents for the industry before re-using them (Nieminen et al., 2020).

Yousef et al. used reagents (DMCHA) and pure Ethanol for the separation process. Six different types of blister packages, including different sizes, colours, and contained pill types, were used. SEM-EDS analysis was used to obtain the metallic layer and location of a polymeric layer in the blister package. Alloying elements such as Ti (titanium), Si (silicon) and Fe (iron) were found in the metal layer. FTIR was used to identify the polymeric layer, and TGA- DSC (thermogravimetric analysis-differential scanning calorimetry) was used to control the forming film's thermal stability and glass transition temperature for each sample. The observation of chlorine indicates that the polymeric layer was PVC and PVDC. The range of thickness of the blisters was 130–250 mm. PVC with varying temperatures is shown in Fig. 4. Colour change was observed at 60 and 80 °C which is a sign of deterioration. Thus, 40 °C was chosen and the DMCHA ratio was determined as 1:3 g/ml (Yousef et al., 2018).

Shukla et al. used acetone and isopropanol for delamination experiments and acetone was diluted with isopropyl alcohol. Experiments were carried out 0–100% (v/v%) with a stirring rate of 600 rpm at 30–50 °C. 13, 10 and 15 wt% of the aluminium layer was separated from the PVC was for blister types 1, 2 and 3 respectively. Aluminium purity was measured by ICP-OES and reported that it was > 99.4% for types 2 and 3. FTIR analysis showed that the plastic layer consisted of PVC and PVDC and the adhesive material between layers was polyacrylic-based. The overall thickness of the blisters ranged from 280 to 365 µm (260–330 µm for the plastic layer and 20–35 µm for the aluminium layer). Shukla et al. concluded that the delamination process for blisters by using acetone and isopropyl alcohol (50 v/v% and 200 ml) was effective (Shukla et al., 2022).

The experimental parameters of all the reagents used in the hydrometallurgical methods are summarized in Table 4.

4.2. Thermal degradation

The most suitable pyrometallurgical method for the separation of plastics and metal in pharmaceutical blisters is the thermal degradation. Due to the high amount of plastic, combustion techniques are not recommended. Thermal degradation occurs in the absence of oxygen. The products of this process can be separated into three fractions: solid, liquid, and gaseous. The non-pyrolyzing elements, or metals, end up in the solid fraction. The metal fraction can be extracted from the char by basic metallurgical procedures (Klejnowska et al., 2020; Pikoń et al., 2021). Klejnowska et al. and Pikoń et al. conducted thermal degradation with pre-consumer and post-consumer pharmaceutical blisters (Fig. 5). Pre-consumer waste materials have no contact with the drugs and transparent plastic was utilized as the lidding material. Postconsumer waste materials have several types of pharmaceutical blisters that removed drugs. Klejnowska et al. analysed them and presented that an analysed part of the postconsumer waste materials containing: Red plastic: 3.9%, Al/Al blister: 9.9%, Orange plastic: 15.0%, Transparent plastic: 32.7%, White plastic: 38.5%.

Chemical analysis was applied to both materials. (See Table 5). The main difference between the two materials is the presence of chlorine. Pre-consumer waste includes higher chlorine than post-consumer waste. The reason for this is lidding mate-rial in pre-consumer. Lidding material is just PVC in pre-consumer, but post-consumer includes several types of materials (Klejnowska et al., 2020; Pikoń et al., 2021).

The thermal degradation experiments were performed at three different temperatures (400 °C, 425 °C, and 450 °C). Off-gas was collected at the beginning, middle, and end of the experiment. FID (flame ionization detector) was used for hydrocarbons and TCD (thermal conductivity detector) was used for inorganic compounds (Klejnowska et al., 2020; Pikoń et al., 2021).

Klejnowska et al. specified the calorific value of the gas at 450 °C for both samples. (21.96 MJ/m^3 for post-consumer and 20.14 MJ/m^3 for pre-consumer). Also, Piko'n et al. stated that at 450 °C, the greatest calorific value of gas was observed for post-consumer waste materials. There were no differences quality of the gas for both samples. In other words, impurities inside both samples did not affect the quality of the gas. Eventually, 450 °C was selected suitable temperature to produce the gaseous fuel (Klejnowska et al., 2020).

Table 3
The FTIR peaks for the identification of polymeric layers (Jung et al., 2018; Liang & Krimm, 1956; Zięba-Palus, 2017).

Polymer	Literature (cm^{-1})	peak assignment
PVC	1427, 1426	CH_2 bend
	1331, 1328	C-H bend
	1255, 1239	C-H bend
	1099, 1095	C-C stretch
	966, 962	CH_2 rock
	616, 609	C-Cl stretch
Acrylic glue	1730	C=O stretch
	1450	CH_2 bend
	1380	CH_2 bend
	1265–1240	C-O-C stretch
	1165	C-O-C stretch
PCTFE	1285, 1279	C-F stretch
	1194, 1191	CF_2 stretch
	1130, 1120	CF_2 stretch
	972, 961	C-Cl stretch
	580, 579	CF_2 wagging
Nylon	3298, 3317	N-H stretch
	2932, 293	C-H stretch
	2858	C-H stretch
	1634, 1625	C=O stretch
	1538	N-H bend, C-N stretch
	1464	CH_2 bend
	1372, 1363	CH2 bend
	1274, 1271	N-H bend, C-N stretch
	1199,1202	CH2 bend
	687	N-H bend, C=O bend

Piko'n et al. separated the char and metallic fraction from the post-consumer waste materials after the pyrolysis process for chemical analyses (Fig. 6). They reported that the separation of aluminium was 85–90% (an average of 86.4% for pre-consumer waste and 88.5% for post-consumer waste). During the thermal process, all coatings and paints were removed. Piko'n et al. calculated the calorific value of samples and mentioned that the sample produced by conducting the process on post-consumer material at 400 °C had the greatest heat of combustion value (32,534 kJ/kg). Table 6 presents ratio of char and the metal fraction for both samples after thermal degradation at 400, 425, and 450 °C. Aluminium separated from the char was remelted. The remelting process was done on a laboratory-scale electric furnace with an addition of $MgCl_2$, NaCl and $Na_3(AlF_6)$ at 800 °C and almost 90% of the aluminium content was recovered (Pikoń et al., 2021).

4.3. Electro hydrophilic Fragmentation (EHF)

Agarwal et al. applied the Electro hydrophilic fragmentation (EHF) technique for type 1 and type 2 blister packages. The phosphoric acid solution in a 4:1 vol ratio was prepared for leaching. Experiments were done with an electrode gap of 40 mm, 300 pulses, frequency of 3 Hz, 130 kV of discharge voltage, and 20 g/L ratios. It was determined by ICP-OES that the blisters contained 10 – 12 wt% aluminium and 88 – 90 wt% polymer fraction. SEM-EDS noted the presence of two polymer layers (possibly PVC) and an aluminium layer in the blisters' inner structure. In addition, it proved to be the EHF parameter with the most significant effect on increasing the separation and recovery of aluminium and polymer fractions and reducing the number of un-separated fractions in which aluminium was lost. It was also determined that the recovery or separation of aluminium was better in type 2 blisters compared to type 1 blisters. Lastly, Energy calculations of the process by Agarwal suggest that EHF could be a potential industrial-scale technique for recycling aluminium from blisters (Agarwal et al., 2020).

5. Discussion

Table 7 shows a summary of the reagents reported in this review work including their chemical behaviour against the metal, plastic, and glue as well

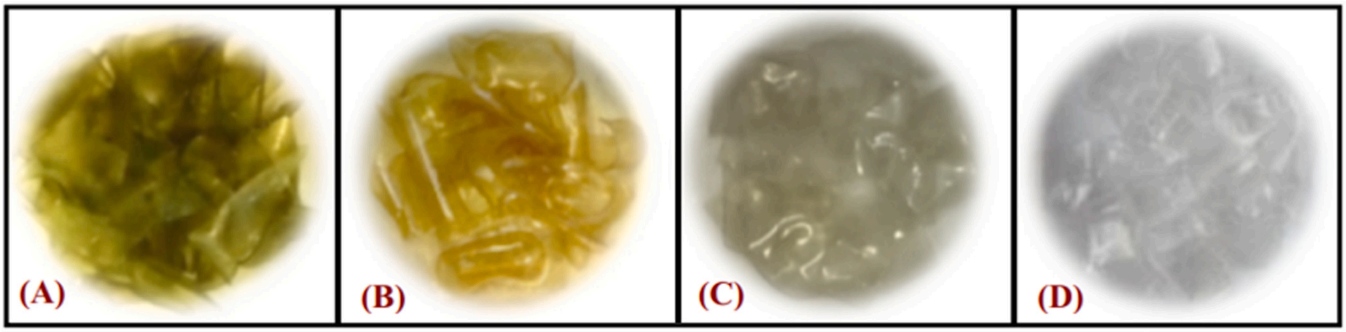

Fig. 4. Forming films recovered at A) 80, B) 60, C) 50, and D) 40, °C (Yousef et al., 2018).

Table 4
Summary of experimental parameters used for the hydrometallurgical separation of blister layers.

Ref	Sample	Reagent	Conditions	Analysis method
(Wang et al., 2015)	type 1	HCl (1.3–2.5 M)	25–50 °C 0–1000 rpm up to 360 min	visible spectrophotometric analysis FTIR
(Wang et al. 2015)	type 1	NaOH (1.25 M)	70 °C 400 rpm 20 min 15:1 solid-liquid mass ratio	
(Rimšaitė et al., 2019)	type 1	CH_2O_2 $C_2H_4O_2$ organic solvent (C_6H_6- $C_3H_6O_3$ – H_2O)	60–100 °C 300 rpm 30 min	visible spectrophotometric analysis
(Nieminen et al., 2020)	type 1, 2, 3	DES $C_3H_6O_3$	80–120 °C 0–200 rpm 50–100 wt% solvent concentration 1:30–3:30 solid-liquid mass ratio	FTIR, SEM-EDS, ICP-MS
(Yousef et al., 2018)	type 1, 2, 3	DMCHA + C_2H_5OH	40–80 °C 120–180 min	SEM-EDS, FTIR, TGA, DSC
(Shukla et al., 2022)	type 1, 2, 3	C_3H_6O + C_3H_8O	30–50 °C 600 rpm 0–100% (VC_3H_6O /VC_3H_8O %)	ICP-OES, FTIR

as their toxicity.

Hydrochloric acid, formic acid, acetic acid, mixed organic solvents, and sodium hydroxide have high toxicity, but DES, lactic acid and mixed acetone-isopropyl alcohol have low toxicity. DMCHA/ethanol has medium toxicity.

Hydrochloric acid, sodium hydroxide and DES completely dissolve the aluminium layer. This is undesirable as it negatively affects the recycling of aluminium economically. The plastic layers can be separated by these reagents however, aluminium cannot be recovered as metal from the aqueous solutions. On the other hand, formic acid dissolves aluminium at a level that can be

Table 5
Chemical analysis of the pre-and postconsumer waste materials [5].

Sample	Content (%)				
	C	H	Cl	N	S
Pre-consumer	45.46	4.47	43.66	0.60	10.83
Postconsumer	44.27	3.37	35.03	0.35	11.33

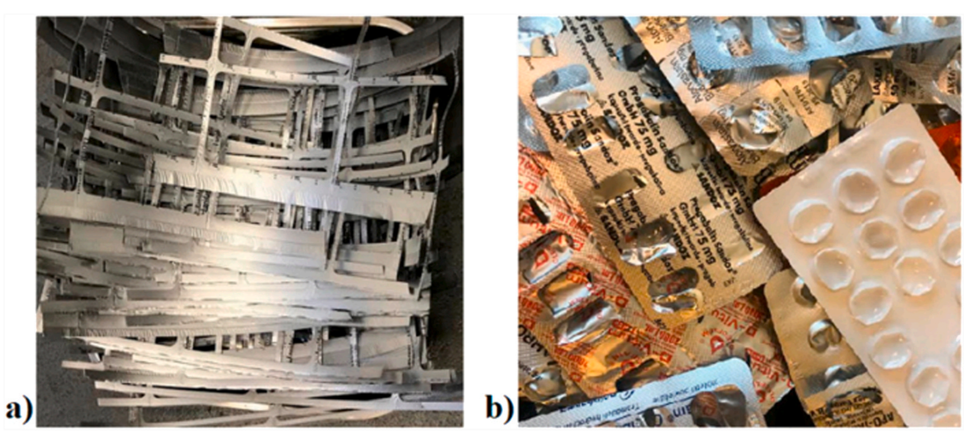

Fig. 5. Analysed materials; (a) pre-consumer waste, (b) postconsumer waste (Klejnowska et al., 2020).

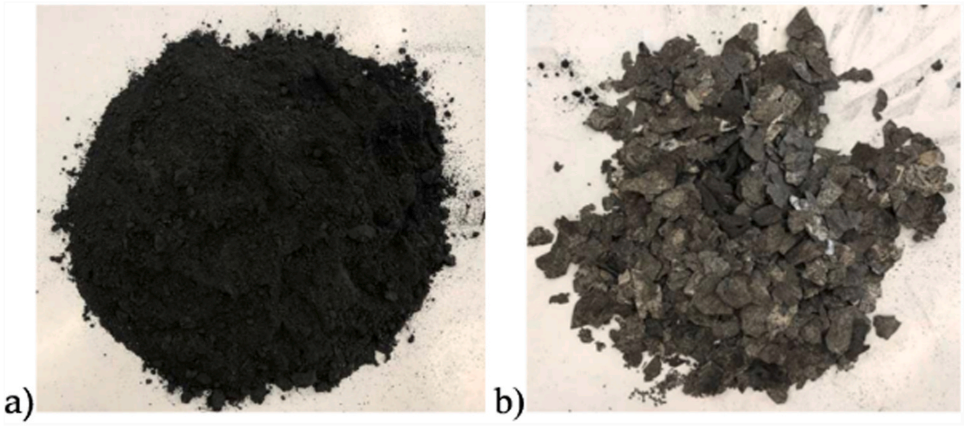

Fig. 6. a) post-pyrolysis char obtained after the separation of the solid fraction. b) Post-pyrolysis metallic fraction obtained after the separation of the solid fraction (Pikoń et al., 2021).

Table 6
The mass distribution of the metal and char after thermal degradation of pre-and post-consumer blisters (Pikoń et al., 2021).

Temperature (°C)	Pre-consumer (wt%)		Post-consumer (wt%)	
	metal	char	metal	char
400	40.5	59.5	36.4	63.6
425	42.6	57.4	37.4	62.6
450	44.4	55.6	39.6	60.4

Table 7
Comparison of different reagents used for hydrometallurgical separation of blister layers.

Reagent	**Toxicity**	**Dissolution of**		
		Metal	**Glue**	**Plastic**
HCl	High	✓	✓	×
$C_2H_4O_2$	High	×	✓	×
CH_2O_2	High	up to 0.08%	✓	×
$C_6H_6 + C_2H_6O$	High	×	✓	×
$[(CH_3)_3NCH_2CH_2OH]Cl + C_3H_6O_3$	Low	✓	✓	×
$C_8H_{17}N + C_2H_6O$	Medium	×	✓	×
$C_3H_6O + C_3H_8O$	Low	×	✓	×
NaOH	High	✓	✓	×
$C_3H_6O_3$	Low	< 5%	✓	×

ignored (0.02–0.08%). Other solvents do not dissolve aluminium and do not create an economic disadvantage in terms of recycling. In addition, all the reagents discussed here dissolve the adhesive, but do not react or dissolve in any way with the plastic layers so they lead to a good separation between the plastic and metal fractions.

Thermal degradation of blisters at 450 °C allows a good separation of aluminium and plastic fractions where the plastic fraction is transformed into carbonaceous materials which can be used as an alternative fuel. An economical and environmental assessment should be performed to analyse the feasibility of this process in terms of cost and environmental impact.

EHF is an effective method to separate aluminium from plastic and EHF provides a reduction of energy consumption.

6. Conclusions

The published studies concerning the recycling of waste pharmaceutical blisters were reviewed and discussed in the current paper. In the light of the cited studies, the following conclusions could be drawn:

- The plastic layers of the blisters contain PVC or PVDC which indicates any thermal treatment may have serious environmental impacts.
- Choline chloride and lactic acid mixture (DES), Hydrochloric acid and sodium hydroxide dissolve the aluminium layers completely and cause unrecoverable loss of the aluminium
- Choline chlorine, lactic acid, acetone, and isopropyl alcohol containing solvents dissolve the glue the between the layers without reacting with aluminium or plastic. By talking their low toxicity into consideration, these reagents can be good options for the separation of the blister layers.

Data availability

Data will be made available on request.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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