UNIVERSIDADE D
COIMBRA

Margarida Pimentel de Amorim Ribeiro

**Relatórios de Estágio e Monografia intitulada "The Issue with Microplastics and their Effects on Human Health" referentes à Unidade Curricular "Estágio", sob a orientação da Dra. Tânia Neves, da Doutora Cátia Augusto e do Professor Doutor André Pereira, apresentados à Faculdade de Farmácia da Universidade de Coimbra para apreciação na prestação de provas públicas de Mestrado Integrado em Ciências Farmacêuticas.**

Setembro de 2022


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Coimbra, 1 de setembro de 2022.

Margarida Pimentel de Amorim Ribeiro

(Margarida Pimentel de Amorim Ribeiro)

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Index

**Parte A - Relatório de Estágio em Farmácia Comunitária**



**Parte B – Relatório de Estágio em Indústria Farmacêutica**

**Parte C – Monografia "The Issue with Microplastics and their Effects on Human Health"**

# Parte A

## Relatório de Estágio em Farmácia Comunitária


Orientado pela Dra. Tânia Neves, de 10 de janeiro a 29 de abril de 2022

## LISTA DE ABREVIATURAS

**BQ** Bioquímicos

**CE** Contraceção de Emergência

**COVID-19** Doença do Coronavírus 19, do inglês *Coronavirus Disease* 19

**DT** Diretora Técnica

**FT** Farmácia Termal

**MICF** Mestrado Integrado em Ciências Farmacêuticas

**MNSRM** Medicamentos Não Sujeitos a Receita Médica

**SARS-CoV-2** Coronavírus de Síndrome Respiratória Aguda Grave 2, do inglês *Severe Acute Respiratory Syndrome Coronavirus 2*

**TRAg** Teste Rápido de Antigénio

## Introdução

O farmacêutico é tido, cada vez mais, como o principal elo entre a população e os serviços de saúde, devido à posição privilegiada de proximidade que com esta mantém. A farmácia é, muitas vezes, o primeiro, e único, local a quem a população se dirige em casos de dúvidas e preocupações com a saúde, demonstrando grande confiança nos conhecimentos e aconselhamentos do farmacêutico. De facto, o farmacêutico é um profissional de saúde capacitado de múltiplos recursos e conhecimentos para proporcionar o melhor aconselhamento, para a resolução ou controlo de problemas de saúde, assim como o correto encaminhamento aos serviços de saúde, quando necessário. Deste modo, torna-se fácil perceber o quão imprescindível o estágio em farmácia comunitária para a formação de novos farmacêuticos, na medida em que permite colocar em prática os conhecimentos adquiridos, bem como a sua consolidação. Proporciona ainda uma excelente oportunidade de aprendizagem de comunicação em saúde, aconselhamento farmacêutico e atendimento ao público.

Nesta conformidade, realizei o estágio curricular na Farmácia Termal (FT), localizada na Curia, entre os meses de janeiro e maio, num total de 670 horas, sob orientação da Diretora Técnica (DT), a Dra. Tânia Neves. Além da DT, a equipa da FT é, atualmente, constituída por mais uma farmacêutica e duas técnicas de farmácia, que tornam a FT numa farmácia extremamente dinâmica, competente e especializada em tudo o que concerne a produtos de saúde e bem-estar, sejam eles fármacos, cosméticos ou fitoterápicos.

A população abrangida pela FT é, tendencialmente, uma população envelhecida. Esta é ainda responsável por um lar de terceira idade. Sendo a Curia uma estância termal, encontramos também vários utentes de passagem.

O presente relatório serve, então, para a avaliação SWOT (*Strengths, Weaknesses, Opportunities and Threats*) deste estágio, analisando de uma perspetiva interna (*Strengths* e *Weaknesses*), bem como de uma perspetiva externa (*Opportunities* e *Threats*) a minha experiência enquanto estagiária na FT.

# 1. Análise SWOT

## 1.1. *Strengths*

### 1.1.1. Serviços Farmacêuticos

A FT dispõe de dois gabinetes de atendimento, de modo a estabelecer uma maior confidencialidade e proximidade com os utentes. Os gabinetes estão equipados com os aparelhos necessários à realização de medições de parâmetros BQ, sendo que um gabinete é preferencialmente utilizado na medição destes parâmetros e o outro para a administração de injetáveis. No fim da avaliação dos parâmetros BQ, é fornecido aos utentes um cartão de registo com os valores devidamente anotados, de modo a que possa proceder a uma monitorização contínua da sua saúde. Durante este estágio relembrei como proceder à medição de diversos parâmetros BQ, como a glicémia, o colesterol e a pressão arterial. Graças à incidência do plano curricular de MICF na análise e interpretação destes parâmetros, consegui retirar conclusões adequadas dos valores apresentados e ainda a comunicá-los aos utentes de modo claro e conciso, bem como a aconselhar alterações de estilo de vida apropriadas ou a encaminhar para o médico em casos mais preocupantes. Constatei ainda a grande preocupação que alguns utentes demonstravam em monitorizar regularmente estes parâmetros, de modo a estarem sempre cientes da sua saúde. No que concerne aos injetáveis, tive a oportunidade de observar, mediante o consentimento do utente, algumas administrações.

### 1.1.2. Análises clínicas

A FT integrou no seu leque de serviços as análises clínicas, em parceria com o laboratório Mário Alvim, perto do fim do meu estágio. Contudo, mesmo tendo sido poucas as vezes que se realizaram enquanto estive na FT, pude constatar uma grande adesão pela parte da população. Mais uma vez, vi o farmacêutico como primeira linha de saúde, pois eram inúmeras as vezes que os utentes se deslocavam até nós para os ajudarmos a compreender os resultados das análises. E, graças ao plano de estudos do MICF, apercebi-me que eram muitas as vezes em que conseguíamos fazer uma interpretação primária e, em certos casos, acalmar o doente enquanto aguardava pela consulta médica.

### 1.1.3. Conhecimentos de inglês

A Curia, além de ser uma estância termal, é também uma localidade com um elevado número de emigrantes e imigrantes. No decorrer do estágio foram vários os utentes estrangeiros, que não falavam português, que se dirigiam à FT na esperança de

aconselhamentos. A proficiência que possuo na língua inglesa demonstrou ser uma mais-valia para a comunicação, na medida em que dilui as barreiras de comunicação.

## 1.2. *Weaknesses*

### 1.2.1. Aconselhamento em puericultura, dermofarmácia e cosmética, e medicamentos veterinários

Apesar do plano curricular de MICF ter uma grande incidência na área de dermofarmácia e cosmética, existe um elevado número de produtos, gamas e marcas disponíveis, adaptados a todas e quaisquer necessidades do cliente. Pese embora as competências de autonomia que detenho na procura de informação e formação, por forma a transformar em conhecimento e colmatar algumas das lacunas sentidas nestas áreas, senti que para fazer o melhor aconselhamento das gamas existentes, é necessário tempo e experiência para se forme conhecimento que nos permita fazer o aconselhamento desejável. Apesar da enorme ajuda da equipa da FT, que se demonstrou sempre disponível a auxiliar o atendimento e a esclarecer as minhas questões, bem como as diferentes formações a que assisti, sinto que o tempo necessário ao correto domínio destes conhecimentos supera a duração do estágio.

No que concerne à puericultura e patologias associadas a bebés, a pouca incidência nestes temas no plano curricular leva a algum desconhecimento e insegurança no atendimento. Porém, pude assistir a uma formação da marca Dr Browns®, que permitiu adquirir novos conhecimentos sobre os diferentes tipos de biberões, chupetas e acessórios de puericultura, e da marca de leites em pó Capricare®, que no imediato consegui aplicar no aconselhamento.

A Curia, não sendo uma área muito urbana, tem um grande número de agricultores e criadores de gado, além de animais domésticos. Embora no plano curricular de MICF esteja englobada a unidade curricular de Preparações de Uso Veterinário, senti que os conhecimentos adquiridos foram mais ao nível das diferentes formas farmacêuticas disponíveis e os seus parâmetros farmacocinéticos. Desta forma, o atendimento com produtos veterinários tornou-se desafiante por não estar tão segura.

Porém, todas estas dificuldades tornaram-se em oportunidades de aprendizagem. Observei atentamente os atendimentos que a equipa realizava, esclarecendo todas e quaisquer dúvidas, o que me permitiu consolidar os meus conhecimentos e proporcionar um melhor atendimento.

### 1.2.2. Desconhecimento de nomes comerciais e embalagens de medicamentos

Devido à instituição da prescrição por Denominação Comum Internacional, no decorrer do percurso no curso de MICF aprendemos a designação dos fármacos pela substância ativa. Contudo, ao chegar à farmácia comunitária, deparamo-nos com vários utentes cuja terapêutica é realizada com o medicamento de marca e só o reconhecem por esse nome o que, por vezes, dificultava o atendimento por não reconhecer essa designação.

Por outro lado, existem utentes cujo medicamento que utilizam é o genérico, e sabem o nome da substância, e por vezes até a cor da caixa, porém não sabem qual o laboratório do genérico. O que leva a algumas situações caricatas no atendimento em que, principalmente no início do estágio quando o conhecimento dos laboratórios existentes na FT ainda era reduzido, tinha de ir buscar uma caixa de cada laboratório existente para que o utente conseguisse identificar o que tomava.

Contudo, com o avançar do tempo, ao começar a familiarizar-me com os laboratórios e com os utentes, consegui com alguma facilidade ultrapassar esta barreira.

## 1.3. *Opportunities*

### 1.3.1. Formações

Sendo que a FT tem um grande portfólio de produtos, é importante que a equipa esteja em constante atualização científica e lhe seja possível esclarecer quaisquer dúvidas rapidamente. Deste modo, foi-me permitido assistir a diversas formações das mais variadas áreas, que me permitiram aprofundar conhecimentos e aprender mais. O que pude pôr em prática nos atendimentos. Foi-me ainda solicitado realizar uma formação sobre suplementos alimentares da SOLGAR® que se constituiu como uma mais-valia para a minha aprendizagem e formação, tanto sobre os produtos como também sobre a comunicação ao público.

### 1.3.2. Integração nas redes sociais e internet

Atualmente a presença *online* é muito importante para o sucesso de um negócio. A FT tem *Instagram* e *Facebook*, bem como um *website* atualizado diariamente. Desta forma, podemos dar resposta a pedidos de população mais distante, que são prontamente entregues por CTT, e também garantimos que os clientes que seguem as nossas páginas têm informações rápidas sobre promoções, consultas, eventos e até concursos e formações na farmácia.

### 1.3.3. Medicamentos Naturais

A fitoterapia recorre a plantas para tratar e até prevenir certas doenças e tem vindo, cada vez mais, a ocupar um maior espaço nas farmácias. A população tende a preferir medicamentos fitoterápicos por estes serem naturais, ao que associam menos riscos e efeitos secundários, e, efetivamente, tendem a aderir mais depressa e melhor a terapias naturais. A FT sendo uma farmácia Apoteca Natura, tem toda a variedade de produtos fitoterapêuticos desta gama e a população que a farmácia abrange demonstra um grande interesse nestes medicamentos. Sendo a FT uma farmácia que aposta em medicamentos naturais, não poderia deixar de referir a PRANAROM®, uma marca de óleos essenciais e fórmulas de tratamento das mais variadas patologias. Portanto, considero que a ampla presença desta classe terapêutica na farmácia, permitiu-me um maior desenvolvimento e aprofundamento os conhecimentos em fitoterapia de um modo que talvez não fosse possível noutro local. De referir que a satisfação dos utentes era notória, sendo que muitos referiam ser o único medicamento que os ajudava e voltando sempre para comprar mais. Realço que foram os conhecimentos adquiridos ao longo do plano curricular, as formações e a ajuda da equipa técnica da FT que me ajudaram a ter a fundamentação necessária para aconselhar estes produtos.

### 1.3.4. Consultas de Podologia, Nutrição e Rastreios Auditivos

A disponibilização destas consultas na FT potenciou o crescimento da minha sensibilidade e conhecimentos nestas áreas. De modo que agora me sinto mais confortável na realização de aconselhamentos de prevenção e tratamento de problemas podológicos, desde pé diabético a infeções fúngicas.

As consultas de nutrição, e a adesão que tinham, fez-me perceber que a nossa população está cada vez mais a investir em Educação para a Saúde. A dinamização destas consultas, permitiu fazer o encaminhamento de alguns utentes que manifestavam desagrado ou preocupação com o seu peso, devido à existência de patologias agravadas pelo excesso de peso, que procurava, dietas necessárias à manutenção de saúde ou até mesmo apenas o desejo de perder peso. Ao disponibilizarmos estas consultas, a população pode ser corretamente acompanhada e aconselhada neste nível.

Relativamente aos rastreios auditivos, estes suscitaram maior interesse e sensibilidade para o problema que é a perda de audição, assim como para os problemas que daí advém, nomeadamente emocionais e relacionais, dada a forma negativa como o utente por vezes reage quando confrontado com a perda de audição. Pelo que me permitiu melhorar a minha capacidade de análise, comunicação e aconselhamento perante este problema.

### 1.3.5. Filosofia *Kaizen*

Pude observar que a introdução da metodologia *Kaizen* na FT, como uma cultura e um sistema de melhoria contínua, me permitiu ser mais organizada e, deste modo, melhorar a minha resposta ao utente, bem como aumentar a minha rentabilidade.

## 1.4. *Threats*

### 1.4.1. Literacia da população

Sendo a população das redondezas um pouco mais envelhecida, vi-me confrontada com várias situações no atendimento para as quais não me sentia bem preparada. Contudo, pedi ajuda à equipa e rapidamente consegui ultrapassar essa barreira. Eram vários os utentes que nos chegavam que não sabiam ler nem escrever, bem como alguns que tinham dificuldades auditivas não tratadas, ou então utentes que simplesmente não entendiam o que o médico lhes tinha explicado. Todos estes veem a FT como um porto de auxílio o que me permitiu desenvolver as competências necessárias de comunicação de saúde ao público.

### 1.4.2. SARS-CoV-2

O meu estágio decorreu de janeiro a abril, que foram ainda meses com elevado número de casos COVID-19. A situação pandémica vivida nestes meses impactou muito o meu estágio, pois, a presença dos acrílicos de proteção tornou-se uma barreira à comunicação, fazendo com que os utentes não nos conseguissem entender tão bem. Por outro lado, sendo que a FT realizava Testes Rápidos de Antigénio (TRAg), a afluência da população das redondezas a este serviço foi notável, provocando mesmo filas de espera. Estas filas impactavam o nosso atendimento, tanto por provocar um sentimento de urgência, em nós e nos utentes, e também porque alguns clientes, ao verem filas grandes na farmácia, desistiam de esperar e iam embora, o que acaba por impactar economicamente a FT.

### 1.4.3. Rutura de *stocks*/Esgotados

No decorrer do estágio, foram diversas as vezes em que me deparei com a impossibilidade de encomendar medicamentos. Esta situação recorrente causa transtornos no atendimento e na relação utente-farmácia. De um momento para o outro o utente depara-se com uma situação não ideal onde não tem acesso à sua terapêutica ideal e vê-se obrigado a substituir o laboratório que é habitual fazer ou, em outros casos, a ter de se dirigir ao médico de modo a alterar a terapêutica. Para além do impacto que isto tem na saúde do utente, tal como referi, prejudica também a confiança que este tem com a farmácia, pois não vê as suas

necessidades satisfeitas. Embora este descontentamento não seja geral, é notório em especial na população mais idosa, que desconfia de outro laboratório que não seja aquele que toma habitualmente, por medo de não fazer efeito ou de não fazer bem.

### 1.4.4. Erros de *stock*

Os erros de *stock*, embora ocasionais, refletiam-se num atendimento mais demorado ao utente. Pude constatar que estes erros se deviam ou a erros na entrada de encomendas ou na saída de produtos e/ou medicamentos. Contudo, a FT promove auditorias de *stocks* mensais, que permitem detetar estes erros antecipadamente. Também ao dar entrada de encomendas e ao arrumar, seguindo a organização *Kaizen* da bancada de receção, podemos também detetar estes erros antes destes impactarem o atendimento.

## 2. Casos Clínicos

### Caso 1

Utente pede pílula do dia seguinte para uma familiar, sabe apenas que a relação sexual foi à cerca de três dias e que a familiar referiu tomar metotrexato para o seu eczema. Não podendo recolher mais informação, como a altura do ciclo menstrual em que se encontrava, e tendo em conta que a relação tinha sido à 3 dias, a hipótese mais segura será Ella-One® (acetato de ulipristal)[1]. Pois Norlevo® (levonorgestrel) é mais eficaz até 72h após a relação[2], enquanto que a Ella-One® é eficaz até 120h. Adicionalmente, o levonorgestrel atua apenas na fase pré-ovulatória precoce e o acetato de ulipristal atua tanto na fase pré-ovulatória precoce como na tardia. Quanto ao metotrexato, não tem interação com Ella-One®.

Dispenso o medicamento e aviso de que a contraceção hormonal, caso a familiar a tome, pode ser retomada de imediato e que deve usar um outro método contracetivo de barreira até à próxima menstruação.

Alerto ainda sobre os possíveis efeitos secundários, como sensibilidade mamária, cefaleias, náuseas e vómitos que, embora raros, podem ocorrer de forma ligeira e transitória.

Por fim, recomendei que, caso não tenha a menstruação dentro de 1 semana da data normal que costuma ter, no máximo, deve realizar um teste de gravidez, pois a CE pode ter sido ineficaz ou a familiar poderia estar já grávida aquando da toma.

### Caso 2

O utente dirige-se à farmácia com queixas de diarreia aquando da toma de antibiótico, que não sabe nomear, e pede Imodium Rapid® [3]. Sendo que a diarreia é um possível efeito secundário do antibiótico, aconselho Prolif® [4]. Prolif® é um probiótico com *Saccharomyces*

*boulardii*, aconselhado no tratamento de diarreia aguda e diarreia iatrogénica. Este probiótico atua aumentando as culturas intestinais de lactobacilos e bifidobactérias, regularizando o trânsito intestinal. Aconselho a toma de um comprimido 2id durante a fase aguda e subsequente redução para 1id até ao fim da toma do antibiótico [4]. Quanto ao Imodium Rapid®, aconselho o uso apenas em caso SOS, como estar sem acesso a uma casa de banho ou estar fora de casa, uma vez que atua através da redução do peristaltismo e consequente aumento do tempo de trânsito intestinal, bem como o aumento do tónus do esfíncter anal. A sua posologia será então 2 comprimidos orodispersíveis e, caso necessário, 1 comprimido orodispersível após cada dejeção. Quanto a efeitos secundários, alerto que o Imodium Rapid®, ao parar o trânsito intestinal, pode causar obstipação e ainda flatulência [3].

**Caso 3**

O utente vai à farmácia pedir um xarope para a tosse do filho de 10 anos. Questiono quanto ao tipo de tosse, se seca ou produtiva, ao que o pai responde que é seca e irritativa. Questiono se o filho tem algum outro problema de saúde, como diabetes, que impeça a escolha de certos xaropes, ao que o utente responde não. Recomendo então a toma de Grintuss Pediátrico® [5], um antitússico com ação demulcente. Este dispositivo médico que vai auxiliar o combate da irritação da mucosa pela tosse seca, favorecendo ainda a hidratação e a eliminação de qualquer muco que se possa também encontrar no organismo da criança. Vai atuar através de um efeito barreira na mucosa, protegendo-a dos agentes irritantes, e através de uma ação lubrificante, reduzindo a fricção que provoca a tosse. Recomendo a toma de 2 colheres doseadoras 2 a 4 vezes ao dia, sendo a última toma à noite, de modo a proporcionar um melhor descanso. Aconselho ainda a toma entre as refeições ou cerca de 15 minutos após estas, evitando também beber água após a toma, de modo a que o xarope tenha tempo de atuar, revestindo a mucosa [5]. Por fim, alerto que deve dirigir-se ao médico caso a tosse persista por mais de 1 semana e se tiver febre.

**Caso 4**

A utente desloca-se à farmácia para pedir xarope para o pai, que tem tosse com expetoração. Questiono a utente se o pai é diabético ou se sofre de algum problema respiratório ou gastroduodenal que possa limitar a escolha do medicamento, ao que a utente responde que o pai é diabético. Deste modo, aconselho Bissolvon Linctus Adulto®[6], composto por cloridrato de bromexina. A bromexina é um mucolítico derivado não sulfonado que atua por reativação do movimento ciliar, facilitando a remoção do muco, e ainda através da diminuição da viscosidade deste. Este xarope não contém sacarose, sendo, portanto, apto para

doentes com diabetes. Aconselho à utente a toma de 5ml 3id e alerto que, inicialmente, irá constatar um aumento das secreções durante o tratamento, o que é normal e expetável, bem como um aumento da tosse para expelir o muco. Aconselho a ingestão de muita água, que irá ajudar também à fluidificação da expetoração, bem como na hidratação do seu pai. Por fim, alerto que deve dirigir-se ao médico caso a tosse persista por mais de 1 semana e se tiver febre.

**Caso 5**

Um utente desloca-se à farmácia, assustado, diz que realizou um teste à COVID-19 num laboratório e este deu positivo, mas não entendeu como. Como o utente se fez acompanhar pelo teste em formato eletrónico, conseguimos visualizá-lo e constatámos que se tratava de um teste serológico sanguíneo. Questionámos o utente se tinha ido realizar o teste por alguma questão em específico, se tinha tido algum contacto de risco ou se necessitava de o realizar para aceder a algum serviço de saúde, ao que o senhor responde que apenas realizou o teste para saber qual o seu estado. Sendo que o teste serológico deteta a presença de anticorpos, questionámos o utente se já tinha tido uma infeção por COVID-19 e se já estava vacinado. De acordo com o senhor, nunca esteve infetado e já tinha a vacinação completa. Portanto, podemos concluir que a presença de anticorpos se devia à vacinação, e transmitimos essa informação ao doente. Contudo, preferiu ainda realizar um TRAg para confirmar, cujo resultado foi negativo, o que comprovou a nossa hipótese.

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# Parte B

## Relatório de Estágio em Indústria Farmacêutica


Orientado pela Doutora Cátia Augusto de 2 de maio a 25 de julho

## LISTA DE ABREVIATURAS

**FFUC** Faculdade de Farmácia da Universidade de Coimbra

**I&D** Investigação e Desenvolvimento

**IF** Indústria Farmacêutica

## Introdução

Presentemente, o curso de MICF na FFUC permite que os alunos realizem parte do estágio curricular numa indústria farmacêutica (IF). Sendo que esta área sempre me suscitou interesse, optei para realizar o estágio curricular nos Laboratórios Basi, no departamento de Investigação e Desenvolvimento (I&D). O estágio decorreu de 2 de maio a 25 de julho, sendo realizadas um total de 424h, sob orientação da Doutora Cátia Augusto.

Os Laboratórios BASI, criados em 1956, têm como principal objetivo transformar-se num *player* global na IF, constituindo-se como uma referência na fluidoterapia, pelo crescimento e expansão nos mercados português e espanhol, através de um investimento contínuo em investigação e inovação, potenciando o aumento da produção tecnológica e processos inovadores, com o crescente turnover das vendas e capacidade de exportação, edução do fabrico em terceiros e o aumento de notoriedade da marca e portefólio Basi. Deste modo, a sua missão passa por desenvolver, fabricar, comercializar e distribuir, a nível global, medicamentos e soluções terapêuticas, de forma competitiva e flexível1.

Atualmente, os Laboratórios Basi contam com mais de 240 produtos registados em 17 áreas terapêuticas. Esta empresa pertence ao Grupo FHC|Farmacêutica, onde também estão inseridas a Empifarma, Overpharma, Phagecon e Zeone Informática[1].

Os Laboratórios Basi possuem duas unidades de fabrico, o IJM (*Injectable Manufacture*) e LSM (*Liquid semi-solid manufacture*), onde se realiza, respetivamente, a produção de injetáveis e de líquidos e semi-sólidos. O departamento de I&D encontra-se no LSM. Este departamento é constituído pelo *openspace*, laboratório de I&D e laboratório de validação de métodos analíticos, com uma equipa multidisciplinar.

O presente relatório tem como objetivo a realização de uma avaliação SWOT (*Strengths, Weaknesses, Opportunities and Threats*) deste estágio, analisando de uma perspetiva interna (*Strengths* e *Weaknesses*), bem como de uma perspetiva externa (*Opportunities* e *Threats*) a minha experiência enquanto estagiária nos Laboratórios Basi.

# 1. Análise SWOT

## 1.1. *Strengths*

### 1.1.1 Conhecimentos prévios lecionados no MICF

A frequência das unidades curriculares de Gestão e Garantia de Qualidade e Assuntos Regulamentares do Medicamento, bem como da opcional de Gestão de Processos Regulamentares constituíram-se como uma grande mais-valia no decorrer deste estágio pois, graças às aprendizagens realizadas detinha alguns conhecimentos que me permitiram um melhor desempenho.

### 1.1.2. Conhecimentos de inglês

O trabalho realizado na secção de suporte científico passou muito por pesquisa de artigos e pesquisa em bases de dados do medicamento, dos mais variados países, para a elaboração de módulos 3.2.P.2 do eCTD (*Common Technical Document*), assim com pesquisas de mercado. Sendo que a maioria dos artigos, bem como livros técnicos (Farmacopeias, *Handbook of Injectable Drugs, Injectable Drugs Guide*), se encontram redigidos em inglês, o facto de possuir proficiência nesta língua, permitiu a compreensão rápida e eficaz da informação necessária.

### 1.1.3. Capacidade de pesquisa

O departamento de I&D, em especial a secção de suporte científico, tem uma grande vertente de pesquisa, que apoia o desenvolvimento de produtos e a elaboração de eCTD. Deste modo, o trabalho realizado passa muito pela pesquisa em bases de dados e de artigos científicos, como referido anteriormente. Nesta conformidade, a capacidade de pesquisa é fundamental.

## 1.2. Weaknesses

### 1.2.1. Desconhecimento de outras línguas

Como anteriormente referido, este estágio baseou-se muito na pesquisa, tanto em bases de artigos científicos, como em bases de dados de produtos farmacêuticos (polacas, holandesas, alemãs, francesas…). Estas últimas, normalmente, encontram-se redigidas na língua nativa, bem como os textos de produto (nomeadamente *Summary of Product Characteristics*). Deste modo, sendo que não possuo conhecimentos técnicos nestes idiomas, a consulta destas bases de dados foi um processo mais demorado e realizado, inicialmente, com menos destreza.

### 1.2.2. Inexperiência

Apesar dos conhecimentos adquiridos ao longo do MICF, foram poucas as oportunidades de os pôr em prática ao longo do curso. Sendo que foi também o meu primeiro contacto com a realidade da IF senti, inicialmente, alguma insegurança, o que se refletiu na demora na realização do trabalho e no surgimento de algumas dúvidas. Contudo, a equipa do I&D mostrou-se sempre pronta a ajudar e esclarecer as minhas dúvidas, pelo que este ponto foi facilmente ultrapassado.

## 1.3. *Opportunities*

### 1.3.1. Formações

No início de qualquer estágio nesta empresa, tanto os estagiários como novos colaboradores, têm de fazer formações. Estas passam por higiene e segurança no trabalho, ambiente e segurança, farmacovigilância e qualidade, entre outros. Já no departamento, tive ainda a oportunidade de ter formação no âmbito do trabalho que iria desenvolver, ou seja, no eCTD, mais especificamente módulo 3.2.P.2., e pesquisas de mercado. Estas formações permitiram-me aplicar e refletir sobre o conhecimento que já detinha e, deste modo, crescer na aprendizagem e na formação de conhecimento mais substancial e fundamentado, que sem dúvida muito me ajudará no futuro.

### 1.3.2. Participação na elaboração de documentos

No decorrer deste estágio foi-me ainda dada a oportunidade de auxiliar no desenvolvimento de pesquisas de mercado, respostas a pedidos de elementos e elaboração do módulo 3.2.P.2. Considero que estas oportunidades me permitiram crescer em conhecimentos, tanto ao nível do trabalho que é realizado em indústria, como também dos produtos desenvolvidos, enquanto substância ativa, excipientes e produto acabado.

### 1.3.3. Visita ao laboratório I&D

Como referido anteriormente, no decorrer do meu estágio participei mais no laboratório I&D, onde tive a oportunidade de assistir à produção de diversos lotes laboratoriais de medicamentos, bem como a vários ensaios ali realizados, sobre os quais não possuía conhecimentos.

## 1.4. *Threats*

### 1.4.1. Pouco contacto com os laboratórios do departamento

Sendo o departamento de I&D constituído por várias secções, trata-se de uma grande equipa multidisciplinar, que trabalha em conjunto e de forma articulada e complementar para o desenvolvimento de novos produtos.

No decorrer do meu estágio, apenas estive no laboratório de I&D, onde o meu trabalho passou pelo auxílio na preparação e finalização de lotes. Portanto, considero que ao não ter passado pelo laboratório de desenvolvimento e validação analítica, não tive uma visão global do funcionamento do departamento.

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# Parte C

Monografia

"*The Issue with Microplastics and their Effects on Human Health*"

Photo taken from https://www.nationalgeographic.com/environment/article/microplastics-are-in-our-bodies-how-much-do-they-harm-us consulted on 10/07/2022

Orientada pelo Professor Doutor André Pereira

## ABREVIATIONS

| | |
|---|---|
| **HDPE** | High Density PE |
| **LDPE** | Low Density PE |
| **MPs** | Microplastics |
| **NPs** | Nanopalstics |
| **PCPs** | Personal Care Products |
| **PE** | Polyethylene |
| **PET** | Polyethylene terephthalate |
| **PP** | Polypropylene |
| **PS** | Polystyrene |
| **PVC** | Polyvinyl chloride |
| **ROS** | Reactive oxygen species |

**Resumo**

Os microplásticos tornaram-se rapidamente uma presença recorrente no ambiente, tanto aquático como atmosférico, bem como no solo. Isto revelou-se uma preocupação pois os investigadores começaram a encontrar estas pequenas partículas em animais, incluindo humanos. Este ano, um grupo de investigadores encontrou partículas de nano plásticos no sangue humano, o que causou alarme na comunidade científica. Esta preocupação advém não só porque os microplásticos são tóxicos, mas também porque podem atuar como vetores para outras toxinas e agentes de poluição. Foram já realizados vários estudos de modo a avaliar o possível impacto destas partículas nos animais e, consequentemente, na cadeia alimentar. Os efeitos descobertos vão desde alterações na sua capacidade de crescimento e reprodução, a *stress* oxidativo e neurotoxicidade. Deste modo, há cada vez mais foco da pesquisa em perceber de que maneira se pode atuar de modo a reduzir a quantidade de microplásticos no nosso ambiente, principalmente através de alterações aos nossos hábitos enquanto consumidores.

**Palavras-chave:** Alimentos; Biota; Consequências; Contaminação; Meio-ambiente; Microplásticos.

**Abstract**

Microplastics have quickly become a ubiquitous presence in the environment, both aquatic and atmospheric, as well as in the soil. This has become an alarming concern as researchers began to encounter these particles in animals, including Humans. This year researchers found nanoplastics particles in samples of Human blood, which caused alarm in the scientific community. This growing concern arises not only because microplastics are by themselves toxic, but also because they can act as vectors to other pollutants and toxins, further increasing the chances of impairment in both animals and Humans. Several studies have been conducted to evaluate this impact on animals and, consequently, on the food chain. These effects range from changes in their growth and reproduction ability, to oxidative stress and neurotoxicity. Recent studies on Humans point also to several effects at an intestinal level as well as respiratory problems, and even certain cancers. Thus, there is an increasing body of research focused on the different ways one could act to reduce the quantity of microplastics in our environment, mainly through changes to our habits as consumers.

**Keywords:** Foodstuff; Biota; Consequences; Contamination; Environment; Microplastics.

## Introduction

We are all aware of the enormous impact of plastic pollution because we can see it. We see inappropriately discarded plastic bags flying around, inevitably finding their way into the water, floating around. We also see numerous photographs of marine life struggling in an environment full of plastics, being stuck in them, eating them, suffocating; and on land, we observe the same effects. We know that plastic takes years to disappear, but does it ever disintegrate? These long travels of plastics and the whole process of degradation never ends, the plastic just becomes smaller and smaller, harder to see, but nevertheless it is still dangerous[1; 2].

Through the same pathways as their predecessors, microplastics (MPs) infiltrate our lives. Ubiquitous, omnipresent, widespread, everywhere, are just some of the words used to describe microplastics. From the water we drink, to the food we eat, the soil we cultivate, the products we use, to the very air that we breathe. Microplastics are everywhere [3; 4; 5; 6; 7; 8].

So why is plastic pollution something so prevalent in our environment?

First, we should start by looking at its history. Plastic was designed to be a material that was "pliable and easily shaped" and synthetic, mankind could now no longer depend solely on Nature for manufacturing. Due to its malleable nature, it was advertised as a perfect substitute for other animal products, such as tortoise shells or ivory. Adding to this fact, and by being industrially manufactured, plastic was cheaper than the other materials it imitated, it is easy to see why it became so popular. Now, with this cheap alternative, it was accessible to everyone, and they could stop using animal products and destroying resources [9; 10].

Plastic, slowly but surely, started making its way into every household, and then World War II broke out. Development skyrocketed, the need for lightweight, cheap, and quickly made materials caused innovation to progress and new types of plastic were synthesised. Plastic was then everywhere. Subsequently, the world became aware of the enormous pollution it was causing and the toxic effects it had. Plastic was accumulating in landfills and, unfortunately, in our environment. It brought concern, since it was not easily degradable and, when it did start to decompose, its smaller particles further polluted our environment [9; 10; 11].

Nowadays, plastic has become more regulated in order to lower its pollution rate. Single use plastics are slowly disappearing, and people are encouraged to prefer sturdier plastic alternatives that can last longer, biodegradable plastics, or even no plastic at all [9; 10]! However, it is important to note that plastic is not only present in packaging but also in textiles and cosmetics, which are also key participants in MPs pollution.

## 1. Plastic polymers

Before defining MPs, we should concentrate on the plastic polymers these particles are Before defining MPs, we should concentrate on the plastic polymers these particles are made of. Plastic can be sorted into two categories, depending on its structure, thermoplastics, or thermosetting plastics. Thermosetting plastics are created by step-growth polymerization. Once formed, they cannot be melted or modified. They have a highly cross-linked structure and, therefore, cannot be recycled. On the other hand, thermoplastics can undergo heat moulding multiple times without changing their chemical composition, which is why they can be recycled. They are "linear chain macromolecules where the atoms and molecules are joined end-to-end into a series of long, sole carbon chains" [12]. In this category there are plastics we hear about every day, which structure we can see in Figure 1, such as [13]:

- Polyvinyl chloride (PVC): Hard and rigid, resistant to chemicals and weathering. Used in medical appliances because it is impermeable to germs and easily disinfected. It also provides single-use applications that reduce infections in healthcare. However, it is very dangerous because it can leach dangerous toxins throughout its lifecycle. It can also be used in pet toys, pipes, medical tubing, oxygen masks, and IV bags.
- Polypropylene (PP): it is very durable and heat resistant. Therefore, it is good for food packaging and storage of hot items or those that need to be heated. Commonly used in straws, bottle caps, and hot food packages.
- Polystyrene (PS): also known as Styrofoam. It is ideal for food packaging and construction industries. However, it can leach harmful toxins, such as styrene, a neurotoxin that is easily absorbed by food and ingested by humans. Usually seen in cups, take out packaging, and insulation.
- Polyethylene (PE):
    - Low Density PE (LDPE) - softer, clearer, and more flexible version of HDPE. Usually used as a liner on the inside of beverage cartons and corrosion-resistant work surfaces. Some examples of products made with LDPE are cling wrap, bread bags, bubble wrap and garbage bags.
    - High Density PE (HDPE) - strong and resistant to moisture and chemicals. Utilized for cartons, containers, pipes and building materials.
- Polyethylene terephthalate (PET): Most commonly used plastic as it is lightweight, strong and transparent. Commonly used in food packaging and fabrics, known as polyester.

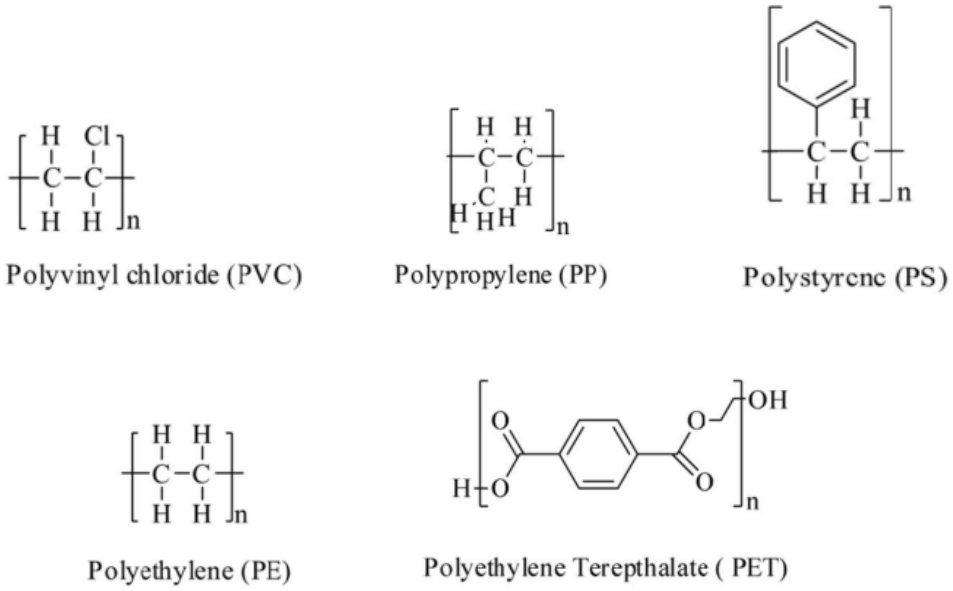
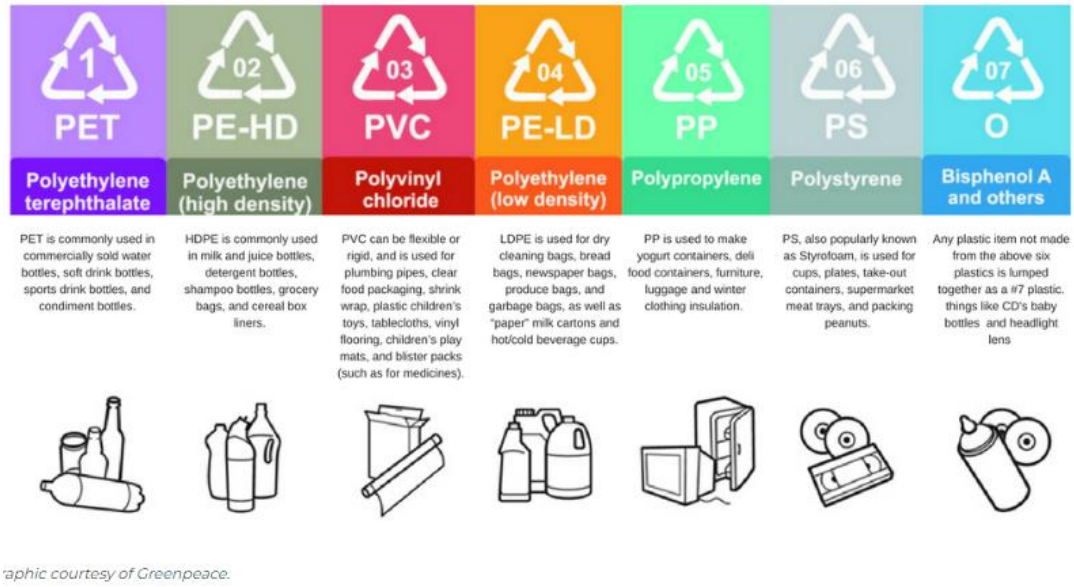



**Figure 1.** Most common types of plastic found as MPs. (Adapted from article "Microplastics in the environment: global concern, challenges, and controlling measures" by Lamichhane, G. *et al.*)[14]

Figure 2 shows the recycling symbols we can find in objects made from these plastic polymers.




'aphic courtesy of Greenpeace.

**Figure 2.** Some uses of the different types of plastic polymers and the recycling symbols found in those items. (From https://plasticoceans.org/7-types-of-plastic/ consulted on 28/5/2022)[13]

## 2. What are Microplastics

As explained above, plastic is used everywhere and, as such, MPs have been found throughout the globe, defining them as ubiquitous [4; 5; 6; 7]. Studies have reported their presence from the top of mountains to the bottoms of the oceans, and from areas with low population density to the biggest cities [3]. So, what are really MPs?

MPs have been defined as plastic particles with a diameter between 5mm and 100nm, as seen in Figure 3, and can be categorized as primary or secondary, regarding their origin, and can be ranged according to their shape and colour. MPs can be originated from insufficient waste management, road traffic and production spill as well as textile fibers from the washing of synthetic material and microbeads in Personal Care Products (PCPs)[3; 8; 15; 16; 17].

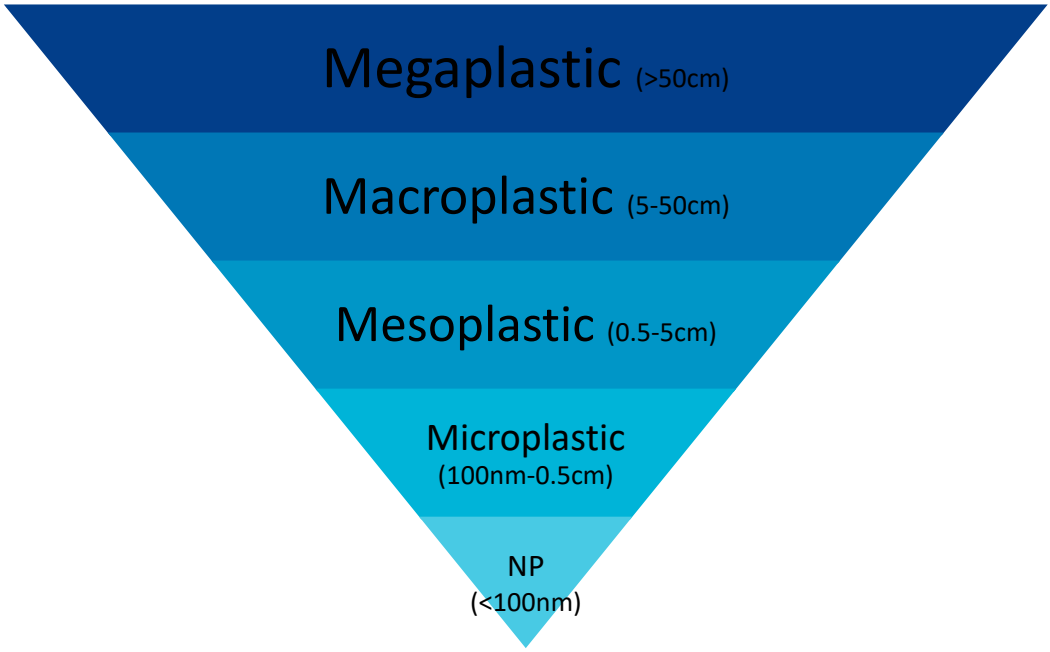



**Figure 3.** Classification of plastic particles according to size.

Primary MPs are those that were intentionally manufactured this size, these are mainly found in textiles, medicines, and PCPs, such as cosmetics, and they are primarily found in domestic and industrial wastewater. Secondary MPs appear as a result of the breakdown and degradation of bigger plastics and are the largest source of this pollutant [3; 4; 15; 16]. This degradation can occur via abrasion, hydrolysis, heat, or microorganisms [15; 16]. Figure 4 shows examples of primary MPs, derived from PCPs, and secondary MPs, derived from synthetic textiles.

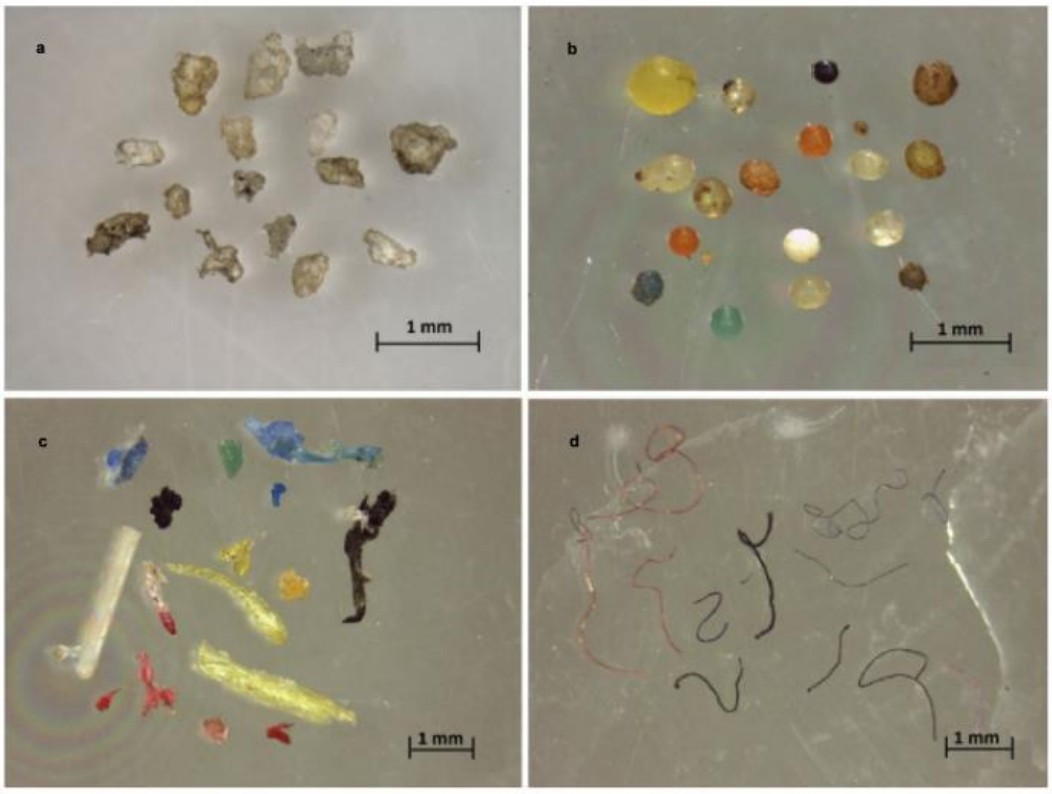



**Figure 4**. "**a, b** Primary microplastics. Microbeads from personal care products. **c, d** Secondary microplastics. Fragments from a breakdown of larger plastics and synthetic textile fibers". (From "Sampling, pre-treatment, and identification methods of microplastics in sewage sludge and their effects in agricultural soils: a review" by Koyuncuoglu, P. and Erden, Gülbin)[18]

MPs can also be categorized by their shape in spheres, beads, pellets, foams, fibers, fragments, films, or flakes. The shape can suggest a specific origin, for example, fibers are commonly a by-product of synthetic fibers and fragments are a result of an exposure to fatigue, strain, and UV radiation [3].

The texture and edges can also help to infer the type of degradation and the time span between their introduction to the environment and their analysis. Sharp edges point to a recent introduction into the environment, as the particles seem not to have undergone enough degradation to smooth them out and, therefore, smooth edges suggest a larger period of residence. These characteristics also play a key role as to whether or not a MP has the potential to cause harm. Thus, smaller angular MPs are more likely to pass membrane barriers, and thinner MPs, like flakes or films, have a larger surface area that can cause greater oxidative stress [3].

Another important aspect that helps researchers deduce the origin of the MPs is their colour, as some colours are more associated with certain types of plastic. For example, clear and transparent particles are often PP, white usually means PE and opaque LDPE [3].

## 3. Microplastics in the air

It is essential to note that MP atmospheric pollution is of extreme importance because the wind can transport these particles everywhere, further altering the marine and soil environment. Therefore, airborne MPs are also one of the greatest contributors to MP pollution in the aquatic environment, being greatly influenced by meteorological conditions and human activities [3; 6; 16; 19].

The first study on the presence of MPs in the atmosphere, suggested that suspended atmospheric MPs (SAMPs), encompassing microfibers, micro fragments, and granules, due to their relatively small size and low density, can easily be carried by the wind to distant places and affect the MP concentration elsewhere [19; 20]. The atmospheric environment includes all sorts of processes that influence MP transport and deposition, wind speed and direction, drafts, turbulence, and other phenomena. As such, the wind itself, is considered an important vector that influences MP transport, affecting plastic pollution in both terrestrial and aquatic environments [3].

Researchers then set out to map the greatest contributors to MP atmospheric pollution, and it comes with no surprise that these match with the most highly produced and in demand plastic types, PE, PP, PET, PVC, and PS [3]. In addition, the main source, besides these polymers, are synthetic textiles, and the predominant shape of MPs are fibers [6].

Other studies investigated the different concentrations of MPs indoors and outdoors. What they discovered was that there was a greater MP concentration indoors (1-60 fibers/$m^3$) than outdoors (0, 3-1, 5 fibers/$m^3$). Then, they hypothesised that this was most likely due to different human activities and rates of air renovation. Most likely due to the presence of furniture and other decorations, cleaning habits and other activities, as well as a lower rate of air renovation, the indoors have a higher concentration of MPs [6; 16].

## 4. Microplastics in the aquatic environment

Microplastic pollution in water bodies can occur in many ways, through deposition of atmospheric MPs pollution, as a direct consequence of human activity, or from wastewater treatment plants effluents and garbage dumping [3; 6; 19; 21].

Since most MPs have a density lower than that of salt or fresh water, they often float on these water surfaces and can travel easily from rivers to oceans. However, MPs come in various sizes. While larger ones are often found in surface ocean waters, smaller MPs, have an increasing density. The smaller the MP, the larger the surface area, as such, smaller MPs have

more interactions with the marine environment, as well as other debris, which leads to their higher density [16].

Among the open sea, MPs concentration seems to be more abundant in areas where there are convergent currents, where litter is accumulated, and, as such, MPs are the largest contributor to marine plastic debris [16]. In addition to this, as mentioned before, the shape of an MP can help infer as to where it originated. Therefore, the MPs most commonly found in the aquatic environment are fibers and fragments, making up about 80% of the total MPs found in the oceans. In the Mediterranean Sea, between 87.7% to 93.2% of the MPs found are fragments [16].

The main contributor, around 80%, to ocean MP pollution are MP polluted rivers. In fact, the Danube River is estimated to release around 530 to 1500 tons of plastic into the Black Sea. Additionally, according to a global model, 1.15-2.41 million tons of plastic enter the ocean through rivers, annually [16]. Their pollution is originated from inland sources and is largely dependent on their proximity to urban areas, population size and hydrological conditions [15]. Moreover, as MP distribution is easily affected by nature, their spatial distribution can be irregular [16; 19; 21].

Seeing that MPs are so present in this environment, it was just a matter of time until they infiltrated the aquatic food chain. Many species have been reported to have been contaminated by this pollutant, such as various fish, turtles, bivalves, shrimp and even zooplankton [6; 21]. Easily, one can see that this contamination of the aquatic food chain, rapidly becomes a contamination of our own food chain. Several studies have evaluated the toxicity that this consumption can have on these organisms and their offspring.

## 5. Microplastics on the soil

MPs on the soil can come from the breakdown of larger plastic items, fertilizers from contaminated sewage sludge, discharges (domestic and production), use and disposal of textiles, irrigation with contaminated waters and atmospheric deposition [6; 18; 19; 21; 22]. Sewage sludge application appears to be one of the greatest contributors to soil pollution, and it is estimated that around 125 to 850 tons of MPs, per million people, was annually introduced to agricultural lands throughout Europe. Considering that sewage sludge is the result of wastewater treatment, one can see why this is also the largest source of primary MPs on the soil. Secondary MPs are often originated from abrasion of other plastic debris and incidental debris inside the soil or at its surface[16; 19].

Once on the soil, denser MPs can remain buried, while the lighter ones are subject to be transported by the wind [19]. While in this environment, MPs can be aged through several

processes, such as, biodegradation, hetero aggregation, and thermal and photo-initiated oxidative degradation. Being hetero aggregation the process where MP interact with aggregates along the soil, like organic matter, mineral colloids, and microbes, and is aged with a modified surface. Many studies found inorganic materials, especially Fe oxides but also Mg, Si and Al, on MP surfaces [22]. Additionally, thermal and photo-initiated oxidative degradation is caused by UV radiation and thermal oxidation that leads to an extensive chemical aging and, consequently, alters MP surface, causing cracks and roughness, polymer structure, charge, polarity and even hydrophilicity [22].

Biodegradation by soil organisms usually involves four steps [22]:

a) Adherence and colonization of the MP surface by microorganisms.
b) Bio disintegration and deterioration.
c) Depolymerisation by microorganisms' enzymes.
d) Assimilation and mineralization, resulting in $CO_2$ and $H_2O$ if under aerobic conditions, or $CO_2$ and $CH_4$ if under anaerobic conditions.

However, the effects of biodegradation on MP usually vary according to polymer type and bacteria species.

This aging affects MPs physiochemical properties, increasing oxygen containing groups and surface roughness, which in turn, enhances mobility and sorption [22]. This higher surface area and sorption leads to a possible interaction with heavy metals and other organic contaminants, consequently, contaminating ecosystems. Likewise, additives in plastic debris, and MPs, can leach into the surrounding soil, further tainting the ecosystems with potentially hazardous chemicals [22]. As observed in aquatic contamination, the presence of these particles in the environment, usually results in their consumption by inhabiting organisms and, consequently, can result in toxic bioaccumulation [22]. While on the topic of inhabiting organisms, it is also important to note a key role these can have on the transport of MP. Smaller animals like worms can transport MPs adhered to them (due to their small size and high surface area) to other areas of the environment, even potentially reaching groundwater [18; 22].

## 6. Microplastics as vectors for other contaminants

Researchers found that "contaminants (heavy metals and toxic chemicals) and microorganisms absorbed onto MP surfaces also pose a substantial threat to aquatic organisms, due to the larger specific surface area and stronger sorption capacities of MPs", not only do they pose a threat to marine life, but to all life [6]. The main additives found in plastics, and consequently in MPs, were bisphenol A, phthalates, polycyclic aromatic

hydrocarbons, polybrominated diphenyl ethers, and polychlorinated biphenyls [7]. Other contaminants found in MPs are Persistent Organic Pollutants and organochlorine, including the pesticide Dichlorodiphenyltrichloroethane, and the insecticide Hexachlorocyclohexane [19; 23]. In addition to this, some microorganisms have also been reported to appear repeatedly in biofilms supported by MPs, like *Vibrio spp*. and *Escherichia coli* [7].

Since MPs have different characteristics, the adsorption of contaminants varies greatly depending on their characteristics and those of the environment, as summarized below in Figure 5.

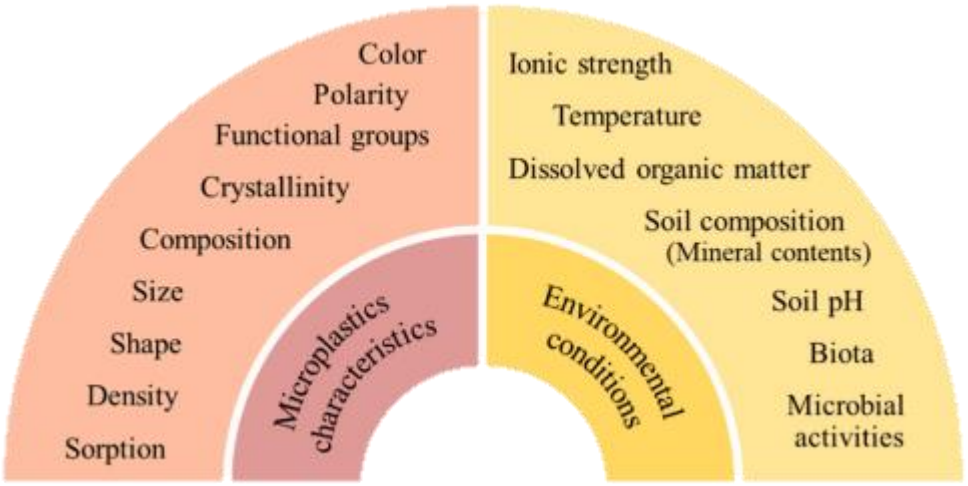



**Figure 5.** Different factors that affect MPs transport in soils. (Adapted from "Microplastics in the soil-groundwater environment: Aging, migration, and co-transport of contaminants – A critical review" by Ren, Zhefan *et al.*)[22]

PE, because of its low density, shows a higher attraction to most chemicals, when compared with PVC and PP. The low sorption of chemicals on PVC and PS seems to be due to their glassy characteristics and high glass transition temperature, as glassy polymers have denser structures and fewer void spaces, which reduces sorption sites [19]. The weathering and aging of MPs will also impact their characteristics. Environmental interactions, such as long-term exposure to the sun, lead to rough surfaces which, in turn, results in a degradation into smaller particles, increasing surface area [19].

The adsorption of heavy metals, either in aquatic or soil environments, is mediated through surface complexation, electrostatic attraction, and precipitation [22]. As seen in Figure 5, environmental conditions affect this sorption, factors like pH or ionic strength "have dominant roles in the sorption affinity between microplastics and heavy metals because (…) [they] could alter the charge of microplastics and heavy metals". The increase in salinity levels decreased this adsorption because MPs interacted not only with heavy metals, but also with other ions. Furthermore, MPs characteristics, like their surface, also affected this action. Aged

surfaces had a stronger sorption, as they had an increase in porosity, specific surface area and polarity [22].

MPs have demonstrated strong sorption capacity of organic contaminants. Although different MPs can exhibit different sorption affinity. Smaller MPs, with an increasing surface area, seem to have stronger sorption affinity to organic contaminants. MPs seem to adsorb through different mechanisms, which are generally determined by their structure and properties, such as:

- van der Waals;
- Electrostatic interaction;
- π-π interactions;
- Hydrophobic interactions;
- Hydrogen bonding;
- Pore filling;
- Cation ligand interactions.

Regarding the aggregation of microorganisms, it is dependent on the species of microorganisms, and on type of polymer and its characteristics, such as surface area available to colonize, rugosity and hydrophobicity. Smooth surface MPs are more hydrophobic and less colonized, whereas rougher surfaces are more hydrophilic, which promotes colonization. This attachment can lead to the formation of biofilms. Additionally, the absorption of pharmaceuticals and heavy metals to MPs possibly contributes to antibiotic resistance. They may help promote horizontal gene transfer between different classes of microorganisms, possibly acting as a hotspot for the creation of drug-resistant microorganisms [7; 19; 23].

## 7. Microplastics in biota

While evaluating MPs levels in the environment, researchers questioned what would be the impact of this pollution in animals. There was a need to evaluate their exposure, as the results could possibly elucidate the effects that the consumption of contaminated animals can have in humans. Therefore, researchers set out to investigate different species from different environments on how they respond to MPs exposure. The results, although sometimes obtained from a high and acute MPs exposure, revealed some alterations that were then seen also in human cells. Table 1 presents some of the species studied, as well as the results observed, and Figure 6 summarizes the effects observed at various levels of organisation [24].

**Table 1.** The effects of MP exposure to certain animals.

| Animal | Effects | Reference |
|---|---|---|
| AQUATIC | | |
| Zebrafish | 5μm PS found accumulated in the gills, liver, and gut<br>20μm PS found accumulated in the gills and gut<br>Inflammation and lipid accumulation<br>Increased activity of superoxide dismutase and catalase<br>Disturbed lipid and energy metabolism | Lu, Yifeng *et al.* [25] |
| Fish | 45nm polymethylmethacrylate particles induced modulation of RNA of peroxisome proliferator-activated receptors related to lipid metabolism, potentially interfering the mobilization of energy reserves | Brandts, I. *et al.* [26] |
| European seabass | Caused inhibition of acetylcholinestearase (AChE)<br>Oxidative stress with increase in lipid peroxidation levels<br>Increase in anaerobic pathway of energy production.<br>Impact swimming performance, a behavioural indicator<br>Reported an interaction of MPs with mercury | Barboza, Luís Gabriel Antão *et al.* [27]<br>Barboza, Luís Gabriel Antão *et al.* [28] |
| Marine copepods | Impedes food intake<br>Blocks the digestive tract<br>Causes physiological stress (immune responses, metabolism disorders, energy depletion, behavioural alterations, growth retardation, and reproduction disturbance) | Bai, Zhuoan *et al.* [29] |
| SOIL | | |
| Soil organisms | Altered and increased the diversity of the gut microbiome, which may lead to an alteration of isotopic and elemental incorporation, growth, and reproduction. | Zhu, Dong *et al.* [30] |
| Earthworm | PE exposure leads to:<br>Skin damage<br>Increased AChE activity<br>Increased catalase activity<br>Increased malondialdehyde levels | Chen, Yuling *et al.* [31] |
| MAMMAL | | |
| Mice | Accumulated in the liver, kidney, and gut<br>Induced disturbance of energy and lipid metabolism oxidative stress<br>Adverse effects on neurotransmission in mice, such as increased activity of AChE and changes in serum neurotransmitters | Deng, Yongfeng *et al.*[32] |
| AIR | | |
| Birds (Japanese quail)* | <u>No evidence of lasting toxicological effects on:</u><br>Mortality<br>Adult body weight<br>Organ histology<br>Hormone levels<br>Fertility<br>Hatch rates<br>Eggshell strength<br><u>They did find that plastic ingestion causes:</u><br>Higher frequency of male reproductive cysts<br>Minor delays in chick growth and sexual maturity, though without affecting ultimate survival or reproductive output | Roman, Lauren *et al.*[33] |

* Plastic was fed to birds to test the consequences of plastic ingestion at relevant loads in Japanese quail.

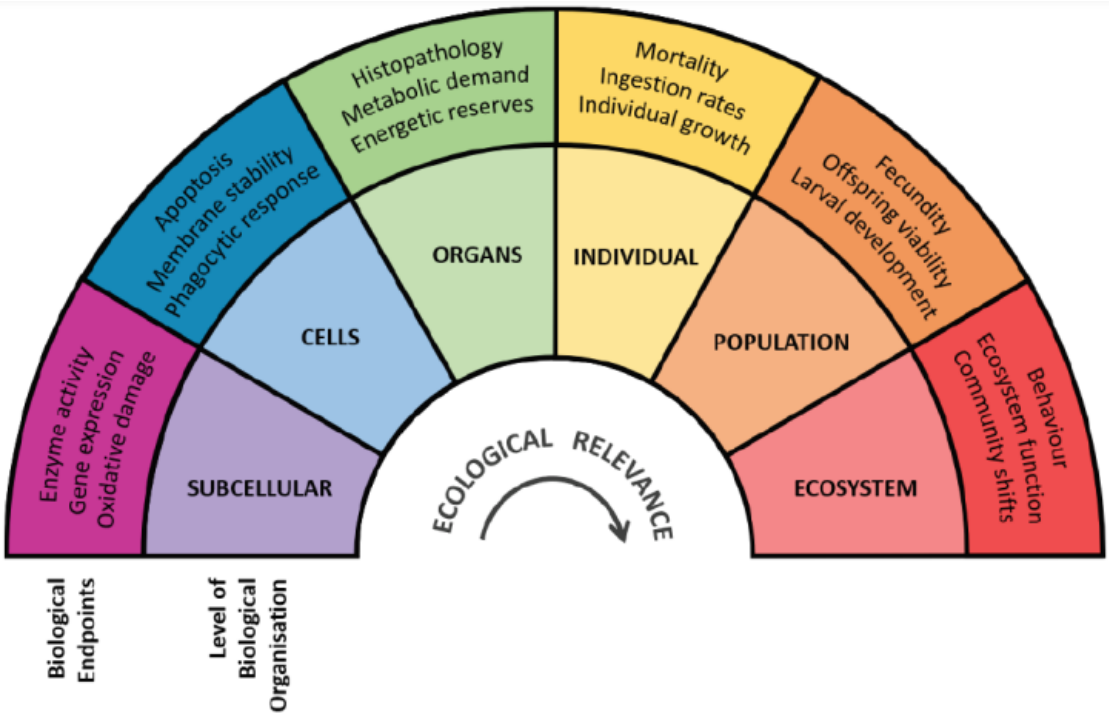



**Figure 6.** "Impacts of NPs MPs on biota reported at various levels of biological organisation (a biological endpoint is a marker of disease progression). Most studies have been at sub-organismal levels and studies at a community or ecological level are relatively sparse" (Adapted from "A Scientific Perspective on Microplastics in Nature and Society" by SAPEA, Science Advice for Policy by European Academies)[34]

Since MPs were found in animals throughout the food chain, some questions were raised on how the contamination of lower trophic, prey, animals could impact higher trophic, predator, animals that eat them. However, there seems to be no agreement, as lower trophic animals seem to have a higher concentration of MPs, bioaccumulation, suggesting that biomagnification does not occur, at least according to recent findings [35].

### 7.1. Plastic-eating microorganisms

Whereas some researchers focused on the impact of MPs on animals, others have been focusing on what microorganisms can be used to degrade plastic polymers. Specifically, studies have focused on what strains of bacteria or fungi, and their enzymes (proteases, lipases, and cutinases), could degrade non-biodegradable plastic polymers (e.g., PET, PP, PE, PVC). These microorganisms work through several possible mechanisms to degrade plastic polymers, directly as a nutritional source, or indirectly through the action of their enzymes. Namely, *Bacillus cereus* helps degrade PET and PS polymers, and *Rhodococcus rubber* PE polymers [12; 36; 37]. Table 2 shows what microorganisms can degrade which polymers; it was adapted to show the most commonly used polymers. [12; 37].

**Table 2.** Plastic eating microorganisms (Adapted from "Rogue One: A Plastic Story" by Patel, Dhara *et al*., and "Biodegradation of plastics: current scenario and future prospects for environmental safety" by Ahmed, Temoor *et al.* [12; 37])

| Plastic Polymer | Microorganism | Reference |
|---|---|---|
| HDPE films | *Aspergillus oryzae* | *Patel, Dhara et al.* [12] |
| PET | *Ideonella sakaiensis*<br>*Bacillus cereus* | *Patel, Dhara et al.* [12]<br>*Ahmed, Temoor et al.* [37] |
| PS | *Bacillus cereus*<br>*Bacillus gottheilii* | *Patel, Dhara et al.* [12] |
| Polyester | *Streptomyces sp.*<br>*Phanerochaete chyrsosporium* | *Ahmed, Temoor et al.* [37] |
| PE | *Brevibacillus borstelensis*<br>*Rhodococcus rubber*<br>*Bacillus gottheilii* | *Patel, Dhara et al.* [12]<br>*Ahmed, Temoor et al.* [37] |
| PP | *Rhodococcus* sp. 36 | *Patel, Dhara et al.* [12] |
| Nylon | *Flavobacterium sp*<br>*Pseudomonas sp.*<br>*Trametes versicolor* | *Patel, Dhara et al.* [12]<br>*Ahmed, Temoor et al.* [37] |
| Starch/Polyester | *Streptomyces*<br>*Phanerochaete chyrsosporium* | *Ahmed, Temoor et al.* [37] |
| Starch/PE | *Aspergillus niger*<br>*Penicillium funiculosm*<br>*Phanerochaete chrysosporium* | *Ahmed, Temoor et al.* [37] |

The complete tables can be consulted in Annex I and Annex II, where it also mentions the microorganisms capable of degrading biopolymers, biodegradable or not, and other fossil-based polymers. These were not mentioned before, as they are still being studied because so far, most are biodegradable in very specific conditions that are hard to mimic in the environment. Although some of them have been around for a while, their use is still scarce as other economic and financial interests arise.

## 8. Microplastics in food

The same concerns raised on how the consumption of prey animals could impact predator animals also applied to us, humans. Not only because of our animal consumption, but also because researchers found MPs in other food categories (fruits, vegetables, salt, sugar, honey, beer, water). Table 3 presents some studies where food contamination was detected, the type of MPs present and its concentration, when mentioned. It is important to note that most values presented are referent to one, or few, geographical regions.

**Table 3.** Exposure to MPs in different food.

| Food | Polymer | Value | Shape | Reference |
|---|---|---|---|---|
| Salt | PET<br>PP<br>PE | 0.007-0.68 particles/g*<br>Portugal particles/kg 0-10 (PET e PE) | Fibers<br>Particles | Peixoto, Diogo *et al.* [38]<br>EFSA COMTA, Panel [39]<br>Kosuth, Mary *et al.* [40]<br>Jin, Mengke *et al.* [41] |
| Sugar | PVC | 343.7±32.08 MP-like particles/kg | Microfibers<br>Spherules | Kosuth, Mary *et al.* [40]<br>Jin, Mengke *et al.* [41]<br>Afrin, Sadia *et al.* [42] |
| Bottled water | PP | Glass bottle – 204 particles/L**<br>Plastic bottle – 1410 particles/L | Fragments | Toussaint, Brigitte *et al.* [24]<br>Manson, Sherri A. [43] |
| Tap water | NA | 0-61 particles/L<br>A mean of 5.45 particles/L | Fibers | Toussaint, Brigitte *et al.* [24]<br>Kosuth, Mary *et al.* [40] |
| Fruit | NA | Apples were found to be the most contaminated fruit | NA | Conti, Gea Oliveri *et al.* [44] |
| Vegetables | NA | Carrots were the most contaminated vegetables | NA | Conti, Gea Oliveri *et al.* [44] |
| Oyster, mussel, manila clam, scallop | PS<br>PP<br>PE<br>Polyester | Average of 0.15 ±0.20 n/g<br>0.97+-0.74 n/individual | Fragments<br>Particles <300 µm | Cho, Youna *et al.* [45] |
| Honey | NA | Average of 0.166 fibers/g<br>0.009 fragments/g | Fibers<br>Fragments | EFSA COMTA, Panel [39]<br>Kosuth, Mary *et al.* [40]<br>Jin, Mengke *et al.* [41] |
| Beer | NA | 0.025/0.033/0.017 per ml, corresponding to the most common shapes | Fibers<br>Fragments<br>Granules | EFSA COMTA, Panel [39]<br>Kosuth, Mary *et al.* [40]<br>Jin, Mengke *et al.* [41] |
| Fish from the Portuguese coast (26 different species) | PP<br>PE<br>alkyd resin<br>rayon<br>polyester<br>nylon<br>acrylic | 0.27±0.63 particles per fish | Fibers<br>Fragments | Neves, Diogo *et al.* |
| Sardine | PET | NA | Fibers | Compa, Montserrat *et al.* [46] |

*As salt is used every day by everyone, it is a long-term route of exposure and can therefore contribute to adverse effects in humans. The values vary greatly depending on the country and place of origin.
**Same brand of water, but different types of bottles (glass and plastic).
NA - Not Available.

As we can see, MPs were found in almost everything we eat or drink on a regular basis. Seafood, when compared to other marine food, is the most studied, as it is consumed whole, and any MPs present are also eaten.

Interestingly, when evaluating if we ingested more MPs from a meal of contaminated mussels or from the environment where the meal was made, researchers found that we were exposed to more MPs from the environment [47].

## 9. The Effects on Human Health

While there is growing evidence that humans are exposed to MPs through several routes (ingestion, inhalation, and dermal contact), there is still limited research on the effects of this exposure. Usually, the effects observed in animals, human cellular lines, and some humans exposed to high concentrations of these particles, is extrapolated to humans. Nonetheless, the evidence discovered suggests some concerning effects [48; 49]. In all biological systems, MPs were found to be a potential cause of toxicity, leading to oxidative stress, cytotoxicity, increased uptake or translocation and inflammatory lesions. This, in addition to the immune's system inability to remove synthetic particles, can lead to an increased risk of neoplasia or chronic inflammation. Additionally, as mentioned before, MPs can act as vectors to other contaminants, and can then release them when ingested by us, leading to further unknown damages [4; 5; 14].

MPs, as mentioned before, are easily transferred and bio accumulated throughout the food chain, there have been many reports of their presence in many foods and beverages [7]. Once ingested, MPs are a serious threat to the human body, they can lead to obstructions, reduced growth rates, reproductive complications, inflammation, and oxidative stress. Some polymers, like PC, PS and PVC, were studied and found to release toxic monomers, associated with cancer, mutagenicity, and reproductive toxicity. Smaller MPs, under 130 μm, can easily translocate into human tissues, triggering a local immune response, releasing monomers, additives, and other pollutants they have absorbed [5; 6; 14].

However, humans are not only exposed to MPs toxicity by ingestion. Several studies also point to the dangers of inhalation, mainly of synthetic textiles, rubber tyres and city dust, and dermal contact, mostly due to the presence of microbeads in PCPs that are in direct contact with the skin [7; 14].

### 9.1. Impact of different routes of exposure

#### 9.1.1. Inhalation

Due to their various shapes, sizes and surface area, MPs have the ability to permeate our cell membranes or be deeply inhaled within the lungs. Usually, inhaled particles suffer clearance mechanisms, such as phagocytosis, mucociliary escalator or even sneezing, which can help prevent the entrance of MPs to the body [6]. In the upper airways, the mucus is thick, and, usually, allows a successful clearance of foreign bodies. Additionally, ciliary movement and the presence of surfactant prevents the smaller particles from spreading and reaching the circulation. In the lower airways, the mucus layer is thinner, which enables an easier particle

diffusion of the MPs able to reach this part of the respiratory system [49; 50]. Here, MPs can stimulate the release of Reactive Oxygen Species (ROS), proteases, and other messengers, causing inflammation to the lungs. Moreover, plastic particles "have been reported to persist in a synthetic extracellular lung fluid for 180 days with no changes in surface area" [6]. Thus, MPs can accumulate and induce inflammation that can persist indefinitely, as well as continuous damage caused by ROS. From here, MPs can spread to the blood, either by diffusion or cellular uptake [50].

It is important to note that some people are at more serious risk of developing MPs-related diseases, especially if proper safety measures are not taken during work. This occupational exposure commonly occurs in the synthetic textile industry, the flock industry, and PVC and vinyl chloride industry [6; 49]. In the synthetic textile industry, workers are exposed to nylon, PE, polyurethane, polyolefin, acrylic, and vinyl-type polymers. Generally, studies linked this exposure to respiratory symptoms. Some researchers also found a possible link between an increased risk of certain cancers and inhalation of synthetic fibers. As for the flock industry, these are made from pulverized or cut fibers, of 0.2 to 5.0mm, usually nylon, polyester, PE, and PP. the inhalation of these particles was found to be the cause of interstitial lung disease - Flock worker's lung - caused by inappropriately ventilated industries. In the vinyl chloride and PVC industry, it is still unclear if it is the PVC dust, the vinyl chloride monomers or the thermal decomposition products that cause toxicity. Some results seem to lead to the conclusion that PVC is the toxic agent, as there were PVC particles found inside macrophages from human patients, alterations in rat lungs when exposed to PVC particles, and symptoms in workers with little exposure to vinyl chloride. Common symptoms to MPs inhalation include asthma-like reactions, chronic pneumonia, chronic bronchitis, and even pneumothorax [49; 51].

As seen in Figure 7, the average inhalation of MPs lies within 35000 - 62000 particles per person per year, depending on sex and age [7].

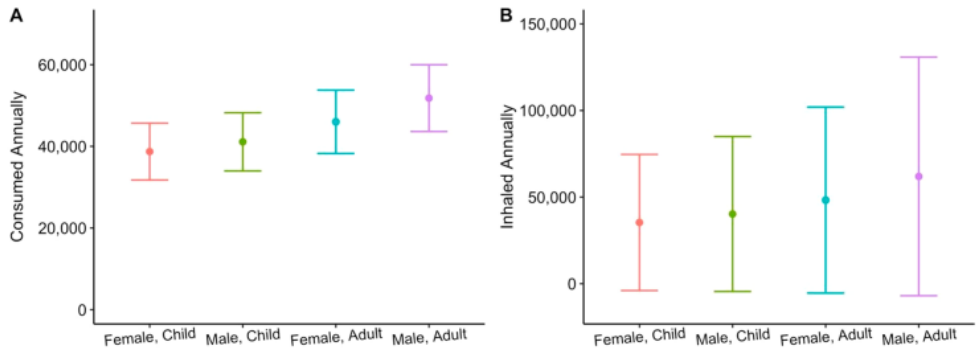



**Figure 7.** "Total microplastic particle (MP) intake for female and male, children and adults from (A) annual consumption of commonly consumed items and (B) annual inhalation via respiration. Points and error bars represent the summation (total) and average standard deviation of all microplastics consumed." (Adapted from "Human Consumption of Microplastics" by Cox, Kieran D. *et al.*)[7]

### 9.1.2. Ingestion

Based on a different study, ingestion is the greatest route of human's exposure to MPs[5]. The estimated consumption of MPs is between 39000 to 52000 particles per person per year, varying according to age and sex, as demonstrated in Figure 7, MPs can enter the gastrointestinal tract by two pathways, either the consumption of contaminated foodstuff or mucociliary clearance.

Due to their ubiquitous presence in our environment, MPs are present in an extremely large range of foodstuff. Because they are present in the oceans and freshwater, they can be found in seafood and fish, as well as drinking water and even salt [41]. As a result of their presence in our soils, they can be found in a lot of our fruits and vegetables, and even honey and sugar. They can even be found in animal products, such as milk. Even food containers have MPs, PET multi-use bottles have between 0.6 to 7.3µg/L of MPs and single-use PET bottles 0.1 to 1.8µg/L[7]. Humans are exposed a great deal to MPs through ingestion.

Through in vivo and in vitro data, researchers say that several uptake mechanisms result in a size-dependent uptake of MPs and nanoplastics (NPs). Greater MPs, >150µm, are not absorbed, remaining bound to the intestinal mucus layer, and coming into direct contact with the apical region of the intestinal epithelial cells. The smaller particles, <150µm, can cross the mucus barrier. After ingestion, these particles can suffer [4; 7]:

- Endocytosis through enterocytes;
- Transcytosis through M-cells, these cover the intestinal lymphoid system (Peyer's patches) - once in the lymphatic circulation, they can reach the blood;
- Persorption, a paracellular transfer through the intestinal epithelium;
- Paracellular uptake.

### 9.1.3. Dermal

This route is linked, mainly, to the exposure to MP's additives and monomers, especially endocrine disruptors such as bisphenol A and phthalates. MPs beads, the principal shape responsible for dermal exposure, is present in facial cleanser and scrubs, toothpaste, soaps, deodorants, moisturizers, sunscreens… They are used to help condition the skin, regulate viscosity, and stabilize emulsions [4; 7].

Moreover, the beads used in PCPs are usually processed mechanically, which may lead to their fragmentation into smaller particles, like NPs, potentially more hazardous [7]. Human epithelial cells were reported to suffer oxidative stress from the exposure to MPs and NPs, although differences in surface properties can lead to distinct outcomes [4].

## 9.2. Oxidative stress

MPs can lead to oxidative stress due to their high surface area, the release of oxidizing species, like metals, from their surface, or due to ROS release during the inflammatory response they cause [4; 14]. For example, after insertion of a PP prosthesis, it was observed an acute inflammatory response [4]. Consequently, there was a release of oxidative species ($H_2O_2$, HClO) that induced hydrolysis, degradation, cracking, and additive leaching of the polymer.

## 9.3. Cytotoxicity

Cytotoxicity is caused by oxidative stress, inflammation, and particle toxicity. PS and PE increased the concentrations of ROS in cerebral and epithelial human cells, contributing to cytotoxicity. PS exposure of macrophages and lung epithelial cell cultures, led to ROS and endoplasmic reticulum stress, which caused autophagic death [4].

## 9.4. Translocation

This process is very probable during inflammation and in the gastrointestinal mucosa, as the epithelial barriers have an increased permeability. While in circulation, either in the blood or lymph, MPs can cause further inflammation, vascular occlusions, increase in coagulation and blood cells cytotoxicity [14]. In a study set out to identify and quantify the polymers present in 22 healthy human volunteers, 17 had a quantifiable mass of plastic particles. The researchers found that most MPs found were PET, PE and PS and the mean sum of these was 1.6µg/ml. PET presented the highest frequency, with a maximum of 2.4µg/ml; followed by PS with a maximum concentration of 4.8µg/ml; and finally, PE, with a maximum of 7.1µg/ml [52]. MPs can reach the liver or kidneys, affecting metabolism and excretion mechanisms, as well as the brain. Researchers also found that MPs, specifically PE and PS, can reach the bone and be responsible

for bone loss, due to an increase in the activity of osteoclasts [4]. The fate of these particles is greatly dependent on whether or not they can be eliminated, via renal filtration or biliary excretion, or if they accumulate in the liver, spleen or other organs. MPs properties, like size, shape, charge and surface, determine its interaction with biological systems [52]. Another study analysed MPs presence in the placenta. Although this study had a small sample size (n=6), it was the first to reveal the presence of coloured MP particles in the placenta. The precise mechanism as to how this occurs is still unknown, but it is possible that MPs entered the circulation through ingestion, followed by endocytosis by M-cells or paracellular diffusion, or through inhalation. As stated, "Potentially, MPs, and in general microparticles, may alter several cellular regulating pathways in placenta", although at this point, the possible implications of this discovery are only extrapolations from other studies [50].

### 9.5. Neurotoxicity

There have been some reports of in vivo neurotoxicity due to exposure of MPs. The mechanism is, most likely, oxidative stress and the activation of microglia after contact with translocated MPs, or through the action of pro-inflammatory cytokines circulating from other inflammation sites. In vivo, MPs have been reported to damage neurons, impacting function and behaviour. Some reports suggest a possible link between exposure to MPs and cognitive impairment, like a higher risk of dementia and Alzheimer's, and neurodegenerative diseases[4; 14].

## 10. Conclusion and future perspectives

It becomes evident the enormous impact something so small can have in our lives. However, despite the rising number of research, investigation on this subject is still in its early stages. We are now more aware of the environmental impact these small particles can have, and the possible consequences of our exposure to them. Nonetheless, more studies are needed to further comprehend the mechanism and the effects of MPs in our environment, in the food chain, and in our bodies. Researchers are also encouraged to re-evaluate the complexity of MPs used in their studies. The particles used are usually very different from the ones found in the environment. Furthermore, they are also encouraged to create and implement standardized protocols to sample, evaluate, identify, and classify MPs, so that the results obtained can be comparable. Most studies so far have also been focused on a high level of exposure for a short period of time, whereas human exposure is usually light but for a larger period of time. Therefore, new methodologies must be developed. Regarding human exposure through ingestion, there are future perspectives to further analyse the

contamination of other food groups that constitute a large part of our nourishment, such as grains, vegetables, and meat.

Concerning the use of plastic itself, legislation has already been put in place, in various countries, to minimize the use of single use plastics, such as plastic bags in the supermarket. Presently, costumers are encouraged to use reusable bags, instead of plastic ones, which now they must pay for. The reduction, reusing, and recycling of plastic materials, leading to an improvement in the circularity of plastic, is also being encouraged. A different use for plastic waste has been the construction of building bricks, or, in alternative, incineration. This is the only process that also destroys MPs, and it can also be used as a waste-to-energy process. The burning of plastic provides a considerable energy recovery, although this does generate a large quantity of $CO_2$. New types of plastic are also being investigated, made from biopolymers or biodegradable materials. Researchers are creating and analysing already existing plastic alternatives as to how they impact the environment, and if they are a better alternative. However, most biodegradable plastics only degrade in specific conditions that are hard to mimic in the environment, and compostable plastics are usually not appropriate for home composting. If these alternatives are mixed into the recycling process, it can affect this process. It is essential to have a well-designed and well-functioning separate collection system, both for recycling and composting. The decline of the use of MPs in PCPs is also being encouraged. Some researchers have also been investigating the use of plastic eating bacteria and/or enzymes to degrade these plastic particles.

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# Annex

## 12.1. Annex 1 – In "Biodegradation of plastics: current scenario and future prospects for environmental safety" by Ahmed, Temoor *et al.*



**Table 1** Some non-biodegradable and biodegradable polymers, their chemical structures, applications, and microorganisms involved in specific biodegradation studies

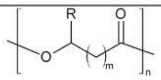
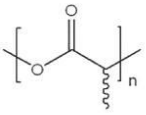
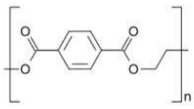
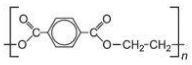
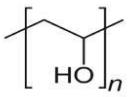
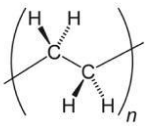
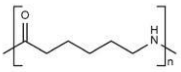
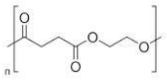
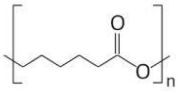
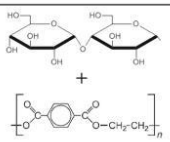
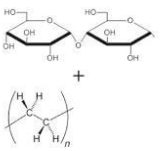
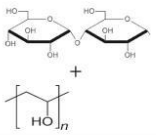
| Plastics | Microorganism | Chemical Structure | Application | Reference |
|---|---|---|---|---|
| **Biobased polymers** | | | | |
| Polyhydroxyalkanoates | *Pseudomonas stutzeri* |  | Packaging materials, disposable diapers, Food ware, Single-Medical devices, Paints | (Muhamad et al. 2015) (Flieger, Kantorova et al. 2003) |
| Polylactic acid | *Bacillus brevis*, *Amycolatopsis* sp., *Penicillium Roquefort* |  | Packaging paper, Coatings, Fertilizers, Films, Compost bags | (Kasirajan and Ngouajio 2012) |
| **Fossil-based polymers** | | | | |
| Polyethylene terephthalate | *Ideonella sakaiensis* |  | Carpets, Shirts, Bags, Plastics bottles, Food packages, Container, | (Yoshida, Hiraga et al. 2016) |
| Polyester | *Streptomyces sp. Phanerochaete chyrsosporium* |  | Fibers, Textiles | (Shah et al. 2008). |
| Polyvinyl alcohol | *Pseudomonas O-3* |  | Adhesives coatings, Ceramics, Reprography, Photography, Medicine, | (Shimao 2001). |
| Polyethylene | *Brevibacillus borstelensis Rhodococcus rubber* |  | Bags, water bottles, Food packaging Film, Toys, Pipes, Motor oil Bottles | (Hadad et al. 2005; Sivan et al. 2006). |
| Nylon | *Flavobacterium sp Pseudomonas sp.* |  | Small bearings, Speedometer gears, windshield Wipers, Water hose nozzels, Football helmets | (Tokiwa et al. 2009). |

**Table 1** (conitnued)

| | | | | |
|---|---|---|---|---|
| Polyethylene succinate | *Pseudomonas* sp. |  | Plastics industry, Shopping bags, Agriculture films | (Tribedi and Sil 2014) |
| Polylcaprolactone | *Clostridium botulinum, C. acetobutylicum, Fusarium solani* |  | Long-term items, Agricultural films, Fibers, Aquatic weeds, Seedling containers | (Abou-Zeid et al. 2001). |
| **Polymer blends** | | | | |
| Starch/polyester | *Streptomyces Phanerochaete chyrsosporium* |  | Present in fibers, Engineering thermoplastics | (Shah et al. 2008) |
| Starch/polyethylene | *Aspergillus niger Penicillium funiculosm Phanerochaete chrysosporium* |  | Highly susceptible to the environmental conditions | (Shah et al. 2008) |
| Starch/PVA Blends | *Alcaligenes feacalis* |  | Agricultural applications, Packaging materials | Tokiwa, Calabia et al. 2009) |

## 12.2. Annex II – In "Rogue one: A plastic story" by Patel, Dhara *et al.*



**Table 2**
Types of bacteria degrading different plastics with different degradation efficiencies.

| Sr no. | Organisms | Plastic | Degradation efficiency | Reference |
|---|---|---|---|---|
| 1 | *A. clavatus strain* | LDPE | 35% | (Gajendiran et al., 2016) |
| 2 | *A. niger* | LDPE | 5.8% | (Gajendiran et al., 2016) |
| 3 | *Actinoplanes* sp. | PE | – | (Rengasamy, 2020) |
| 4 | *Anabaena spiroides, Scenedesmus dimorphus,* and *Navicula pupula* | PE | 8% | (Sarmah and Rout, 2018) |
| 5 | *Aspergillus clavatus strain JASK1* | LDPE Films | 35% | (Raddadi and Fava, 2019) |
| 6 | *Aspergillus favus* | HDPE | 8.51 ± 0.1% | (Chaudhary and Vijayakumar, 2020) |
| 7 | *Aspergillus flavus* | LDPE Powder | 20.63% | (Raziyafathima et al., 2015) |
| 8 | *Aspergillus flavus* | Disposable plastic films | 46.5% | (Raziyafathima et al., 2015) |
| 9 | *Aspergillus glaucus* | Polythene<br>Plastic | 20.80%<br>7.26% | (Raziyafathima et al., 2015) |
| 10 | *Aspergillus japonicas* | LDPE | 11.11% | (Gajendiran et al., 2016) |
| 11 | *Aspergillus niger* | Polythene bags<br>Plastic cups | 12.25%<br>12.5% | (Raziyafathima et al., 2015) |
| 12 | *Aspergillus niger* | Powdered LDPE | 5% | (Raziyafathima et al., 2015) |
| 13 | *Aspergillus oryzae* | HDPE Films | 72% | (Raziyafathima et al., 2015) |
| 14 | *Aspergillus terreus MF12* | HDPE | 20% | (Balasubramanian et al., 2014) |
| 15 | *B. cereus* | PE<br>PET<br>PS | 1.6%<br>6.6%<br>7.4% | (Auta et al., 2017) |
| 16 | *B. gottheilii* | PE<br>PET<br>PP<br>PS | 6.6%<br>3.0%<br>3.6%<br>5.8% | (Auta et al., 2017) |
| 17 | *B. pumilus* | PE | 1.5% | (Auta et al., 2017) |
| 18 | *B. sphericus (Alt)* | LDPE<br>HDPE | 10%<br>3.5% | (Kumari et al., 2019) |
| 19 | *B. subtilis* | PE | 1.75% | (Auta et al., 2017) |
| 20 | *Bacillus cereus* | Polyethylene | 7.2–2.4% | (Raziyafathima et al., 2015) |
| 21 | *Bacillus cereus* | Polythene | 12.5% | (Raziyafathima et al., 2015) |
| 22 | *Bacillus cereus* | Polypropylene Granules | 12% | (Helen et al., 2017) |
| 23 | *Bacillus cereus* | PE<br>PET<br>PS | 1.6%<br>6.6%<br>7.4% | (Roager and Sonnenschein, 2019) |
| 24 | *Bacillus cereus* | PE | 14.6% | (Roager and Sonnenschein, 2019) |
| 25 | *Bacillus cereus* | PET | 60.2% | (Roager and Sonnenschein, 2019) |
| 26 | *Bacillus cereus* | PS | 67.5% | (Roager and Sonnenschein, 2019) |
| 27 | *Bacillus cereus BF20* | LDPE<br>HDPE | 5%<br>2% | (Roager and Sonnenschein, 2019) |
| 28 | *Bacillus cereus BF20* | LDPE | 5% | (Roager and Sonnenschein, 2019) |
| 29 | *Bacillus cereus BF20* | HDPE | 2% | (Roager and Sonnenschein, 2019) |
| 30 | *Bacillus gottheilii* | | | |

(continued on next page)

**Table 2** (*continued*)

| Sr no. | Organisms | Plastic | Degradation efficiency | Reference |
|---|---|---|---|---|
| | | PE | 6.2% | (Roager and Sonnenschein, 2019) |
| | | PET | 3.0% | |
| | | PP | 3.6% | |
| | | PS | 5.8% | |
| 31 | *Bacillus gottheilii* | PE | 56.6% | (Roager and Sonnenschein, 2019) |
| 32 | *Bacillus gottheilii* | PET | 27.4% | (Roager and Sonnenschein, 2019) |
| 33 | *Bacillus gottheilii* | PP | 32.9% | (Roager and Sonnenschein, 2019) |
| 34 | *Bacillus gottheilii* | PS | 52.9% | (Roager and Sonnenschein, 2019) |
| 35 | *Bacillus pumilus M27* | LDPE | 1.5% | (Roager and Sonnenschein, 2019) |
| 36 | *Bacillus pumilus M27* | LDPE | 18.3% | (Roager and Sonnenschein, 2019) |
| 37 | *Bacillus* sp. | PP | 4.0% | (Auta et al., 2018) |
| 38 | *Bacillus* sp. | PP | 4% | (Roager and Sonnenschein, 2019) |
| 39 | *Bacillus* sp. *27* | PP | 36.5% | (Roager and Sonnenschein, 2019) |
| 40 | *Bacillus sphericus* | LDPE | 10% | (Roager and Sonnenschein, 2019) |
| | | HDPE | 3.5% | |
| 41 | *Bacillus sphericus Alt* | LDPE | 10% | (Roager and Sonnenschein, 2019) |
| 42 | *Bacillus sphericus Alt* | HDPE | 3.5% | (Roager and Sonnenschein, 2019) |
| 43 | *Bacillus subtilis H1584* | LDPE | 1.75% | (Roager and Sonnenschein, 2019) |
| 44 | *Bacillus subtilis H1584* | LDPE | 21.3% | (Roager and Sonnenschein, 2019) |
| 45 | *Brevibacillus borstelensis* | Polyethylene | 2.5% | (Kumari et al., 2019) |
| 46 | *Cephalosporium* sp. | HDPE | 7.18 ± 0.15% | (Chaudhary and Vijayakumar, 2020) |
| 47 | *Enterobacter asburiae YT1* | PE | 6.1 ± 0.3% | (Yuan et al., 2020) |
| 48 | *Enterobacter* sp. | PS | 12.4% | (Paço et al., 2019) |
| 49 | *Exiguobacterium* sp. | PS | 7.8% | (Paço et al., 2019) |
| 50 | *K. palustris* | PE | 1% | (Auta et al., 2017) |
| 51 | *Kocuria palustris M16* | LDPE | 1% | (Roager and Sonnenschein, 2019) |
| 52 | *Kocuria palustris M16* | LDPE | 12.2% | (Roager and Sonnenschein, 2019) |
| 53 | *Lasiodiplodia theobromae* | PP | <4% | (Paço et al., 2019) |
| 54 | *M. rouxii NRRL 1835* | Disposable plastic films | 28.5% | (Raziyafathima et al., 2015) |
| 55 | *Masoniella* sp. | Plastic cup | 27.4% | (Raziyafathima et al., 2015) |
| 56 | *Micrococcus luteus* | Plastic cup | 38% | (Raziyafathima et al., 2015) |
| 57 | *Paenibacillus* sp. | LDPE | 30.8% | (Bardají et al., 2019) |
| 58 | *Pencillium pinophilum* | Powdered LDPE | 11.07% | (Raziyafathima et al., 2015) |
| 59 | *Penicillium chrysogenum* | PLA | 14.8% | (Nair et al., 2016) |

**Table 2** (*continued*)

| Sr no. | Organisms | Plastic | Degradation efficiency | Reference |
|---|---|---|---|---|
| 60 | *Phanerochaete chrysosporium* | Polythene | 50% | (Raziyafathima et al., 2015) |
| 61 | *Phanerochaete chrysosporium* | PVC | 11% | (Paço et al., 2019) |
| 62 | *Phormidium lucidum*- and *Oscillatoria subbrevis*- | PE | 30% | (Sarmah and Rout, 2018) |
| 63 | *Pseudomonas aeruginosa* | Polythene | 35% | (Raziyafathima et al., 2015) |
| 64 | *Pseudomonas aeruginosa* | LDPE | 20% | (Kyaw et al., 2012) |
| 65 | *Pseudomonas aeruginosa* | LDPE | 11% | (Kyaw et al., 2012) |
| 66 | *Pseudomonas putida* | Milk cover | 75.3% | (Raziyafathima et al., 2015) |
| 67 | *Pseudomonas putida* | LDPE | 9% | (Kyaw et al., 2012) |
| 68 | *Pseudomonas* sp. | Natural | 46.2% | (Raziyafathima et al., 2015) |
| | | Synthetic polythylene | 29.1% | |
| 69 | *Pseudomonas* sp. | Natural | 31.4% | (Raziyafathima et al., 2015) |
| | | Synthetic polythylene | 16.3% | |
| 70 | *Pseudomonas* sp. | Natural | 39.7% | (Raziyafathima et al., 2015) |
| | | Synthetic polythylene | 19.6% | |
| 71 | *Pseudomonas* sp. | Polythene | 20.54% | (Raziyafathima et al., 2015) |
| | | Plastic | 8.16% | |
| 72 | *Pseudomonas* sp. | Polythene | 12.5% | (Raziyafathima et al., 2015) |
| 73 | *Pseudomonas* sp. | LDPE Powder | 37.09% | (Raziyafathima et al., 2015) |
| 74 | *Pseudomonas* sp. | Polythene | 11% | (Singh et al., 2016) |
| 75 | *Pseudomonas stutzeri* | PP | 0.25% | (Paço et al., 2019) |
| 76 | *Pseudomonas syringae* | LDPE | 11.3% | (Kyaw et al., 2012) |
| 77 | *Pseudonocardia* sp. | PE | – | (Rengasamy, 2020) |
| 78 | *Rhodococcus* | PP | 6.4% | (Auta et al., 2018) |
| 79 | *Rhodococcus ruber (C208)* | Branched lowdensity (0.92 g $cm^{-3}$) | 7.5% | (Raziyafathima et al., 2015) |
| 80 | *Rhodococcus ruber strain C208* | PE Films | 7.5% | (Raddadi and Fava, 2019) |
| 81 | *Rhodococcus* sp. | PP | 6.4% | (Auta et al., 2018) |
| 82 | *Rhodococcus* sp. | PP | 6.4% | (Roager and Sonnenschein, 2019) |
| 83 | *Rhodococcus* sp. *36* | PP | 58.4% | (Roager and Sonnenschein, 2019) |
| 84 | *Sporichthya* sp. | PE | – | (Rengasamy, 2020) |
| 85 | *Sporosarcina globispora* | Polypropylene Granules | 11% | (Helen et al., 2017) |
| 86 | *Staphylococcus* sp. | Polythene | 52% | (Singh et al., 2016) |
| 87 | *Streptococcus lactis* | Polythene bags and plastic cups | 12.25% and 12.5% | (Raziyafathima et al., 2015) |
| 88 | *Streptomyces KU8,* | LDPE Powder | 46.16% | (Raziyafathima et al., 2015) |
| 89 | *Streptomyces* sp. | LDPE | 46.7% | (Raziyafathima et al., 2015) |
| 90 | *Streptomyces* sp. | PE | 20% | (Rengasamy, 2020) |
| 91 | *Thermobifida fusca* | PET | 12.9% | (Paço et al., 2019) |
| 92 | *Trametes versicolor* | Nylon | 54% | (Paço et al., 2019) |
| 93 | *Zalerium maritimum* | PE | 70% | (Paço et al., 2019) |
| | | LDPE | | |
| | | HDPE | | |