

Review

Fluoropolymers as Unique and Irreplaceable Materials: Challenges and Future Trends in These Specific Per or Poly-Fluoroalkyl Substances *

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* Dedicated to my friend and coworker, Professor George Kostov, in the occasion of his 80th birthday.

Abstract: In contrast to some low-molar-mass per- and polyfluoroalkyl substances (PFASs), which are well established to be toxic, persistent, bioaccumulative, and mobile, fluoropolymers (FPs) are water-insoluble, safe, bioinert, and durable. These niche high-performance polymers fulfil the 13 polymer-of-low-concern (PLC) criteria in their recommended conditions of use. In addition, more recent innovations (e.g., the use of non-fluorinated surfactants in aqueous radical (co)polymerization of fluoroalkenes) from industrial manufacturers of FPs are highlighted. This review also aims to show how these specialty polymers endowed with outstanding properties are essential (even irreplaceable, since hydrocarbon polymer alternatives used in similar conditions fail) for our daily life (electronics, energy, optics, internet of things, transportation, etc.) and constitute a special family *separate* from other “conventional” C_1 – C_{10} PFASs found everywhere on Earth and its oceans. Furthermore, some information reports on their recycling (e.g., the unzipping depolymerization of polytetrafluoroethylene, PTFE, into TFE), end-of-life FPs, and their risk assessment, circular economy, and regulations. Various studies are devoted to environments involving FPs, though they present a niche volume (with a yearly production of 330,300 tons) compared to all plastics (with 460 million tons). Complementary to other reviews on PFASs, which lack of such above data, this review presents both fundamental and applied strategies as evidenced by major FP producers.

Keywords: end of life; fluoropolymers; per- and polyfluoroalkyl substances (PFASs); polymerization aids; recycling; regulators; surfactants



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1. Introduction

According to the Organization for Economic Co-operation and Development (OECD) [1,2], perfluoroalkyl (and polyfluoroalkyl) substances (PFASs) are artificial/anthropogenic products that contain multiple C–F bonds [3–9]. Because of their unique hydrophobic/lipophobic physicochemical properties, this specific group of chemicals displays quite different physical, chemical, and biological properties [5–9] than other hydrocarbon compounds and have been involved in many applications in different areas [5–10]. The OECD [1] has reported more than 4700 PFAS molecules and, according to the US Environment Protection Agency [3,11], this number reaches more than 12,000 compounds [12]. However, PFAS molecules, especially those of low molar mass, have been found in many soils, waters, seas, and oceans as reported by a plethora of articles and reviews [4–10]. Thanks to the high electronegativity and small radii of the fluorine atom that confers a short and quite stable C–F bond, fluorinated products have remarkable chemical inertness and thermal stability (the dissociation energy of this C–F bond is worth ca. 120 kcal·mol^{−1} [7,9]). However, such characteristics further induce some limitations, since PFASs are known to be water-soluble, mobile, toxic, persistent, and bioaccumulable [9,12–14]. Since 2000, many regulations have been proposed, modified, and multiplied [5–8,10,12–17]. Various fluorinated compounds

have been banned for several years and continuous procedures from competent authorities still maintain the pressure to impose drastic legislations/regulations [16].

Thomas et al. [17] comprehensively reported the global situation on the regulation of PFASs in both the scientific and legislative communities, and analyzed the different regulatory actions launched both in Europe and in the USA (including federal- and state-level initiatives). These authors supplied an exhaustive list of different dossiers of legislation and carefully reported how regulators have approached the concerns regarding PFASs from different perspectives. Last March 2023, China added PFOA and PFOS to its list of New Pollutants for Priority Management to modify their production, use, import, and export [18]. Presently, 152 countries have ratified the Stockholm Convention, which puts in place the elimination and restriction of listed PFASs with exemptions for specific uses such as hard metal plating and firefighting foams (AFFFs). As of 5 April 2023, Israel, Haiti, the USA, Malaysia, and Brunei Darussalam have not ratified the convention. Although ratified, there is no indication that a number of the member nations have made efforts to regulate PFASs via other independent mechanisms [17].

This review aims first at making a distinction between various classes of PFASs, showing major issues from low-molar-mass ones in contrast to the high-molar-mass fluoropolymers, which display specific advantages (safety, bioinertness, non-toxicity, and fulfilling the 13 polymer-of-low-concern (PLC) criteria in their conditions of use).

In addition, advanced technologies from industrial manufacturers of FPs have led to recent innovations such as the use of non-fluorinated surfactants in the aqueous radical (co)polymerization of fluoroalkenes to yield FPs with similar performances. These above innovations have unprecedentedly been reported before. This review also aims at showing how these specialty polymers endowed with outstanding properties are essential (even irreplaceable) for our daily life (in electronics, energy, optics, internet of things, transportation, etc.) and constitute a special family that is *separate* from the other “conventional” C₁–C₁₄ PFASs found everywhere on Earth and its oceans. Furthermore, some information reports on their recycling (e.g., the unzipping depolymerization of polytetrafluoroethylene, PTFE, into TFE), end-of-life FPs, and their risk assessment and circular economy. Various studies are devoted to environments involving FPs, though they represent a niche volume. Complementary to articles on PFASs, which lack the information above, this review gathers both fundamental and applied strategies as evidenced by major FP producers. Various features are still attracting huge interest from both academic and industrial players.

2. History of PFASs

Fluorinated polymers have been known for eighty-five years [14] and a brief historic sketch showing their extraordinary evolution is depicted in Figure 1, which includes fluorinated gases (discovered in the 1920s), intermediates, monomers, oligomers, and polymers, as well key methods to supply them either via electrochemical fluorination [9] or telomerization [19]. Among them, surface-active products (surfactants) are specific amphiphilic PFASs that display much lower surface tension and surface energy than hydrocarbon surfactants [9,20]. They are currently used in more than 200 applications, such as aqueous firefighting/film-forming foams [20–22], food packaging, cosmetics, photoacid generators [9,10,20], paints, semiconductors, in electroplating [22], and as polymerization aids in the emulsion radical polymerization of fluorinated alkenes [9,22]. There are many examples related to PFASs including their production sites [12] or storage areas such as military bases equipped with extinguishers [23,24] and airports [25,26], where many PFASs have been found. Ruyle et al. [24] analyzed groundwater samples from a fire training area between September 2007 and July 2021 (six time points; Figure 2). All groundwater measurements were from samples collected from the same well to control the hydrological variability. The samples represent concentrations in the upper 2–3 m of groundwater. These authors directly compared the PFAS concentrations to those of samples collected in 2007. Their analyses were achieved in order to supply quantitative and qualitative information from complementary techniques such as liquid chromatography–tandem

mass spectrometry (LC-MS/MS), combustion ion chromatography, high-resolution mass spectrometry, and a comparison of measured and library MS/MS spectra.

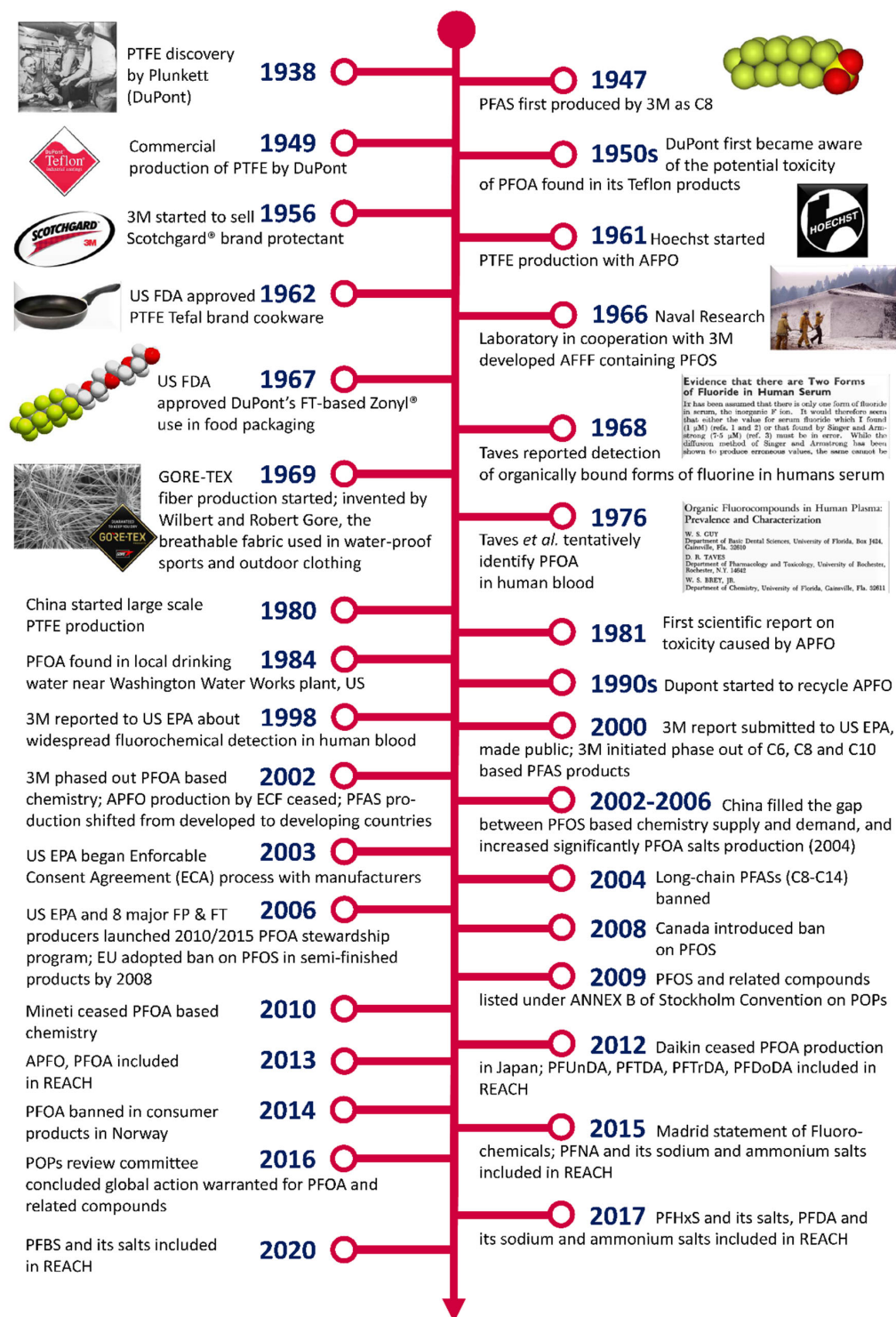


Figure 1. Historical scheme of the fluorine chemistry, from the discovery of polytetrafluoroethylene (PTFE) to REACH regulations (Reprinted with permission from Ref. [9]. Copyright 2022 Royal Society of Chemistry) (APFO, ECF, EPA, FT, PFBS, PFCA, PFNA, PFOA, PFOS, POP, and REACH stand for ammonium perfluorooctanoate, electrochemical fluorination, Environment Protection Agency, fluorotelomer, perfluorobutanesulfonate, perfluorocarboxylic acid, perfluorononanoic acid, perfluorooctanoic acid, perfluorooctanesulfonic acid, persistent organic pollutants, and Registration, Evaluation, Authorisation and Restriction of Chemicals, respectively).

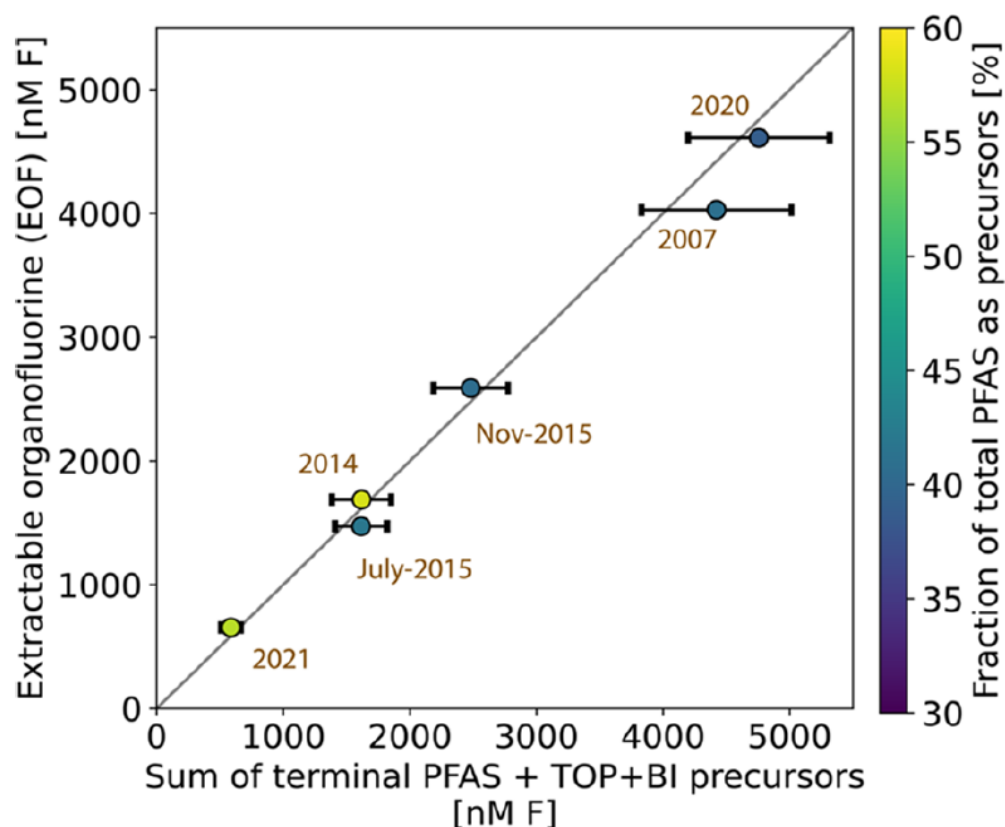


Figure 2. Mass budget for PFASs in groundwater below the fire training area at Joint Base Cape Cod, USA: Comparison of detected extractable organofluorine (EOF) and PFAS concentrations. The x -axis represents the sum of terminal PFAS and oxidizable precursors inferred from the total oxidizable precursor (TOP) assay using Bayesian inference. The sum of differences from duplicate extracts for targeted PFAS (9%; $n = 1$) and the standard deviation of inferred precursor concentrations are shown by x -axis error bars. Circles are shaded in purple according to the fraction of EOF explained by oxidizable precursors. The one-tone line (gray) is used to compare the sum of terminal PFASs and precursors measured using targeted analysis and the TOP inference with EOF. Reprinted with permission from Ref. [24].

3. Issues on Mobility, Persistency, Toxicity, and Bioaccumulation of PFASs

As a matter of fact, major concerns arise from their high water solubility [27] and thus mobility, as well as their chemical stability, toxicity, persistence [26,28–30], and bioaccumulation in the environment, in the food chain, and in humans [5,6,10,12,23,28–31]. Growing attention has been paid to PFASs as a specific chemical class [4,7,31] because of their adverse health effects, modes of action, and physical and biochemical properties [4], mainly linked to their too-stable small perfluorinated chain that cannot degrade or be metabolized.

Actually, modern powerful analytical apparatus and machines are able to detect very low chemical concentrations (as low as several tenth of ppb [32] (or even hundreds of ppt); knowing that one ppb is a drop of water in an Olympic-size swimming pool!).

Globally, environmental officials from five member states [16] launched actions to push regulatory agencies (as Registration, Evaluation, Authorisation and Restriction of Chemicals: REACH) and consequently the EU to restrict PFASs (including FPs) with some plans to ban all PFASs by 2030 [33]. In addition, more than a dozen states in the USA have been also influencing authorities to ban PFASs in the coming years (Maine and Minnesota have already started). Consequently, synthesizing alternatives to face perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) issues (since 2006, PFOA and PFOS, their salts, and similar compounds have been banned in many countries) led to a large amount of research that has been well summarized in various reviews [21] or book

chapters [22,34] (though China is still currently using PFOA as polymerization aid as well as other PFASs containing shorter chain lengths). On the other hand, Chemours and Dyneon industrially produced hexafluoropropylene oxide dimer ammonium carboxylate (Gen[®]X or HFPO-DA) and 4,8-dioxa-3H-perfluorononanoate (Adona[®]), respectively, enabling FPs to be yielded, the quality and performances of which were similar to those of the FPs obtained in the presence of PFOA or PFOS. However, several years later, these surfactants had also been detected in soils and rivers, probably because of their persistency and mobility issues [9,34,35].

4. Different Categories of PFASs

PFASs have been categorized into two distinct families of fluorinated compounds [4, 7,27,36], the major differences being their molar mass (Figure 3) and dispersity for their separate uses.

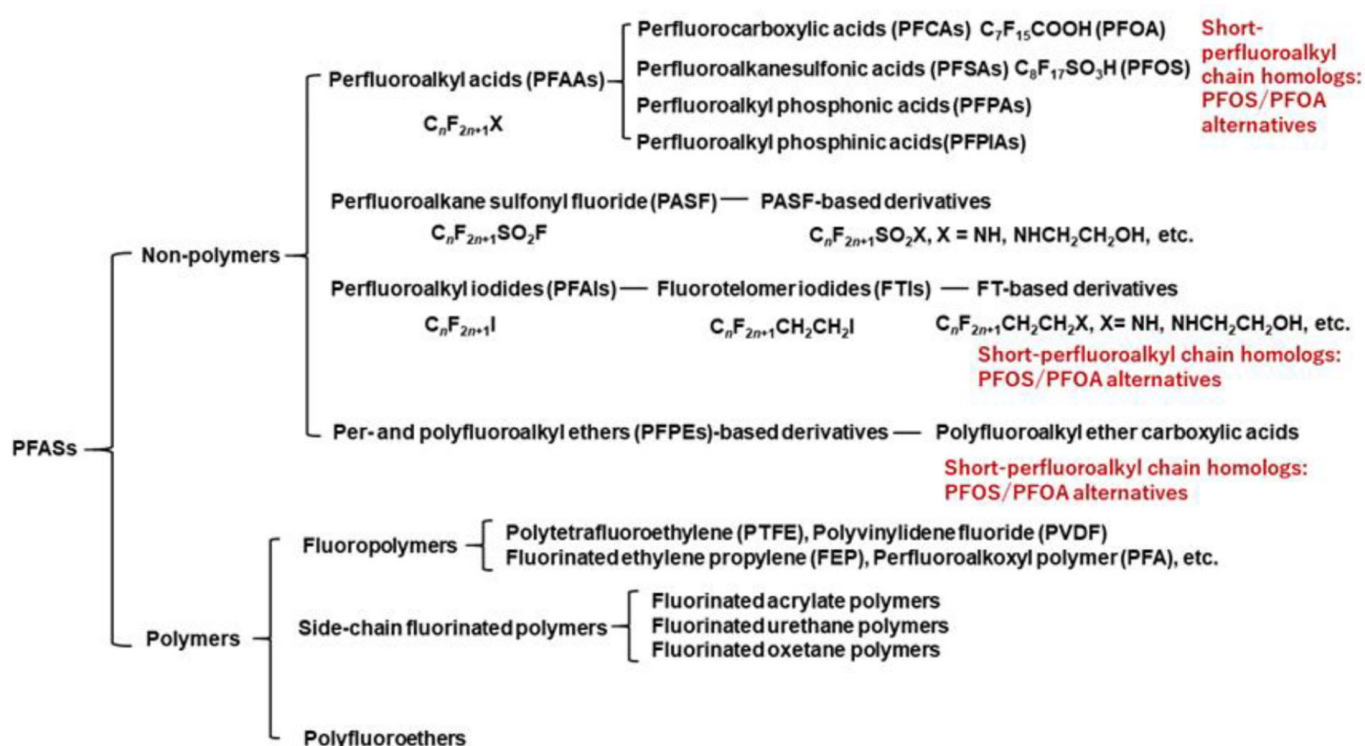


Figure 3. General classification of PFASs according to the Organization for Economic Co-operation and Development (OECD) [1].

4.1. Non-Polymeric PFASs

4.1.1. Introduction

Low-molar-mass PFASs ($<1000 \text{ g}\cdot\text{mol}^{-1}$), including PFOA, PFOS, and fluorinated telomers (Scheme 1) [9,19], have contaminated many places on Earth and its oceans or decompose in the stratosphere, leading to trifluoroacetic acid (which is extremely difficult to separate from water) and trifluoroacetate [37], polluting waters and soils and thus bringing negative impacts. These compounds also cross the cellular membranes of animals and human beings [1,32,38].

4.1.2. Strategies to Eliminate Low-Molar-Mass PFASs

Beside the thermal (low [39] or high [40,41]), biological [42], and microbial [43] degradation and that occurs under subcritical water [44], which has been well summarized by Mueller and Yingling [45], a variety of porous sorbents such as carbon-based materials, ion-exchange resins, or polycationic gels have been investigated to remove

PFASs [46–49]. The adsorption behaviors of PFASs are dramatically affected by the pH values of environmental conditions, as well as substances of several orders of magnitude higher concentrations than PFASs in natural water sources [46–48]. Therefore, selective PFAS separation under environmentally friendly conditions has been revealed to be highly challenging [49,50]. In reality, endowed with their fluorophilicity feature, fluoropolymer nanoparticles (FPNPs) (e.g., star polymers with fluorinated nanogel cores and hydrophilic poly(ethylene oxide) arms able to remove PFOA from 10 ppm to ppb levels [51,52]) are interesting candidates for PFAS adsorption because they display strong and selective affinity to PFASs. FPNPs, being highly resistant to non-fluorinated ions, are able to spread in the environment.

In addition, Song et al. [53] recently succeeded in eliminating PFOA via chlorine-radical-triggered electrochemical oxidation, while Chen et al. [54] synthesized an original FPNP-embedded hydrogel for PFAS adsorption. These FPNPs were produced from tandem photo-mediated RDRP (Figure 4). The FPNPs showed significant adsorption performance for many cationic, anionic, neutral, and zwitterionic PFASs. The strong and selective affinity toward fluorinated compounds enabled clearance of PFASs at highly environmentally relevant concentrations in water without being dramatically disturbed by acidic/basic conditions. Furthermore, such FPNP-embedded hydrogel displayed good mechanical properties inclined to facilitate its separation, regeneration, and recycling.

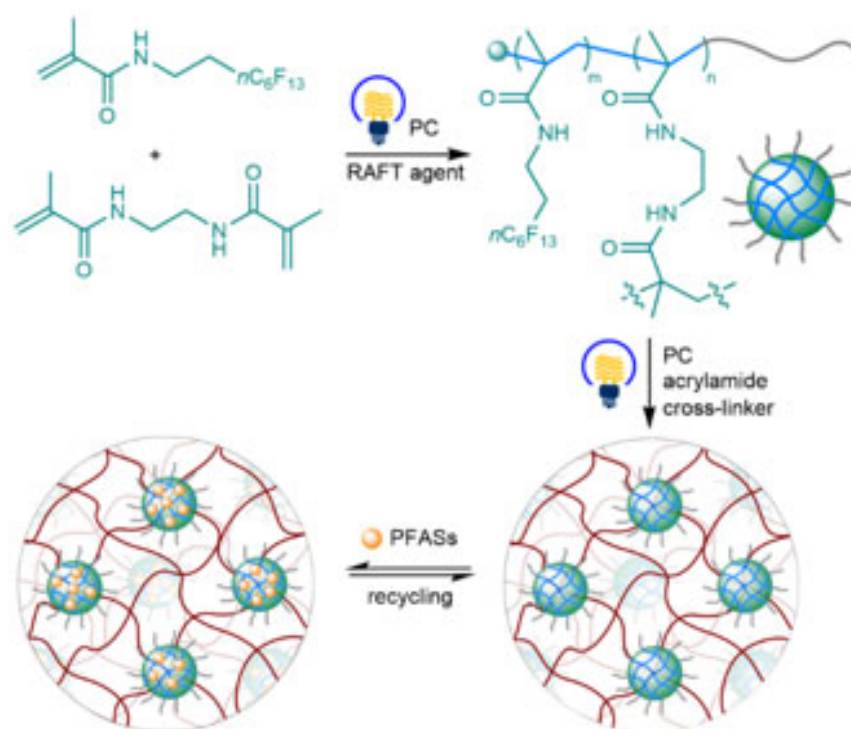
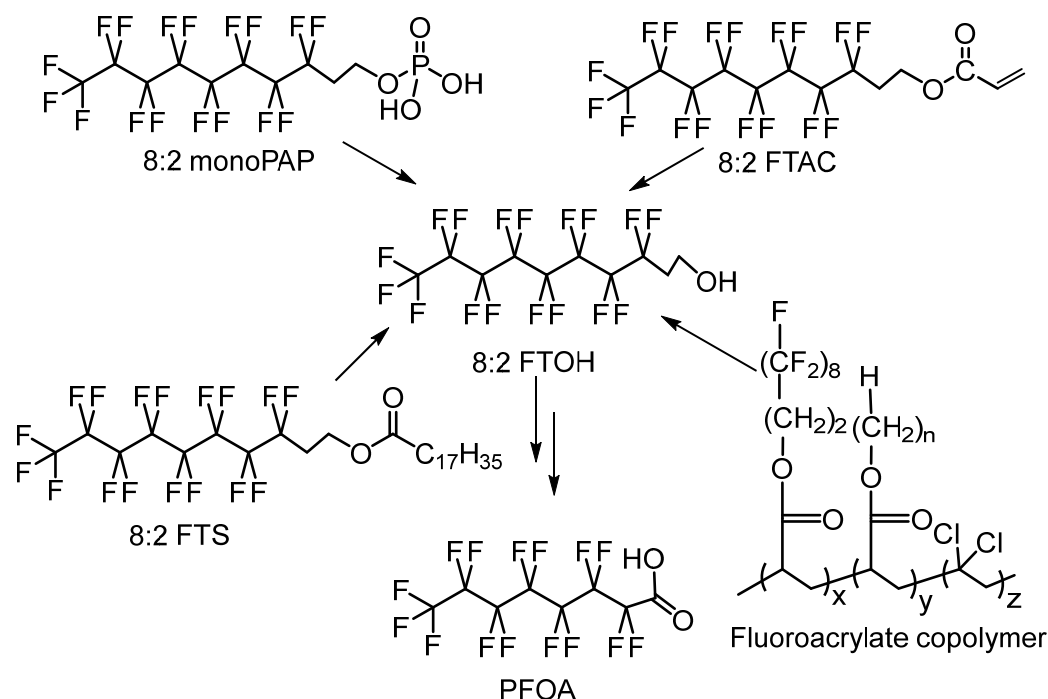


Figure 4. Synthesis of fluoropolymer nanoparticle (FPNP)-embedded hydrogel and study on PFAS adsorption. Adapted with permission from Ref. [54]. Copyright 2020 American Chemical Society.

Beyond FPNPs, other fluorinated sorbents have been reported as relevant host molecules for PFAS guests. One example deals with cross-linked fluoropolymer gels [46,49], while β -cyclodextrin-based polymers [55] and granular activated carbon [41] are evidenced to capture neutral and/or anionic PFASs efficiently. The outstanding performance of these FPs further highlights that the fluorophilicity effect could be used as a basic feature to promote PFAS adsorption toward a sustainable society.



Scheme 1. Illustration of microbial degradation of poly(fluoroacrylate) that generates 8:2 fluorotelomer derivatives. Adapted with permission from Ref. [43]. Copyright 2013 Elsevier.

4.2. Fluorinated Polymers

4.2.1. FPs Containing Fluorinated Side Chain or Oxygen Atoms

A wide variety of fluorinated polymers have been reported in some monographs [56–59] and reviews [60–64]. While fitting the PFAS definition because of their chemical composition, structure, and presence of fluorine atoms [4,7,64], FPs represent a specific family and are significantly different from other substances of the PFAS category (Figure 3). Indeed, they can be composed of (i) polymers bearing fluorinated dangling chains such as poly[fluoro(meth)acrylate]s [65,66], or fluorinated polyurethanes or poly[fluoro(oxetane)]s; (ii) perfluoropolyethers, PFPEs, prepared via ring-opening polymerization of either hexafluoropropylene oxide (HFPO) or oxetanes, or achieved from the photochemical polymerization of TFE and hexafluoropropylene (HFP) in the presence of oxygen [67]; and finally (iii) polymers containing carbon and fluorine atoms in their backbones. As an example, from durable water repellent (DWR) clothing, poly[fluoro(meth)acrylate]s [66] undergo some leaching out of the fluorinated side groups through weathering yielding, PFASs (mainly fluorinated hydroxy telomers).

Furthermore, the microbial degradation of polymers bearing (per)fluorinated side groups represents a major issue, as evidenced by Liu and Avendaño [43]. It can be assumed that, because of their high chemical and ageing stability, to the best of our knowledge, no similar study has yet been reported on FPs bearing fluorine atoms in the backbone. These poly(fluoroacrylate)s possessing ω -perfluorinated dangling moieties have led to 8:2 fluorotelomer derivatives (Scheme 1), while several studies have described the decomposition and release of the fluorinated side chain under various conditions [66].

4.2.2. Fluoropolymers (i.e., Backbone Containing C-F Bonds)

Valuable Fluoropolymers with Exceptional Properties

This sub-section is devoted to polymers bearing C-F bonds within the backbone, and it is divided into four parts. These unique specialty polymers are niche products (production: 330,000 tons/year [64] compared to >400 million tons/year of all polymers), known to be safe, bioinert, persistent, and not degradable under environmental conditions. These durable materials display outstanding properties [56–64], prolonged lifetimes, increased

fire safety, reduced maintenance needs, and good performances (even in extreme conditions or aggressive/corrosive media) where other materials fail. One example is the dramatic Challenger explosion in 1986, 73 s after liftoff, related to poly(thioether) seals that had too-high T_g values. Since then, all shuttle packings and gaskets have been made of fluoroelastomers [68]. Advantageously, they are the unique candidates displaying the best heat and oil resistance (e.g., aircraft fluids such as Skydrol®) [69] (Figure 5) and excellent flexibility. Essential for our daily life [63] and involved in many high-tech areas, FPs are endowed with exceptional features [56–64], with their molar masses being able to reach several million $\text{g}\cdot\text{mol}^{-1}$ (like PTFE). Because of the growing need for higher requirements and engineering materials that combine specific properties for high-tech applications, FPs are currently undergoing increasing development [70].

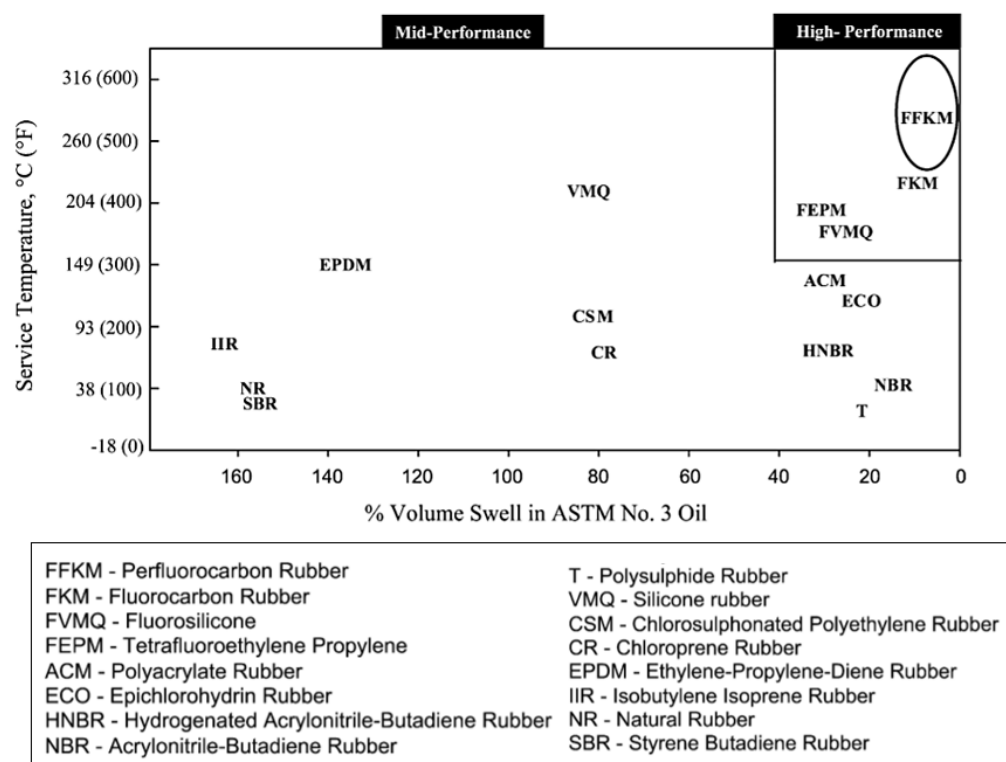


Figure 5. Compared relative heat and oil resistances of elastomers (ASTM D2000). Adapted with permission from Ref. [69]. Copyright 2003 Elsevier.

One example is poly(vinylidene fluoride), PVDF, which satisfies stringent leachable limits and other national health regulations, ensuring that it is safe for use in water treatment. In addition, this FP is durable, withstanding high pressures while maintaining structural integrity.

Currently, these specialty polymers are also involved in specific UV and aging resistant coatings and have been involved in many other applications: (i) Wires and cables in wide domains such as aerospace (because of their high limiting oxygen index value, PTFE coatings ensure fire retardancy in several-hundred-kilometer cables and connections in planes), insulation (insulation resistance $\geq 1500 \text{ M}\Omega\cdot\text{km}$), electrical applications, and high-frequency (5000 V) performance in coaxial cables for avionics and high-temperature-resistant cables for aeroengine services [71]. The resilience and inertness of crosslinked elastomers provide exceptional performance to gaskets in shuttles [72]. (ii) Materials for energy storage and conversion (as key candidates for the energetic transition: cathode binders in lithium ion batteries, proton exchange fuel cell membranes, backsheets of photovoltaic panels, electroactive (piezoelectric and electrothermal) devices [73], haptics, printed electronics, dielectrics, for virtual reality, and actuators for artificial muscles, and are

indispensable drivers of the European Green Deal). (iii) The chemical process industry (e.g., injection-molded PVDF tower packing is used over and over in sulfuric acid and chlorine scrubber systems and does not lose its properties like other polymers when exposed to harsh chemistries and high temperatures). (iv) Transport (transmission fluids and specific seals and gaskets) [57,74], telecommunications (optical fibers, among more than 4 million km of undersea cables, are carrying information via a huge network) [75], food and water treatment, electronics [76], and pharmaceutical and medical devices [77–82].

FPs should only be involved in uses required for health, safety, or when they are critical for the functioning of society and no alternatives are available [9,63,64,83,84]. In addition, searching for alternative materials would reduce the time required for toxicological analyses.

The most prevalent materials are PTFE [61], PVDF [73,85], poly(chlorotrifluoroethylene), PCTFE [86], and the copolymers based on tetrafluoroethylene, TFE [87], and vinylidene fluoride, VDF [88], which can be either thermoplastics or elastomers [72]. Usually, in their conditions of uses, FPs are safe, stable (thermally, chemically against UV and aging, and biologically), durable, non-toxic, non-bioaccumulative, insoluble in water and thus non-mobile, hydrolytically stable, and are not subject to hydrolysis-catalyzed or -metabolized degradation. For these features, they are not considered as substances of very high concern (SVHC) and fulfil the 13 criteria (see Section Polymer-of-Low-Concern Criteria) [35,89,90]. Furthermore, their relevant combinations of properties are not matched by any of the alternative hydrocarbon polymers [9,63,83,84], hence making them so unique and valuable.

Regulatory agencies, such as Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) [32], the Toxic Substances Control Act (TSCA), and the Japanese Existing New Chemical Substances Inventory (ENCSI), support initiatives aimed at regulating the substances of greatest concern. They will endeavor to contribute to the broad and complex scientific, technical, but also economic forthcoming debate on those substances. Currently, FPs seem to be impacted by the upcoming restrictions on PFASs under the EU REACH Regulation, published in February 2023 [32].

Improvement in FP Production in More Environmentally Friendly Processes

Because they are concerned about the negative aspects of the fluorinated polymerization aids (FPAs or surfactants) currently used to replace PFOA, FP manufacturers have been overcoming the great challenge to produce FPs free from FPAs. They are currently searching for solutions for both replacing such PFAs with non-FPAs (NFPAs) and processing by reducing fluorinated effluents and gas emissions. Indeed, a few years ago, the companies Chemours and Dyneon developed and used Gen[®]ex and Adona[®], respectively, though these FPs have been found as traces in rivers and soils [34]. However, the regulatory agencies are currently pushed by various authorities towards helping the industry to swiftly move towards sustainable technologies, and many efforts from these FP producers have been recently taken two main strategies: (i) The absence of FPA as well as matching the PLC criteria are more appropriate to specific syntheses (such as FKM). A lot of progress has been observed in the last decade after several FP manufacturers modified their production using NFPAs (or surfactants), leading to major innovations in the whole industry (such as 3M [91], AGC [92], Arkema [93], Chemours [94,95], Daikin [96], Gujarat Fluorochemicals [97–99], Solvay [100], and others), with multiple patents being filed claiming such “NFPA Technology” for various products (Table 1) [101].

However, the use of NFPAs in a specific recipe (for example, in the aqueous radical polymerization of M1 fluoromonomers, e.g., TFE) does not necessary lead to the same success as that of another M2 monomer (e.g., VDF or a mixture of various fluorinated comonomers). The legislation process should be focused on the use of FPs and the emissions of fluorinated derivatives. In this regard, a regulatory decision tree was suggested [101] (Figure 6), linked to the manufacturing of FPs in the presence or absence of such surfactants (with process abatement to obtain a PFAS concentration lower than 25 ppb [38]),

to provide essential use criteria in terms of safety, performance, health, improvements in the process, and alternatives.

Table 1. Industrial developments of non-fluorinated polymerization aid (NFPA) technology in the manufacturing of fluoropolymers.

Type of Fluoropolymer	References
PTFE Aqueous dispersions	[83,93]
PTFE Fine powders	[90,94]
PVDF	[88,93,95]
FKM	[89,92,95]
PFA	[94]

FKM stands for poly(VDF-*co*-HFP) or poly(VDF-*ter*-HFP-*ter*-TFE) copolymers while PFA means poly(TFE-*co*-perfluoroalkyl vinyl ether) copolymer, respectively.

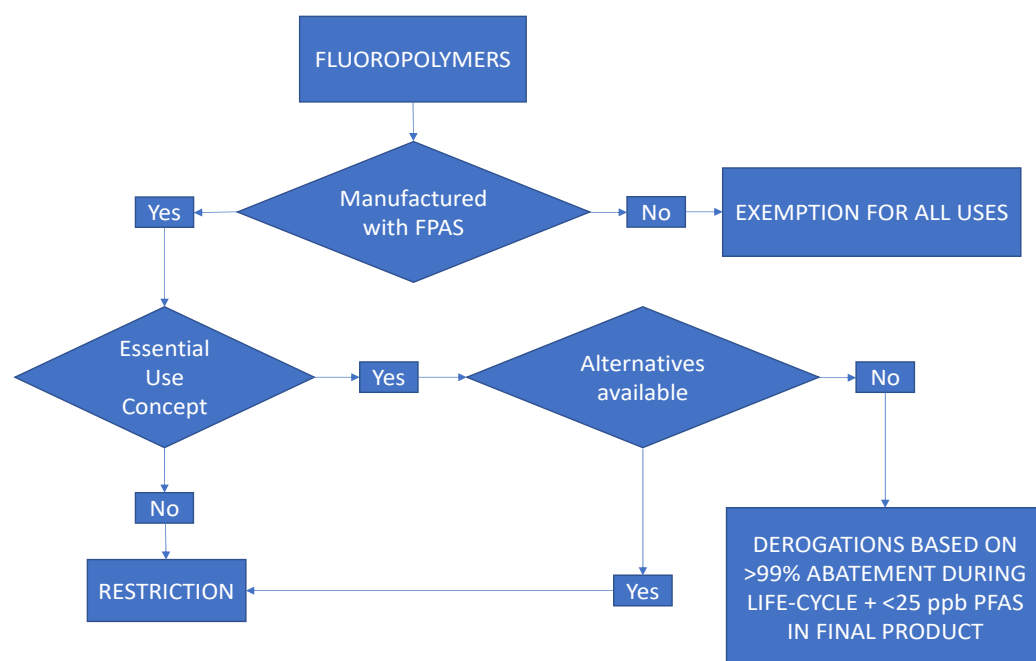


Figure 6. Regulatory decision tree for fluoropolymers. Reprinted from Ref. [101].

Hence, FPs produced without any FPAs should be exempt for all uses across all industries including consumer applications as they raise no risk to the environment or to mammal and human health, in addition to the fact that FPs also match the PLC criteria.

(ii) Manufacturing modification. The second action taken by many FP manufacturers aims at changing their process to eliminate fluorinated side-products such as residual reactants, oligomers, low-molar-mass derivatives and intermediates, aqueous residues, and volatiles. Actually, improving the abatement processes and PFAS recovery in the manufacture of FPs has enabled a reduction of 99% in fluorosurfactant emissions since the 1990s [102], while recent studies have brought it as high as 99.99% [103]. For example, though critical analyses were published in the last decade [104], the Arkema Company strongly reacted and announced that, since February 2023, this innovative solution has made it possible to reduce C₆F₁₃-telomer sulfonate (6:2 FTS) emissions by more than 90% and that the emissions of such a telomer now represent less than 1 kg per day [105] in FP manufacturing in Pierre-Bénite (France) without the use of any fluorosurfactants. Actually, by the end of 2024, a similar process will equip all its other production sites around the world [105].

Other companies have also been modifying their process to significantly reduce their emissions, with many of them having announced such strategies [105–112]. An abundant body of literature is available in relation to the control and treatment of emitted PFASs from industrial processes [43–45], while many studies are still ongoing [39,113].

Polymer-of-Low-Concern Criteria

More recently, the American Chemical Council led the Fluoropolymer Industry Group (*Fluoropolymergroup*) to investigate a similar study on 14 additional fluorinated (co)polymers [90]. FPs and the Stockholm Convention persistent organic pollutants (POPs) criteria meet the persistence criterion only, but not the bioaccumulative, toxic, or mobile criteria.

According to the OECD definition [1,36,114], the criteria for polymers of low concern (PLC) that result from the combined experience and knowledge of global regulatory authorities on predictive parameters of health and environmental hazards induced by polymers have been extensively reported in several reviews [114–116]. Indeed, to be regarded as a PLC, a polymer must not have any known hazard classification while it should also commit to the following criteria:

(i) A high average molar mass number (M_n) and a minimum oligomer amount are the most important requirements for PLC assessment, as claimed by the EU: [115] *“most potential health concern polymers have a low number average molecular weight, M_n , (<1000 Da) and an oligomer content >1%.”* The higher the number of oligomers, the more eco-toxicological the polymer is [114]. By comparing the potential health concern of polymers with varying oligomer percentages, *“the distribution of potential health concern polymers showed an increased incidence of higher oligomer content that began at 5% for <1000 Da and 2% for <500 Da oligomeric content”* [114];

(ii) Reactive functional group (RFG) requirements;

(iii) Solubility in solvents and in water lower than $10 \text{ mg} \cdot \text{L}^{-1}$;

(iv) Other criteria such as a low cationic density, not containing any CF_2 or CF_3 groups, being stable under the conditions in which it is used. The primary concerns for such FPs are their degradation in the environment to release persistent, bioaccumulative, or toxic products, not being a high-molar-mass water-absorbent polymer ($\geq 10,000 \text{ g} \cdot \text{mol}^{-1}$), and having any known hazard classification.

Indeed, regarding the RFGs and RFG ratio to M_n [90,115,116], FPs fulfill the PLC criteria. A PTFE most typically bearing terminal $-\text{CF}_3$ groups [36] is not considered as an RFG. Furthermore, the M_n value is an important feature of biological effect because very large molecules (>1000–10,000 Da) are too big to cross the cellular membrane [117–119] and thus cannot react with “target organs”, such as the reproductive system. Hence, as the M_n of a polymer increases, a reduced incidence of potential health concern effects might be expected [114], and, as proof, expended PTFE (e-PTFE) materials are currently used for stents, cardiovascular prostheses, and many other medical items [80,81].

In contrast and as expected, a polymer does not meet the PLC criteria if it decomposes considerably, or degrades or depolymerizes during use. In other words, it undergoes a deep modification into simpler, lower-molar-mass chemicals as the result of oxidation, hydrolysis, heat, sunlight, attack by solvents or microbial action, or any other reaction(s). Indeed, FPs are resistant to such reactions/decompositions [59]. Based on such relevant features and the above PLC criteria, Henry et al. [35] supplied key evidence on four main FPs (PTFE, FEP, PFA and ETFE) matching the 13 PLC criteria [120]. Using gas chromatography/mass spectrometry (GC/MS) and liquid chromatography/mass spectrometry (LC/MS) analyses, these authors characterized the extractable fractions from these FPs and detected that less than 2 ppm was leachable from PTFE (Table 2) [35]. As expected, since the monomers are gases, they were not detected.

Table 2. Results of gas chromatography/mass spectrometry and liquid chromatography/mass spectrometry analyses of extractable fraction from PTFE to match the PLC criteria (readapted with permission from Wiley) [36].

Final PTFE Results		
Properties of interest	Concentration	PLC Criteria
* % oligomer	Not detected	<2% w/w (20,000 ppm)
** residual monomers	Not detected	No limit established by OECD, 2009
Low-molar-mass leachables and extractables	# 2 ppm	No limit established by OECD, 2009

* Polymers of potential health concern have an increased incidence of higher oligomer content that began at 5% for <1000 Da and 2% for <500 Da oligomeric content (OECD, 2009). The table lists the lower limit, 2%. ** The data set used by OECD [114] to establish the PLC criteria was insufficient to establish a universal limit for all residual monomers, though residual monomer content was established as a PLC criteria [108]. According to U.S. EPA's Safer Choice criteria (SCP, 2015), TFE is a residual of concern, which is not allowed to be present in Safer Choice-recognized products at 0.01% or higher. There is no specific limit on residual monomers in the PLC criteria [114]. # Isopar K, an unavoidable ambient air contaminant adsorbed to PTFE fine powder, was detected at ≤ 2 ppm.

Advantageously, as with most FPs, PTFE is insoluble in water and, therefore, is not mobile in the environment. Using the descriptive solubility table from the US Pharmacopeia [121], the water solubility of PTFE would be classified as insoluble (10^{-5} mg·L $^{-1}$ or 0.01 mg·L $^{-1}$) to very slightly soluble (10^{-4} mg·L $^{-1}$ or 0.1 mg·L $^{-1}$).

The polymer policies of 10 countries, including the EU REACH handling of polymers, were examined [114] and it was concluded that “Polymers with <1% of M_n < 1000 Da and low water extractivity are not able to cause systemic effects which are toxicologically or ecotoxicologically relevant”. In the case of high-molar-mass FPs, such characteristics are not observed (Table 2).

Among all FPs, PTFE is not a substance currently registered under REACH regulations supplying the definition of a polymer substance: “a molecule that contains a sequence of at least 3 monomer units, which are covalently bound to at least one other monomer unit or other reactant” [122]. But, because PTFE, like all FPs, is an identifiable organic substance, the suggested Universal Basic Asset (UBA) framework for assessment using the proposed PMT criteria (persistent, mobile, and toxic) would be applicable. Moreover, PTFE is highly stable in the environment and is resistant to thermal degradation. It is stable for years at temperatures up to 260 °C [36,123,124], it is stable to hydrolysis, oxidation, and light, as well as to anaerobic and aerobic degradation [125]. Therefore, PTFE would fulfill the UBA's proposed persistence criterion.

As stated by USEPA, regarding PFASs and PFCA, the regulatory agency suggests a clarification about the nature of the linkage, stating “How these materials are incorporated into the polymer is immaterial (they may be counter ions, terminal/end capping agents, or part of the polymer backbone)” [126]. Surprisingly, the key characteristic is the presence of a $-\text{CF}_3$ group that is attached to, or forms part of, the polymer backbone and “this link (between the polymer backbone and the $-\text{CF}_3$ group) is susceptible to degradation and cleavage” [126]. Thus, based on a USEPA report, the presence of the $-\text{CF}_3$ group is relevant since it provides a structural alert to consider potential degradation products [127]. This statement is quite surprising since a CF_3 end-group prevents depolymerization via unzipping [59].

As listed in Table 2, these FPs are not subject to degradation.

Another advantage of PTFE is its non-toxicity. Thanks to the too-high (several million) average M_n of PTFE mentioned above, it cannot cross the cellular membrane, indicating it is not toxic or bioavailable. Indeed, this polymer has been extensively tested in the European Union and USA to allow commercial applications for global medical device regulations, food contact, and surgery [77–81]. Furthermore, FPs contain none or tiny monomer(s) (which are gaseous), oligomer(s), and leachable amounts of or no reactive functional groups with high toxicity (Table 2) [36]. These comparisons of PLC and various regulatory assessment criteria demonstrate that, in contrast to conventional PFASs, high-

molar-mass FPs display quite different characteristics. Therefore, they should fall into a separate class of materials that must be determined on their own features.

More recently, the American Chemical Council led the Fluoropolymer Industry Group (*Fluoropolymergroup*) to investigate a similar study on 14 additional fluorinated (co)polymers [90]. FPs and the Stockholm Convention persistent organic pollutants (POPs) criteria meet the persistence criterion only, but not the bioaccumulative, toxic, or mobile criteria. Moreover, their physico-chemical properties prevent bioavailability, bioaccumulation, toxicity, and degradation. Presently, 96% of FPs fulfill these 13 PLC criteria.

Recycling, End of Life, and Reuse of FPs

Recycling is the re-introduction of utilized compounds (or polymers) into the cycle of products (i.e., polymers in the context). They are collected, sorted, and refined to be re-used as materials or energy source. Recycling should help to preserve resources and to avoid waste [128–130]. Indeed, the recycling of plastics is a real challenge [131–133] since only ca. 9% of polymers is recycled, which is just under three times more than FPs [134]. The global plastics production was 460 million t (Mt) in 2021 [131], and is predicted to reach 1120 Mt annually by 2050 [132], and should increase up to 1231 Mt by 2060. In the 2000–2019 period, the growth of plastics has outpaced that of economic growth by almost 40%. MacLeod et al. [133] highlighted the global threat induced by plastic pollution based on the high environmental persistence of plastics. In contrast to commodity polymers, the consumption of FPs represents quite a small volume (estimated at 330,300 metric t in 2021 [64], hence representing less than 0.1% among all polymers). In 2015, its global consumption was 270 kt, evidencing a 22.2% increase since then. Actually, the global situation of the fate of FP waste is as follows: 83.5% is incinerated, 13.1% goes to landfill, and 3.4% is recycled [134,135]; this is briefly summarized hereafter.

(i) Different techniques of recycling.

FP waste from commercially available and industrial waste manufacturers is either pre-sorted or arises from dismantling processing, and can also be incinerated for energy recovery. Fractions of pre-sorted FP waste are devoted to recycling, either to be exported for recycling in various countries [134–136] or to domestic recyclers. Other forms of recycling include sintering, re-grinding, or chemical recycling of FP materials. Four main methods of recycling are possible: [128] (i) primary (or mechanical) recycling; (ii) secondary recycling; (iii) tertiary recycling; and (iv) quaternary (or energy) recycling.

(ii) Decomposition and recycling of FPs

Several examples are supplied hereafter:

PTFE. The thermal degradation and pyrolysis of PTFE was studied by many authors. In 1947, it was pioneered by Lewis and Naylor (under vacuum at 600 °C) [137], 9 years later by Wall and Michaelson (at 450–510 °C, under the presence of various gases) [138], then reported by Simon and Kaminski [139] (who pyrolyzed PTFE at 500–600 °C in a fluidized bed reactor, with the primary products of decomposition being TFE and $\bullet\text{CF}_2\bullet$ bisradicals), comprehensively described by Ellis et al. [140], followed by Schlipf and Schwalm [141], further updated by Puts and Crouse [142,143], and then carefully reviewed by Lakshman and Chakraborty in 2015 in a book [144]. Puts and Crouse [142,143] were able to deeply detect and quantify the released fluorinated compounds (especially fluoroolefins and octafluorocyclobutane, OFCB) in the pyrolysis of PTFE from 35 °C to 800 °C in the presence or absence of various metals or salts. These authors highlighted that, in the absence of salts, TFE was produced in 98% while the nature of the salt induced the release of other gases with the influence of inorganic oxides of Al, Cr, Co, Cu, Fe, Ga, In, La, Mn, Ni, V, Zn, and Zr (Scheme 2) [142,143].

Industrially, while various thermal processes (smoldering, pyrolysis, open burning, etc.) were claimed in the patent literature (recently summarized) [136], the reuse of fluoromonomers has scarcely been reported. However, it was scaled up in a pilot plant at Dyneon Company [145,146] (Figure 7), via a robust process called “FP upcycling technology”,

yielding more than 90% TFE/HFP. This technology was scaled up into a new demonstration plant (capacity is presently >500 t year).

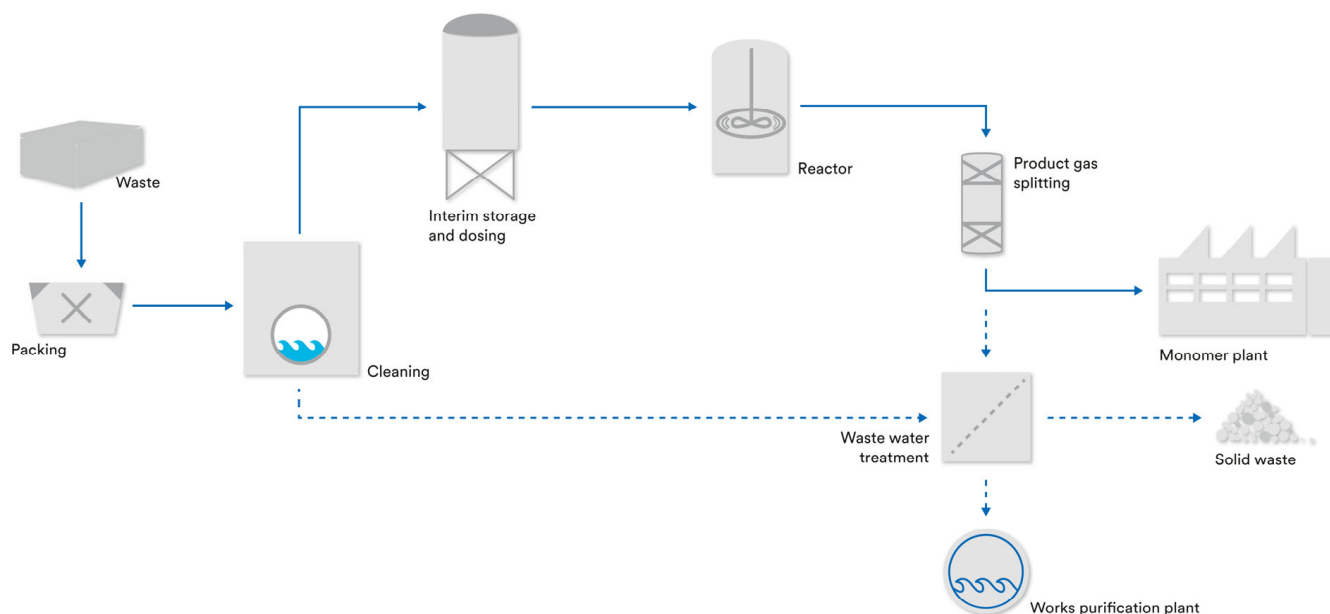


Figure 7. Sketch of the world's first pilot plant for recycling perfluorinated polymers in Germany. Reprinted with permission from Ref. [145]. Copyright 2016 3M/Dyneon GmbH.

Recycling of other thermoplastics. The company Arkema [141,142] claims to use PVDF copolymers as a processing and recycling aid (PPRA) for polyethylene and polypropylene films, pipes, cables, and injection-molded parts. Such a PPRA increases output and flow, enhances surface finish, reduces extruder pressure, and allows for steady gauge control and processing at lower temperatures. This company has adopted a process that enables only 20–30% of materials to be recycled before losing some features and being reprocessed, and up to 90 or even 100% of recycled materials are required to make such above items [147]. Materials already containing recycled PPRA behave almost the same as a virgin material in which a polymer processing aid (PPA) was added as a master batch in the extruder [148]. PVDF and VDF copolymers are currently assisting the reprocessing of high-volume polyolefins as a PPRA. In addition, Takahara's group [149] reported that PVDF used for fishing lines could not be degraded via UV radiation and biodegradation and, thus, may be recycled after use.

Recycling of Fluorinated Elastomers. The recycling of fluorinated elastomers has been reported in a few studies, which have been well summarized by Schuster et al. [150]. These authors reported only two relevant methods to achieve the recycling of poly(VDF-*ter*-HFP-*ter*-TFE) terpolymers (also named FKM) in an industrially acceptable way: (i) via milling FKM into fine powders to be mixed to virgin FKM and (ii) through the mechanical devulcanization of FKM, followed by successive compounding with virgin rubber. Both techniques give suitable thermostable products by preserving the mechanical features of original FKM. Indeed, these authors' review mainly cites many patents, while the quoted articles just refer to the degradation and not to de-vulcanization. These authors concluded that recycling FKM is possible and leads to products with competitive properties to those obtained in the presence of virgin FKM. But, as is known, Schuster et al. [150] stated that fluorinated elastomers are usually crosslinked and thus recycling is rather complex, in addition to the fact that they also contain fillers and additives.

Degradation and recycling of perfluorosulfonic acid membranes. Another key functional FP is a copolymer based on TFE and a perfluoroalkyl sulfonyl fluoride vinyl ether further processed into proton exchange membranes for fuel cells (PEMFC), such as Nafion®, Flemion®, Fumion, and Aquivion®, called perfluorosulfonic acid (PFSA) membranes (Figure 8) [151].

These high-performance polymers are also involved in chloro-alkali processes to produce chlorine and sodium hydroxide from brine, in desalination for drinkable waters, and in electrolyzers able to produce “clean” hydrogen from water. Though the thermal degradation of Nafion® N117 membranes was reported by Feng et al. [152] and by Zaton et al. [153], its recycling is very challenging.

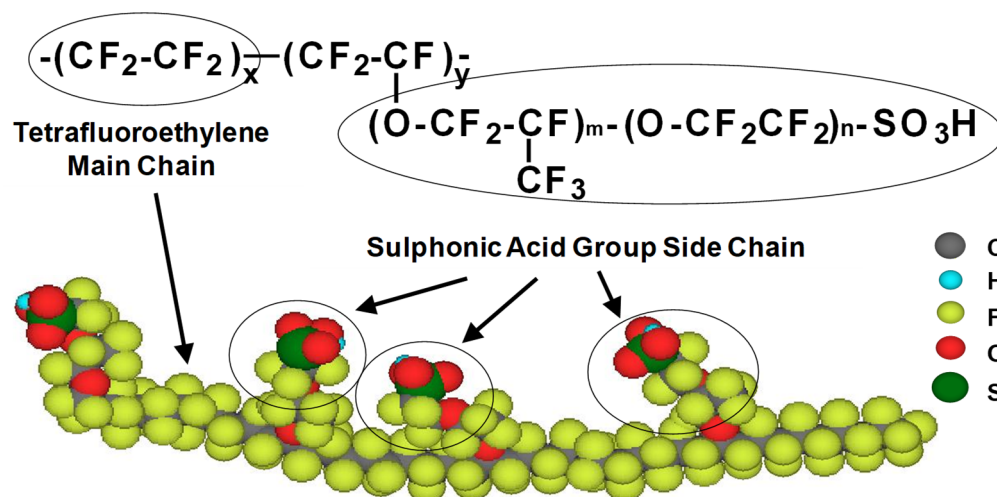


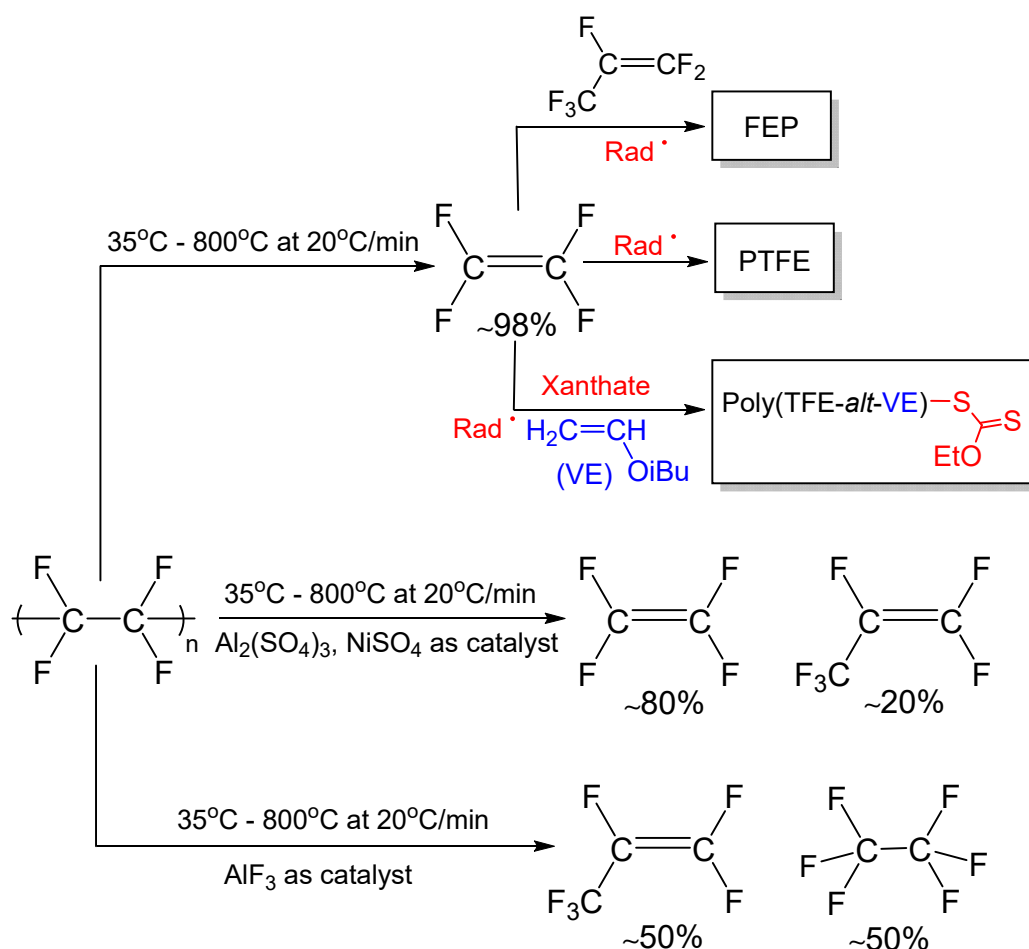
Figure 8. Perfluorosulfonic acid (PFSA) for PEMFC membranes used in fuel cells and electrolyzers. Reprinted with permission from Ref. [154]. Copyright 2016 Royal Society of Chemistry.

Nowadays, no alternative is foreseen to be able to substitute such high-performance materials [9,59,63,83,84], which are essential to the functioning of the hydrogen value chain and electrolyzers. These are produced and used in a highly controlled industrial environment, where their emissions are negligible and, due to their high initial price, their reusability and recyclability are actively investigated. So far, a patent from Grot [155] (involving dissolving the membrane and separating the components), a report from Park [156], and a British Research and Innovation project, called Frankenstack [157] (dealing with the recovery and reuse at the end of the lifecycle membrane) are the only documents describing the recycling of PFSA membranes.

Chemical Recycling to Monomer and Reuse of the Released Fluoromonomers

The chemical recycling of FP to fluoromonomers (CRM) is a real challenge. An example is illustrated by Scheme 2 that represents the depolymerization of PTFE into TFE or other fluorinated compounds according to the conditions. The generated TFE could be involved in various reactions enabling the loop to be closed: (i) in radical homopolymerization initiated by peroxides or persulfates to lead to PTFE [158]; (ii) via conventional radical copolymerization of either HFP [159] or isobutyl vinyl ether (iBuVE) [160] to produce either poly(TFE-co-HFP) copolymer (or FEP) or alternated poly(TFE-co-iBuVE) copolymer (as commercially available Zeffle® homologues [154]), and finally (iii) under reversible addition–fragmentation chain transfer (RAFT) copolymerization of TFE and iBuVE, controlled by a xanthate, to yield well-defined poly(TFE-co-iBuVE) copolymers [160].

Anastasaki et al. [161] reported the catalyst-free depolymerization of poly(2,2,2-trifluoroethylmethacrylate), PTFEMA, at 180 °C. This polymer was previously synthesized via reversible addition–fragmentation chain-transfer polymerization (RAFT) of TFEMA controlled with a trithiocarbonate (TTC). The kinetics of depolymerization, monitored via ^1H NMR spectroscopy, evidenced the unzipping reaction and evidenced that at the end of the reaction only TFEMA and the TTC remained in the flask (Figure 9). Though it required heat, that reaction did not need any toxic reactants.



Scheme 2. Thermal decomposition of PTFE in absence or presence of various metals or salts to lead back to TFE (and other fluorinated compounds) [142,143]. The recovered TFE was homopolymerized [157], or copolymerized with HFP [158] or isobutyl vinyl ether (iBuVE) [159], to produce PTFE, poly(TFE-co-HFP) copolymer (i.e., FEP), or alternated poly(TFE-co-iBuVE) copolymer [159].

Reuse of Degraded FP

Bai's team [162] described that a commercially available FKM elastomer (poly(VDF-co-HFP) or poly(VDF-ter-HFP ter-TFE) fluoroelastomers, $M_n > 300,000 \text{ g}\cdot\text{mol}^{-1}$), the average molar mass in number and dispersity of which were $M_n = 134,000 \text{ g}\cdot\text{mol}^{-1}$ and $PDI = 3.7$ (while the VDF:HFP molar ratio was 3:1), could undergo tertiary recycling, yielding cooligomers. The M_n of the latter ranged between 3300 and $10,400 \text{ g}\cdot\text{mol}^{-1}$. This reaction occurred in the presence of sodium hydroxide, hydrogen peroxide, and triethyl ammonium chloride. These transparent dicarboxyl telechelic cooligomers were first chemically changed into diacrylates and then photocrosslinked. The resulting network exhibited suitable mechanical and hydrophobic properties [162].

A more recent work on the use of FEP waste for transparent soils was achieved through the coating of specific terpolymers onto such waste (thanks to fluorine–fluorine interactions). The growing of lettuce roots was monitored using an optical system and the roots were able to live in such an environment [163].

Incineration

Incineration is the last method to process end-of-life FPs. Recent studies on the disposal of end-of-life PTFE have highlighted incineration as an appropriate method to dispose of FP too, with no environmental concerns. It is a high-temperature flaming process, which takes place in an open-air space, whereas smoldering is a flameless

combustion process that occurs on the surface of a condensed fuel. While both methods can be utilized to decompose fluorinated waste, the main difference is that smoldering is self-sustaining and, hence, is more energy-efficient compared to incineration, which needs a continuous energy input.

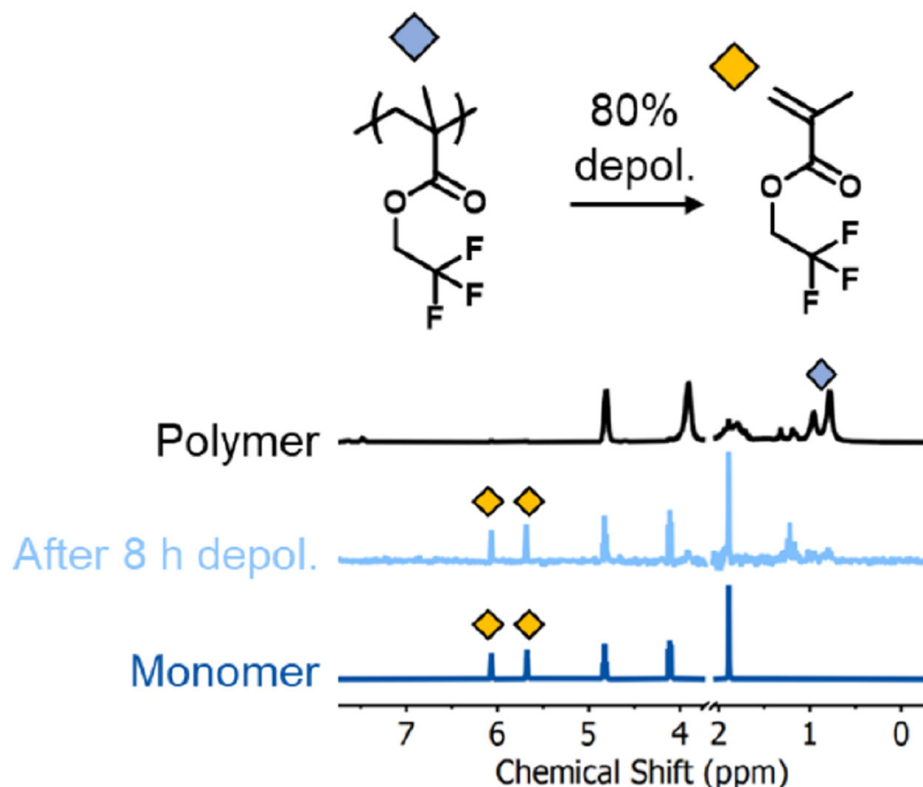


Figure 9. Reaction scheme of the thermal depolymerization of poly(2,2,2-trifluoroethylacrylate), PTFEMA, and ¹H NMR spectra of PTFEMA (up), of the total product mixture after 8 h (middle spectrum), and of TFEMA after depolymerization (bottom). Adapted from Ref. [161].

Incineration or combustion differ from thermolysis in that a source of fuel is used in order to purposefully favor a complete degradation of FPs (as a source of trifluoroacetic acid or acetate, TFA, and chlorodifluoroacetic acid, CDFA) [140]. Furthermore, due to the high temperatures and oxidizing conditions used, they are unlikely to produce environmentally significant levels of TFA or TFA precursors. On the other hand, the low-temperature burning of domestic waste, as an important source of furans and polychlorinated dioxins to the atmosphere, may analogously be a huge source of fluorinated acids.

Incineration has been adopted by various countries [134,135,164,165]. In the case of Norway [165], though municipal solid waste incineration (MSWI) conditions are achieved at about 850 °C, emissions of FP degradation products from household waste incineration have not been investigated yet. However, at the laboratory scale, the decomposition of PTFE and other FPs was comprehensively studied in the 700–1050 °C temperature range, yielding the release of various main products such as CF₄, CHF₃, C₂F₆, TFE, HF, and OFCB (Table 3) [124,140,165–171].

Most of these substances are non-toxic, but highly toxic ones like perfluoroisobutylene (PFIB) or fluorophosgene (COF₂) may possibly be released under some severe conditions.

Wang et al. [172] suggested that PFASs may be generated from FP waste via an MSWI process, probably at temperatures lower than 500 °C. Thanks to its high thermal and chemical stabilities, PTFE is inert in the environment and Taylor et al. [173] found that municipal waste incinerators operating with an average gas temperature of 1000 °C can be used to totally decompose PTFE.

Table 3. FPs and their main decomposition products at various temperatures from the literature. In parenthesis: PFC code [165] (reproduced with permission from Norwegian Institute of Air Research).

Polymer	T (°C)	Main Products	References
PTFE	450	COF ₂ , HF	[124]
	400–500	TFE, HFP, PFIB	[166]
	500	HFP, TFA	[140]
	530	CF ₄ , C ₂ F ₆ , TFE, HFP, <i>c</i> -C ₄ F ₈ (<i>c</i> -OFCB)	[167]
	550	CF ₂ O, C ₂ F ₆ , CF ₃ CFO,	[168]
		C ₅ F ₄ , CF ₃ CF ₂ CFO,	
		(CF ₂) ₃ O ₂	
	600–700	TFE, OFCB	[169]
	750–800	HFP	[169]
	850–900	PFIB	[169]
	800	CF ₄	[124]
	>900	C ₂ F ₆	[124]
	850	HFP, TFE	[170]
	750–1050	C ₂ F ₆ , CF ₄	[170]
ETFE	350	COF ₂ , PFBE, TFE, CO	[124]
ECTFE	500	TFA, CDFA	[124]
FEP	400	COF ₂ , HFP, TFE, PFIB	[124]
PFA	400	COF ₂	[124]
PEEPE	500	TFA	[140]
CPTFE/ PCTFE	500	CPFP, CDFA	[124]
PTFE/PFA+ PTFE/FEP	800	CH ₄ , CHF ₃ (HFC-23), C ₂ F ₆ (PFC-116)	[171]

In contrast, in Germany, Aleksandrov et al. [174] reported that the incineration of PTFE, using the best available techniques (BATs), did not release any PFAS. By comparing with the possible formation of 31 PFAS compounds as references, these authors noted that PTFE could almost fully decomposed into fluorine (as HF) and concluded that the municipal incineration of PTFE should be considered as an acceptable form of waste treatment. They tested for the presence of 31 different PFASs and 11 of these were detected but deemed to be due to contamination from the environment. A constant mass flow of wood pellets was utilized while these authors added PTFE into the reactor to maintain a consistent thermal profile, as shown in Figure 10.

Furthermore, the Dutch Institute for Public Health and Environment (RIVM) [164] drew slightly fewer concrete conclusions, mentioning that although it can be assumed that the polymers are destroyed with the gasification process, this does not provide enough information on the kind and degree of by-products formed or on the rate of mineralization.

In the EU, the overall situation of the fate of collected FP waste involved in recycling, recovery, reuse, and landfill, proposed in the Conversio Report, is illustrated in Figure 11 [134,135], indicating that, globally, ca. 23.5 kt of FP waste was collected in 2020 (<0.01% of the total waste). To compare, ca. 29,450 kt of plastics was gathered in 2020 (<5% of the total collected waste excluding mineral fractions). Moreover, about 84% (20.4 kt) of the total FP collected waste in Europe in 2020 is either thermally destructured or (co-)incinerated, while 3.1 kt (13.1%) went to landfill. Finally, 0.81 kt was gathered separately for recycling, whereas a significant amount was exported for recycling (e.g., to Asian countries) [130].

Beside incineration, a more severe degradation of FPs can be obtained through various methods including smoldering and pyrolysis. These are efficient to treat fluorinated waste [136], with the first one being self-sustaining. As a high-temperature process used for thermal decomposition, pyrolysis is similar to incineration except it is achieved in an inert atmosphere. For efficient degradation, a temperature greater than 900 °C is preferred. These techniques enable a total destruction of released hazardous PFASs. Several studies have tested the efficiency of these methods to determine if they reach temperatures high enough

for a sufficient duration to enable complete degradation [174,175]. Other techniques of incineration [136], such as the mineralization (vide infra) of FPs during thermal treatment, or a plasma-based water treatment, are also being investigated as they may be safer and more efficient to treat waste.

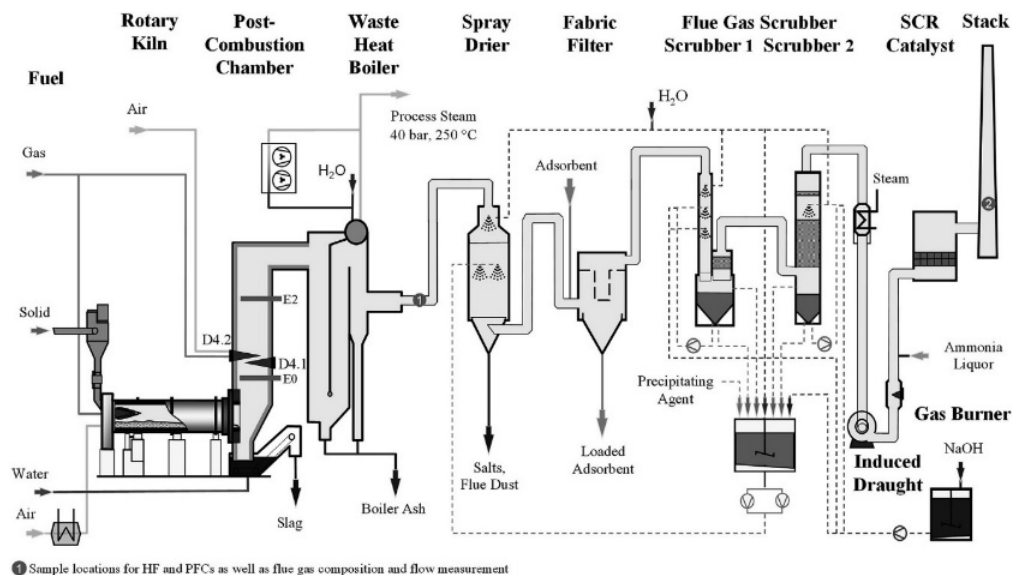


Figure 10. Engineering drawing of the “Brennkammer mit Dampfkessel” (BRENDA) (German acronym) pilot combustion facility at Karlsruhe Institute of Technology. Reprinted with permission from Ref. [174]. Copyright 2019 Elsevier.

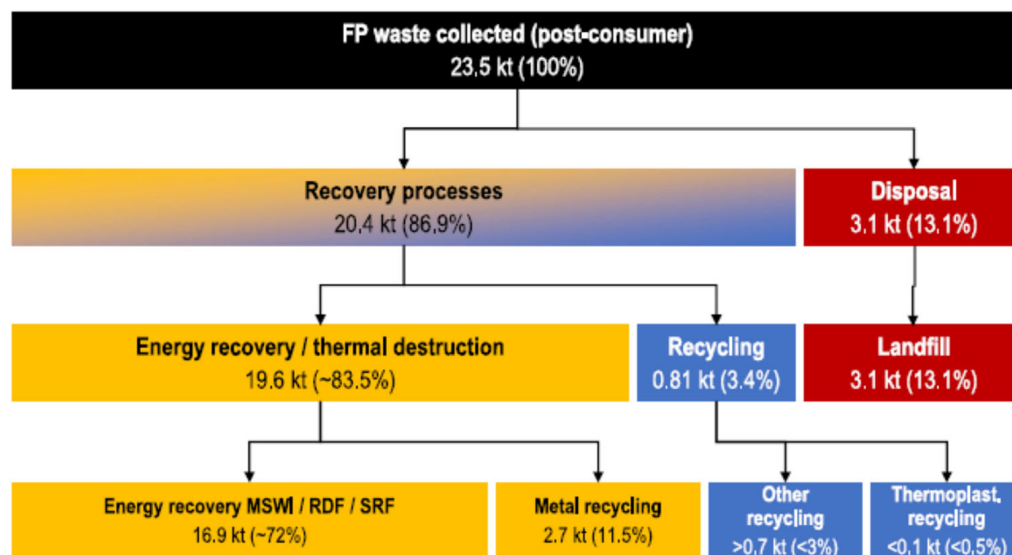


Figure 11. Fate of collected FP waste and tonnages (percentages) involved in recycling, recovery, reuse, and landfill in EU. Reprinted with permission from Ref. [134]. Copyright 2020 Conversio Market & Strategy GmbH.

End of Life

Several authors have studied the end of life of FPs [136]. When an FP has fulfilled its intended use and will be disposed of, the fate of the FP must be investigated.

Many reports have concluded that FPs such as PTFE do not degrade in the environment and do not release any compounds hazardous toward mammals, human beings, and the environment [102,123,165,176,177]. Thus, the downstream, end-of-life process of incineration should lead to more studies.

In addition, though FPs match the PLC criteria (Section Polymer-of-Low-Concern Criteria), the circular economy of FPs deserves more interest, and Wahlström et al. [165] have comprehensively proposed an overall approach including several flows (Figure 12) ranging from the manufacture of FPs to their use and their recycling (also analyzing the depolymerization of PTFE into TFE as explained in the sections above).

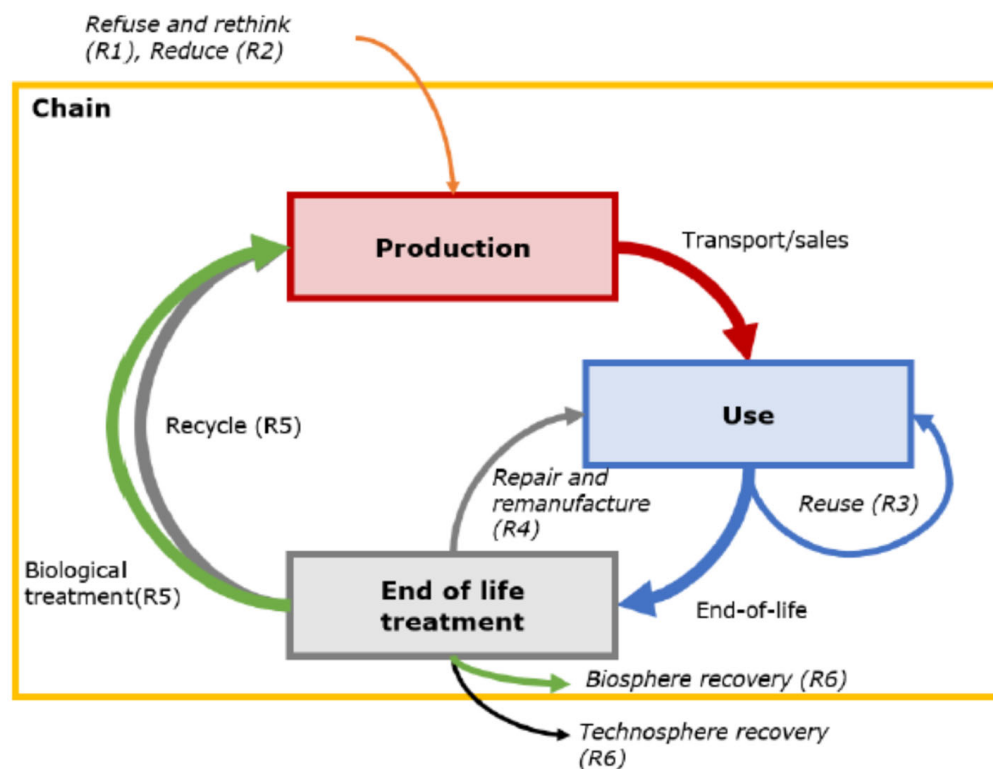


Figure 12. Sketch of flows of materials in a circular economy. Reprinted with permission from Ref. [165]. Copyright 2021 European Topic Centre Waste and Materials in a Green Economy.

The Conversio report [134] extensively provided the results of the treatment of FP waste in different industry segments (automotive, aerospace, semiconductors, electronics [76], and chemical industries) in the EU in 2020 regarding collected waste, energy recovery, landfill, and recycling, as well as the co-treatment of FP and associated waste streams. Figure 13 represents the overall circular economy situation of FPs in the EU, involving pre-consumer processing losses during the manufacturing of FP products and applications [134,135]. Most FPs are (co-)incinerated in MSWI plants or dedicated hazardous waste incineration plants that treat different wastes from chemical waste producers. Indeed, two main methods of recycling have been used (Figure 13): the mechanical and the chemical ones enabling the recycling of melt-processible FPs (such as PVDF or PFA), non-melt-processible ones (as achieved at Dyneon [145,146] or Karlsruhe Institute of Technology [174]), or virgin raw FPs.

The processing of FP materials such as the machining of PTFE rods and cubes for the manufacturing of various milled and drilled parts results in pre-consumer FP processing losses. Currently, ca. 20–25% of FP producers claim to perform their own internal re-processing steps for their process losses. This is the case for Dyneon [145,146], Arkema [147,148], and other companies. Then, 30–35% report that they send their pre-consumer FP waste to external material re-processing companies while 15% export their pre-consumer wastes to other companies inside the EU. Around 5–10% mention that their FP processing losses are exported outside the EU for re-processing, e.g., to Asian countries [130]. Finally, 5% of them state that they do not have any information on their process losses. These companies usually sub-contract waste companies.

Fluorspar / calcium fluoride (CaF_2) is a limited resource. The circularity of FP materials could offer a way to cope with the growing market demand for FP materials and the tight supply situation (import dependency) for relevant secondary raw materials.

Mechanical recycling of FP

- Melt-processable FP such as PVDF or PFA
- Re-grind and processing of not melt-processable FP materials into powders etc.

Chemical recycling of FP

- 3M recycling plant for not melt-processable FP materials
- Virgin-like raw material quality for the manufacturing of new FP products & applications

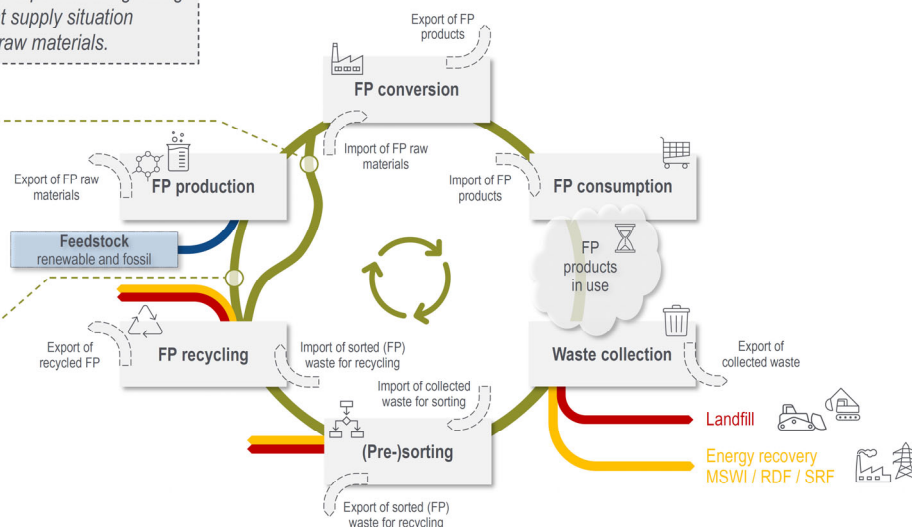


Figure 13. Circular economy situation of FPs: lifecycle of FPs from feedstocks extraction to end of life in EU. Reprinted with permission from Ref. [134]. Copyright 2020 Conversio Market & Strategy GmbH.

Mineralization

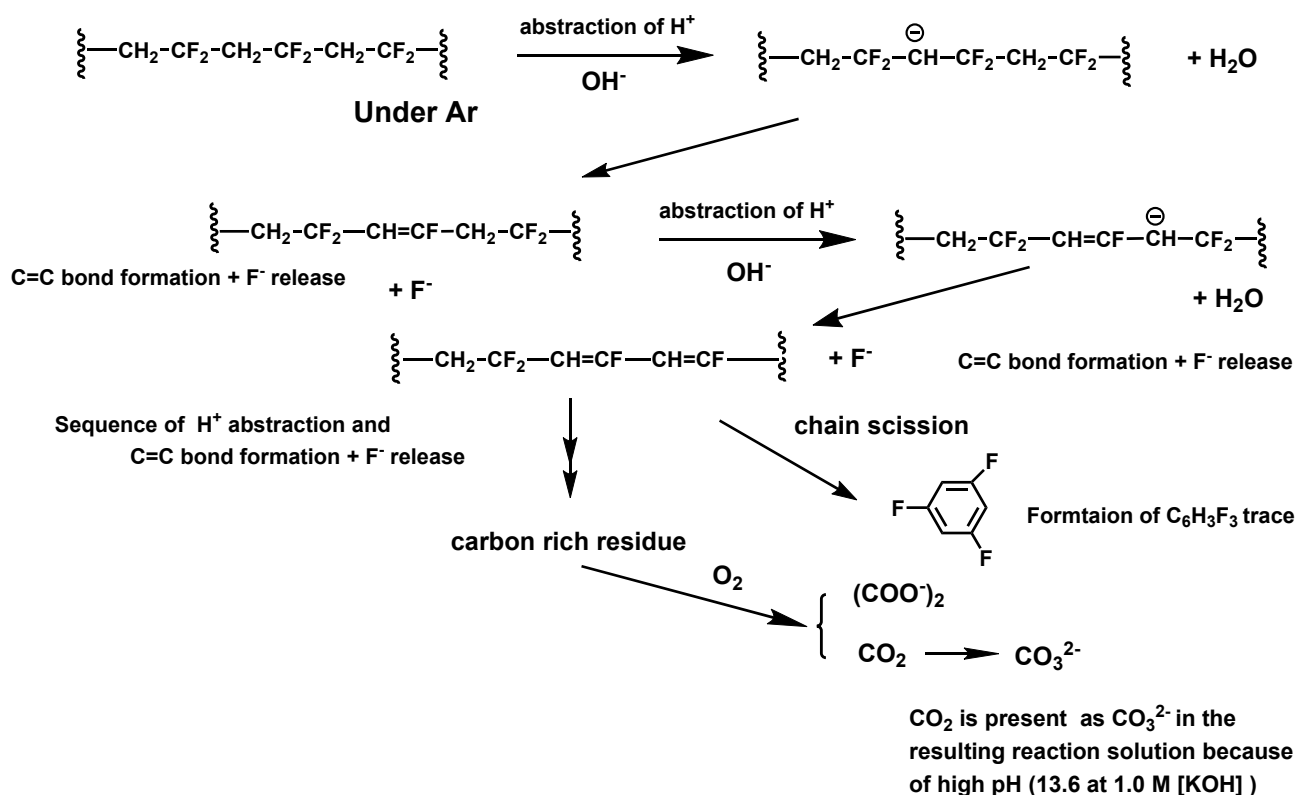
A total degradation of FPs is desired to avoid any release of oligomers that impart severe persistent and toxic issues. Mineralization, which yields fluoride anions, appears to be an attractive and environmentally friendly method. As reported for low-molar-mass PFASs [44], the mineralization of FPs has been deeply studied by Hori's group for more than 10 years by means of subcritical (or superheated) water [178]. These conditions can be reached at the critical temperature (374 °C) and pressure (>22.1 MPa) of water [178–184] for which this fluid displays low viscosity, high diffusivity, and an ability to hydrolyze and mineralize many organic compounds. Indeed, reactions requiring subcritical water are considered environmentally benign with the goal of recycling the fluorine element. In the case of FPs, using this technique, Hori's team mineralized PVDF [179,180] (decomposed into F^- and CO_2) as well as the VDF copolymers poly(VDF-co-HFP) [180], poly(VDF-co-CTFE) [179], poly(VDF-co-PMVE) [181], and poly(VDF-co-MAF) [182] copolymers (where MAF stands for methacrylic acid) and a poly(VDF-ter-HFP-ter-TFE) terpolymer [183]. This led to a *quasi*-complete mineralization of PVDF performed at 250 °C as well as for poly(VDF-co-HFP) and poly(VDF-co-CTFE) copolymers [179,180].

Scheme 3 supplies a suggested mechanism of the decomposition of PVDF. Advantageously, by reacting Ca^{2+} cations (from $\text{Ca}(\text{OH})_2$) with released fluoride anions, these authors examined that CaF_2 formation [180–183] could close the loop on the fluorine element, since CaF_2 is the source of all fluorinated compounds.

These authors also extended that strategy to the mineralization of poly(VDF-co-HFP) and ETFE copolymers [180] and PFSA membranes [184] in much more attractive conditions than those reporting the degradation of PFSA membranes generating perfluoroalkanoic acids [151] and perfluoroalkane sulfonic acids [185].

A different approach from another Japanese team [186] involved the use of molten alkaline metal hydroxide at 400–600 °C to mineralize PTFE. This two-step process allowed for efficient mineralization in chemical recycling. However, the process appears surprising since PTFE can be etched by liquid sodium and also degrades from 500 °C, as seen in the Recycling, End of Life and Reuse of FPs section. First, PTFE (as well as PVDF, PCTFE, and poly(VDF-co-HFP) copolymer) was decomposed into soluble alkaline fluorides via a degradation in molten hydroxides at high temperatures and atmospheric pressure. Then, CaF_2 , considered the main source of organofluorine chemistry, was produced through

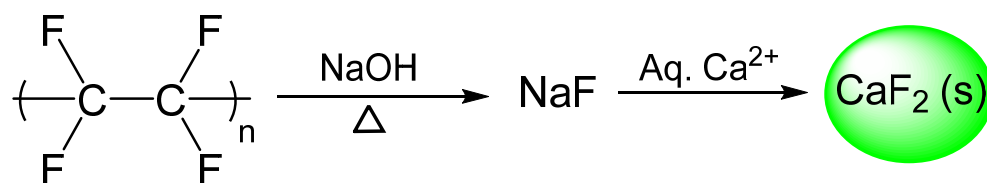
treatment of the former aqueous solution with CaCl_2 . When PTFE was heated with a large excess of NaOH at 500°C , a 74% yield of CaF_2 was obtained (Scheme 4) with respect to the initial PTFE amount.



Reaction under Ar: Efficient F^- formation + carbon rich residue

Reaction under O_2 : Efficient F^- formation + no residue

Scheme 3. Proposed mechanism for the H_2O_2 -induced decomposition of PVDF. Reprinted from Ref. [180].



Scheme 4. Proposed procedure for the mineralization of PTFE using molten NaOH .

Indeed, such high temperatures are not far from the thermal conditions that favor the unzipping depolymerization of PTFE [102,137–144,158] and, consequently, for other less-thermostable FPs than PTFE, degradation should also happen even without any base. These authors noted that (i) there was no decomposition with molten NaOH below 400°C , whereas (ii) from 600°C , the yields of CaF_2 fell down to 46% (from 67% and 74% at 450 and 500°C , respectively).

More recently, Sheldon et al. [187] reported that a nucleophilic magnesium reagent (Figure 14 and Scheme 5) could enable the defluorination of PTFE powder under mild conditions (room temperature and 1 atm), releasing a molecular soluble magnesium fluoride coordination product (2) that was separated from the surface-modified FP. This kinetically stabilized species could be utilized as fluoride carrier and appeared more reactive than the inorganic metal fluorides $\text{MF}(\text{s})$ or $\text{MF}_2(\text{s})$, which suffer from high lattice enthalpies

and high stability. This proof of concept evidences that the fluorine atoms in PTFE can be harvested and reused in coordination synthesis.

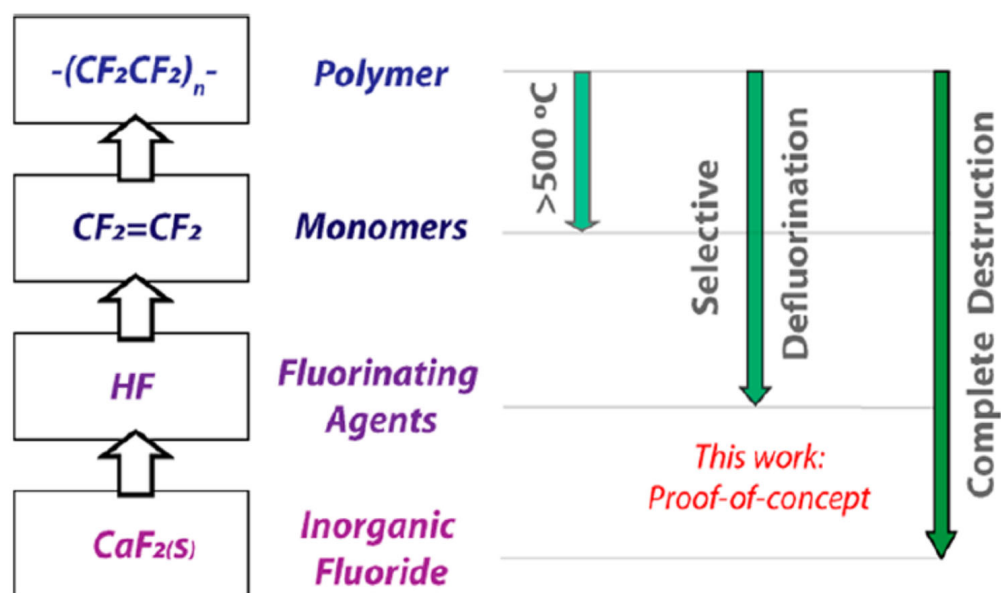
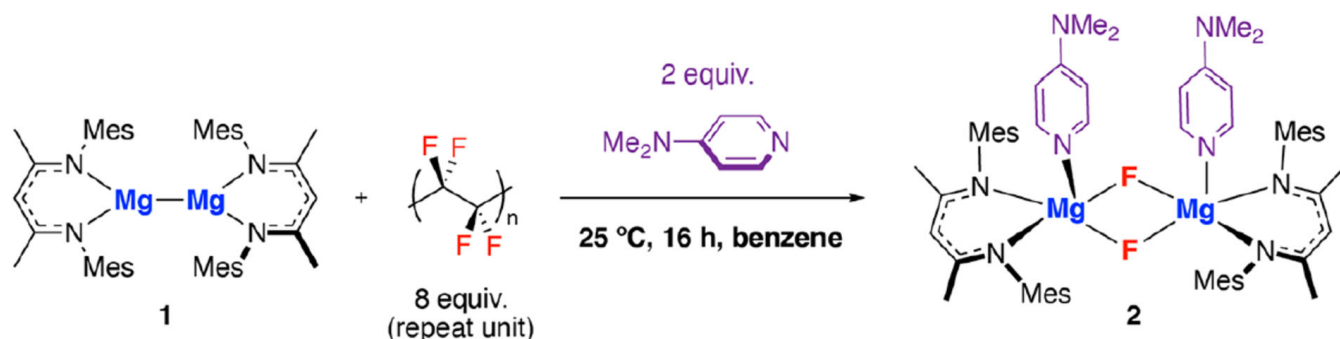


Figure 14. Cycle of fluorine chemistry from fluorspar (CaF_2) to PTFE, along with potential routes for recycling, including thermal depolymerization (above 500 °C), selective defluorination to form fluorinating agents, and complete destruction back to inorganic metal fluoride. Reprinted from Ref. [187].



Scheme 5. Room-temperature reaction of a nucleophilic magnesium reagent (1) with PTFE to generate an organometallic fluorinated magnesium complex (2). Reprinted from Ref. [187].

5. Conclusions and Discussion

PFASs cover more than 12,000 synthetic compounds containing a carbon–fluorine bond. With such a broad scope, not all PFASs are the same and it is likely that the impact of a possible restriction on PFASs on the global industry will be a shocking prospect, particularly since the recent proposal does not differentiate between substances that may have different toxicity profiles and applications. Indeed, the justification to launch a restriction on PFAS as a group is based on the ‘persistence and other concerns’ related to these chemicals and the fact that previous initiatives to regulate PFAS chemicals individually have resulted in the substitution of one PFAS molecule by another molecule that also matches the definition of PFASs, and may exhibit similar toxicological properties.

While most PFASs have not yet undergone toxicology assessments or been linked to health harms, many efforts have been devoted to the detection and remediation in both solid and aqueous media to ensure that contamination is limited to safe levels.

Because of their chemical composition, structure, and much higher molar masses, fluoropolymers are significantly different from other substances in the PFAS family.

The only main reason for the concern associated with FPs deals with the use of non-polymeric PFASs as polymerization aids during the manufacturing process (the radical polymerization in an aqueous medium has required a hydrocarbon surfactant to be used for a couple of years).

With such high molar masses (several million for PTFE), FPs cannot migrate through the cellular membrane, hence displaying their non-bioavailability and non-toxicity. Furthermore, due to recent improvements in their manufacturing without any use of fluorinated surfactants, in addition to their high chemical, thermal, and aging stabilities, they contain no or quite tiny oligomer or organic leachables. In addition, their physico-chemical properties prevent bioaccumulation and degradation. Advantageously, as with most FPs, PTFE is insoluble in water and, therefore, is not mobile in the environment. Consequently, the outcomes of such features (in addition the other 13 requirements) are that ca. 96% of the global commercial FPs satisfy the accepted OECD PLC criteria.

In reality, FPs exhibit exceptional properties while preserving their high performance even under aggressive chemical and thermal conditions. These niche technical polymers are stable against hydrolysis, UV, oxidation, and biodegradation. Their applications encompass health, safety, performance, and the functioning of society and they are used in strategic sectors and high-tech industries (e.g., aerospace, electronics, energy, optics, medicine). Their relevant combinations of outstanding features are not observed in any of the alternative hydrocarbon polymers [9,63,83,84], hence making them unique and valuable. Presently, alternatives to FPs, which should be assessed based on criteria such as *performance, safety, accessibility, resource efficiency, waste generation, cost, availability, stability, and lifetime*, do not exist. Furthermore, various reports indicate that FPs (especially PTFE) have been extensively tested to fulfil the Japanese [130], US, and EU food contact and global medical device regulations (e.g., Japan Pharmaceutical and Medical Device Agency, US Food and Drug Administration, Korea Ministry of Food, China Food and Drug Administration, and Drug Safety, including ISO 10,993 for biocompatibility testing and preclinical animal testing).

As presented throughout this review, FPs could potentially present environmental challenges across international borders. Since their inception and widespread commercial and industrial utilizations, these materials have become essential for many everyday applications and are not considered to be a health hazard during their typical life cycle. At their end of life, possible low-molar-mass compounds that are dependent upon certain conditions may become an issue that needs to be easily detected and removed from the environment. Many techniques on the remediation of PFASs have already been achieved.

FPs and the Stockholm Convention persistent organic pollutant (POP) criteria meet the persistence criterion only, but not the bioaccumulative, toxic, or mobile criteria.

Furthermore, the main concerns have been recently addressed, both in using NFPA and controlling >99% PFAS emissions linked to appropriate abatement technology in industrial FP productions. As a result, FPs produced with NFPA technology have led to commercial success and further motivate the industry to work harder in this direction. In addition, there is a search for various solutions for recycling, reuse, circular economy, and life cycle analysis. In this vein, several Occidental companies have already found strategies to depolymerize, recycle ("close the loop", even in pilot plants), or reuse FPs. Among the annual plastic production of more than 460 million tons [131], only 9% has been recycled while the data fall to 3.4% for FPs (for a yearly production of 330,300 tons [64]). Further efforts on the recycling of clean FPs (e.g., PTFE), FEP, PFA, and PVDF waste or scraps generated in production have already achieved success (e.g., by Dyneon for PTFE, FEP, and PFA at a pilot scale [145,146], by Arkema for PVDF [147,148], and at Karlsruhe Institute of Technology [174]); however, the recycling of FPs in consumer articles is not well clarified because they are usually contaminated by several (inorganic) fillers and substances, which hamper that process.

Various studies have shown, on small and pilot (500 tons/year [188]) scales, the ability to upcycle FPs back to their monomers (via recycling to monomers) and to use the generated

fluoromonomers (e.g., TFE) for further (co)polymerizations. Though such an approach to a closed-loop economy for FPs has already been scaled up, it is expected that additional studies on the recycling and reuse of FPs are currently continuing.

To overcome the limitations of incineration (especially HF release), recent alternative processes regarding the thermal treatment (mineralization to release fluoride anions, precursors of CaF_2 as the starting point of the fluorine chemistry chain) of FPs either under subcritical water or with molten sodium or a magnesium complex are quite relevant to close the loop and deserve to be further scaled up.

Research is needed to determine the possible emissions from thermal disposal of FPs. Furthermore, methods of thermal degradation and waste treatment of polymers containing PFASs can be greatly expanded on to enable environmentally safe and conscientious processes. In addition, PTFE is known to undergo quite low decomposition above the application temperature of 260 °C for months while 400 °C is required to favor a major degradation. Hence, incineration may potentially degrade FPs, and from 850 °C a total decomposition is observed without releasing any PFAS. Such a growing topic allows efficient degradation temperatures, the potential to release compounds of incomplete combustion, deposition onto land, stack gas analyses, and other risk factors to be evaluated. In addition, reactive extrusion processing has been reported as a versatile technology to recycle melt-processible polymers [189], and could be extended to FPs (except PTFE).

Though many reports evidence that FPs (i) do not degrade in the environment or (ii) do not generate harmful compounds, their incineration requires further innovations. Labelling should comply with eco-labelling standards and thus help EoL managers in identifying and sorting hazardous fluoropolymer waste from other plastic waste during the EoL process.

Though the demand for FPs is still increasing [190], future works should deal with FP manufacturing, highlighting the safety, health, and environmental management practices, under applicable regulations.

FPs could be impacted by the upcoming restriction on PFASs under the EU REACH regulation, the proposal of which was published in February 2023 [33]. A lot of progress has been made in industry over recent years in relation to the control of PFAS emissions due to their use in fluoropolymer production. The FP-industry-representative [191] *FluoroProducts and PFAS for Europe* group (which represents producers, importers, and users of fluorinated products and PFASs across Europe) has issued a six-point action plan, which includes derogations for key applications that are not time-limited.

In addition, the FP industry in Europe [192,193] evaluated the contribution brought by FP manufacturers regarding revenue, investment, and employment, while many more significant benefits can be released along the value chain via the use of FPs in many high-tech applications.

For these reasons and because of their usefulness, inertness, non-toxicity, non-bioaccumulation, and non-mobility, and the growing interest even in upcoming technologies, FPs cannot be in the scope of the PFAS restriction. Moreover, the main concerns linked to the industrial productions of FPs have been addressed (improvement in abatement techniques, removal of PFAS polymerization aids, and introducing alternative technologies). They show that these high-value-added polymers must be separated from conventional PFASs, are essential for everyday life, and are irreplaceable materials.

Hence, the data presented demonstrate that the FP class of PFASs is well defined, safe, and an essential subset of PFASs. Though the dossier is still under evaluation [33] after more than 3000 answers to the consultation, the restriction of FPs under REACH regulations may significantly slow down the EU strategic sustainability ambition [194] as well as the ecological transition. For example, in the hydrogen sector, such a PFAS ban, without granting any exemption, would have catastrophic consequences on the industry's EUR 30 billion worth of investment in a decade [195] (only including electrolyzers and fuel cells). Such a ban would also jeopardize up to 200,000 direct jobs and over 260,000 indirect

ones within 10 years in a market with a potential value of EUR 820 billion that should employ 5.4 million people by the middle of the century.

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At \$76M, is the 5th largest manufacturing industry in the state.



Provides 940 direct jobs and anchors 940 related jobs.



Pays \$63M in wages.



Has an average wage of \$65,186, 25% higher than the average manufacturing wage in New Mexico.



Generates \$11M in state & local taxes, and \$20M in federal taxes.



Invests \$50M across New Mexico to build & update equipment and facilities.



Ships \$270M in products to customers around the world.



Generates an additional 940 jobs in plastics & rubber products.



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940
Direct Jobs

\$11M
State & Local Tax

\$50M
Capital Expenditure s

40
Establishme nts

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Average Wage

\$780M
Shipments

940
Indirect Jobs

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Total Wages

\$270M
Exports

\$25M
Federal Tax

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direct jobs.

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chemistry average
wage**

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average
manufacturing wage.**

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3. Prioritize energy independence and bolster our sector's trade surplus
4. Safeguard our communities and incentivize job creation
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Case Study: Agriculture

U.S. chemical manufacturers produce materials used in fertilizers, insecticides, pesticides, herbicides helping boost crop production, irrigation tubing and greenhouse panels and walls just to name a few.

Acrylonitrile: used in the production of a wide range of chemical products (mainly ABS/SAN resins, acrylic fibers, acrylamide, nitrile rubber, adiponitrile and carbon fibers). Plant and seedling/nursery trays as well as greenhouse tapes (e.g., repair tape, batten tape and vent tapes) can be made from ABS (or polypropylene).

Ethylene oxide: utilized to produce a wide variety of active ingredients used in insecticides, pesticides, and herbicides, helping to protect crops and boost crop production.

Acetaldehyde: used as an intermediate for pyridine which is used in a variety of agricultural chemicals

Formaldehyde: is used in pork and poultry production as well as aquaculture to prevent disease and infection.

Methylene chloride: used to produce polycarbonate which is used in greenhouse panels and walls.

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Case Study: Infrastructure

U.S. chemical manufacturers produce materials used in road construction, bridges, dams, water treatment and distribution, rail, energy-efficient buildings, electricity transmission, and EV charging stations.

N-Methyl-2-pyrrolidone (NMP):

used as a solvent in the production of paints and coatings, caulk and sealants.

Ethylene Oxide:

Used to develop polyester resins that are used in concrete to lengthen the life of bridges and roads.

1,3-Butadiene: used to make structural cements and bridge mounts.

Formaldehyde:

formaldehyde-based resins are used to manufacture composite and engineered wood products used in cabinetry, countertops, molding, furniture, shelving.

1-Bromopropane: used as a solvent in asphalt production.

Ethylene Oxide: Used to develop polyester resins that are used in concrete to lengthen the life of roads.

Methylene Chloride: used as a solvent for traffic paints and other coatings where fast solvent



Investigation of γ -irradiated polyvinylidene fluoride and its acute toxicity

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ABSTRACT

Polyvinylidene fluoride (PVDF) is an industrial polymer with many applications. The EPR spectrum of polyvinylidene fluoride (PVDF) irradiated by γ -rays at low temperature (-196°C) provides evidence for the presence of radicals formed by loss of a fluorine atom from PVDF, and polyenyl radicals. Polyenyl radicals dominate in the polymer irradiated at room temperature. Peroxide radicals formed as a result of oxidation of primary free radicals by atmospheric oxygen are observed in the EPR spectrum of a polymer irradiated in air, or when air is introduced to a polymer irradiated in a vacuum. Carbonization and oxidation of γ -irradiated PVDF were observed in the XPS spectrum. A model for polymer degradation based on correlated G3(MP2) molecular orbital theory electronic structure calculations is described. The presence of HF in the products and a low yield of products with the composition $\text{C}_x\text{F}_y\text{H}_z$ indicate the absence of noticeable thermal destruction of the main polymer chain upon heating to 220°C of both the initial and γ -irradiated PVDF. Although any HF released during the PVDF dehydrofluorination would be toxic, a study of the acute toxicity of γ -irradiated PVDF showed that the polymer does not exhibit toxicity after a single intragastric route of administration to mice.

1. Introduction

Polyvinylidene fluoride (PVDF) is an industrial polymer [1,2,3,4] with high strength (up to 90 MPa) that does not have a cold flow under load, has an increased elasticity, and is resistant to abrasive wear. Low molecular weight PVDF dissolves relatively easily in aprotic solvents and is also easily processed from the melt at relatively low temperatures at all molar masses. The operating temperature range of PVDF is from -40°C to 135°C . Due to its increased resistance to backbone bond cleavage from ionizing radiation and ultraviolet light, [2,5] PVDF is a promising fluorine-containing polymer for use in nuclear power and new technologies. A number of studies of the effect of various types of radiation on PVDF have been reported. [6–19] It is known [5] that during the radiolysis of partially fluorinated polymers, such as PVDF, crosslinking and destruction of the polymer chain can occur simultaneously. The relative rates depend on the irradiation conditions and the fluorination of the polymer. Under certain conditions of radiolysis, PVDF can undergo preferential crosslinking in vacuum. [5] The results obtained by Long [11] made it possible to determine the values of the

radiation-chemical yield of crosslinking ($G_c = 2.0$) and destruction ($G_d = 0.3$) during the course of γ -irradiation of PVDF.

The main molecular product of the radiolysis [1] and pyrolysis [20] of PVDF is hydrogen fluoride. The process for radiation dehydrofluorination of PVDF has been described in detail. [6,8,9] This process can give the polymer new useful physical and chemical properties, [1,6] and the carbon-carbon bonds formed by loss of HF can be interconnected to form chain structures with either double (polycumulenes) or alternating single and double (polyene) carbon-carbon bonds. [21,22] The ready elimination of highly toxic HF from the PVDF macromolecule may make it dangerous to use materials based on PVDF in the presence of certain chemicals, radiation, heat, etc., that can initiate the HF elimination. HF elimination may also occur during the initial melt processing of PVDF as this is outside the normal operating temperature range of PVDF. This prompted an investigation of the effects of γ -irradiation on the acute toxicity of irradiated PVDF. A reason to pursue this study is that PVDF has novel piezoelectric and pyroelectric characteristics, so it is a promising ferroelectric polymer that can be used in a polarized state in different applications [23], including the medical field. [24] Even

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though irradiation of PVDF has been previously studied, there are still questions on the mechanism of how the polymer changes as well as how the HF elimination occurs. We have studied the molecular-topological structure of PVDF after irradiation with γ -rays from ^{60}Co [25], from an infra-red laser [26], X-rays [27], accelerated MeV protons [28], and helium ions. [29] The purpose of the current investigation is to use X-ray photoelectron spectroscopy (XPS), electron paramagnetic resonance (EPR), and computational models to study γ -irradiated PVDF, as well as to determine the acute toxicity of the irradiated polymer. The results of this study will inform the community about the proper conditions for the use of PVDF in applications where γ -rays are present, such as nuclear power and the medical field.

2. Results and discussion

It is known [1] that the appearance of unsaturated bonds during γ -radiolysis of PVDF is accompanied by the release of HF. The process of releasing HF from PVDF has some similarities to the evolution of H_2 during the radiolysis of hydrocarbon polymers such as polyethylene (PE). However, there is a significant difference in the processes of γ -radiolysis of PVDF and PE as the radiation chemical yield of paramagnetic centers in PVDF ($G_R = 2.2$ [30]) is significantly lower than in PE ($G_R = 6.4$ [31]). A paramagnetic center yield that is lower than in a hydrocarbon polymer is a characteristic of γ -radiolysis of all fluorine containing polymers, especially for polytetrafluoroethylene ($G_R = 0.4$ [32]).

2.1. EPR spectra of γ -irradiated PVDF

EPR spectra of the irradiated polymer were taken to determine the nature of the radicals formed during γ -radiolysis of PVDF. Figure 1a shows the EPR spectrum of PVDF irradiated at -196°C . At low temperatures, the anisotropic hyperfine splitting on the alpha fluorine atoms is not averaged and can reach up to 20 mT. [33] Thus, we assign the singlet with a width of ~ 17 mT in Figure 1a to a radical with one alpha fluorine atom, which is formed by radiolytic detachment of a fluorine atom from the PVDF macromolecule as given in reaction (1) to form R_1 radical



species. On the sides of the wide singlet band, there is a doublet with a splitting of 50.4 mT attributed to trapped hydrogen atoms formed during the radiolytic rupture of C-H bonds in PVDF. An increase in the γ -radiation dose to 600 kGy leads to a linear increase in the intensity of all components of the EPR spectrum. The EPR results are summarized in Table 1.

When a polymer sample irradiated at -196°C is heated to room temperature, most of the paramagnetic centers are eliminated. The spectrum of paramagnetic centers that remained stable at room temperature has a poorly resolved hyperfine structure with a total width of about 29 mT (Figure 1b), which may encompass a range of radical sites. The intensity of the signal of paramagnetic centers stable at room temperature is almost three orders of magnitude lower than the intensity of

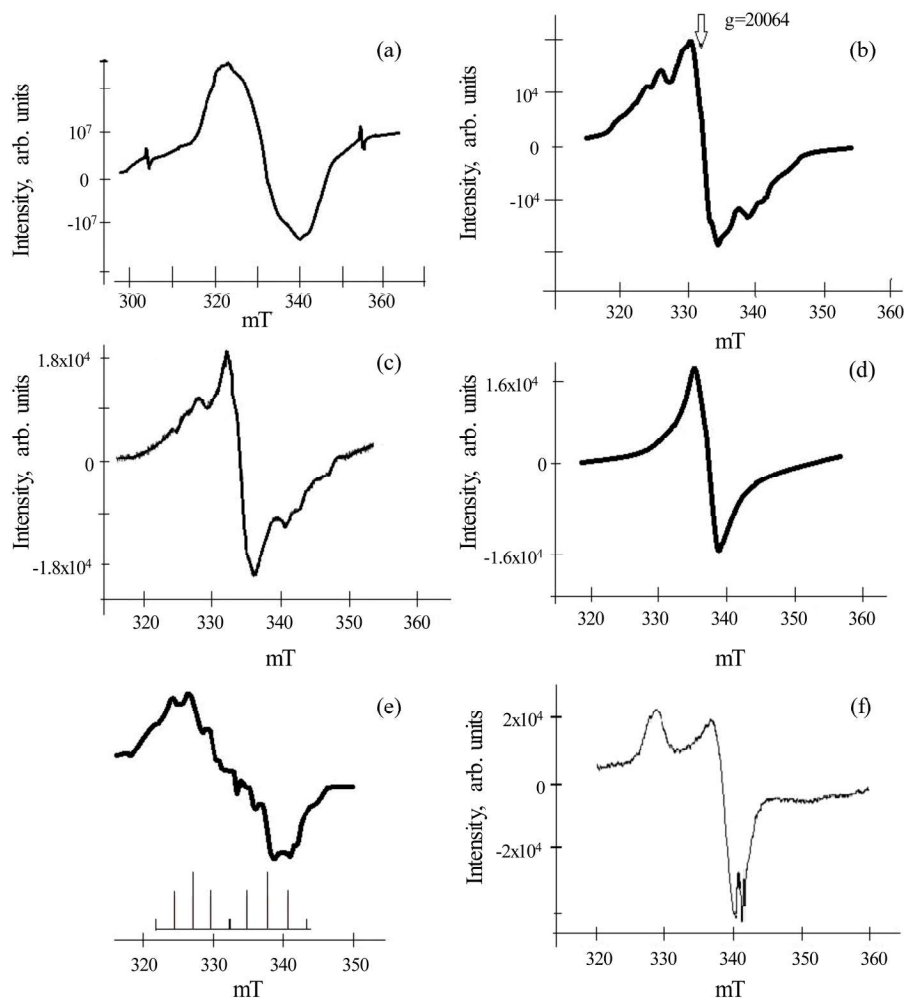


Figure 1. EPR spectra of PVDF irradiated with γ -rays of ^{60}Co . Dose of γ -irradiation is 600 kGy (a, b, c) and 140 kGy (d, f). The irradiation temperature is -196°C (a, b, c, f) and 27°C (d). The temperature of recording of the EPR spectra was at -196°C (a, f) and 27°C (b, c, d) before (a, b, f) and after storage of the irradiated samples at room temperature for 24 hours (c, d). Spectrum e was obtained by subtracting spectrum d from spectrum b.

Table 1

Experimental EPR hyperfine splitting (HFC in mT) and computational model assignments.

HFC	Figure	Assignment
17	1a	$\sim\text{CH}_2\text{C}^*\text{FCH}_2\text{CF}_2\sim (\text{R}_1) \alpha\text{F}$
50.4	1a	H^*
29	1b	Group of radicals
11	1b	$\sim\text{CH}_2\text{C}^*\text{FCH}_2\text{CF}_2\sim (\text{R}_1) \alpha\text{F}$ at 27 °C
2.6	1b	$\sim\text{CH}_2\text{C}^*\text{FCH}_2\text{CF}_2\sim (\text{R}_1) \beta\text{H}$
3.7	1d	Higher conjugated $\text{CH}_3\text{CF}_2\text{C}^*\text{HCF}=\text{CHCF}=\text{CHCH}_3 \alpha\text{F}$
3.2	1d	Higher conjugated $\text{CH}_3\text{CF}_2\text{C}^*\text{HCF}=\text{CHCF}=\text{CHCH}_3 \alpha\text{F}$

the initial EPR spectrum of the polymer irradiated at -196 °C (Figures 1a and 1b). In the spectrum of paramagnetic centers stabilized at room temperature, one can distinguish lines with splittings of 11.0 mT and 2.6 mT, assigned to hyperfine coupling (HFC) in the radicals R_1 with values $a_{\alpha}\text{F} = 11.0$ mT and $a_{\beta}\text{H} = 2.6$ mT. The HFC constants of this radical are close to the values ($a_{\alpha}\text{F} = 10.9$ mT and $a_{\beta}\text{H} = 2.5$ mT) reported previously. [34]

Radiolytic dissociation of a hydrogen atom from a PVDF macromolecule results in the formation of radicals with one alpha hydrogen atom (R_{II}) as given in equation (2).



It was not possible to distinguish characteristic lines of the radical R_{II} in the spectrum of PVDF irradiated at -196 °C. This is due to the relatively low content of the R_{II} radicals in irradiated PVDF, and, as a result, their EPR signal is covered by the background of the intense spectrum of R_1 radicals. According to the literature, [30,34] an unpaired electron interacts with one α hydrogen and four equivalent β fluorine atoms in the macroradical R_{II} leading to a doublet of quintets in the EPR spectrum. However, the literature values report somewhat different HFC constants for the fluorine and hydrogen atoms in R_{II} : $a_{\alpha}\text{H} = 1.6$ mT [30], $a_{\alpha}\text{H} = 2.3$ mT [34], $a_{\beta}\text{F} = 5$ mT [30], and $a_{\beta}\text{F} = 4.25$ mT. [34] Thus, the observed EPR spectra of PVDF irradiated at -196 °C show that the dominant species are macroradicals formed when a fluorine atom is detached from the PVDF macromolecule. The EPR spectra of stable radicals change during storage of irradiated polymer at room temperature leading to an increase in the relative intensity of the central part of the spectra as observed in Figures 1b and 1c.

A singlet is observed in the EPR spectrum of PVDF irradiated at room temperature (Figure 1d). Its width narrows with an increase in the radiation dose. After irradiation of the polymer by doses of 100 and 350 kGy, the singlet widths are 3.7 mT and 3.2 mT, respectively. Similar singlet lines in the EPR spectra of γ -irradiated hydrocarbon and hydrogen/fluoride polymers have been reported and attributed to polyenyl radicals. [35] The width of their singlet spectrum narrows with increasing length of the conjugated chain. So, at $n = 2$ (n is the number of double bonds in the polyenyl radical), the singlet width in PE is 4 mT, and at $n = 10$ –12, it has narrowed to 2.5 mT. The narrowing of the singlet width with an increase in the γ -radiation dose is due to a decrease in the spin density at each carbon atom because there is an increase in the conjugation length leading to an increase in the delocalization of an unpaired electron over a larger number of polyene carbon atoms. This leads to an increase in the number of unresolved HFC components and to a narrowing of the envelope. Polyenyl radicals, due to delocalization of the radical site over the adjacent unsaturated bonds, have a lower chemical reactivity, and are characterized by higher thermal stability. This contributes to an increase in the proportion of polyenyl radicals in the EPR spectrum of the polymer irradiated or recorded at room temperature.

Figure 1e shows the spectrum obtained by subtracting the spectrum (Figure 1d) of polyenyl radicals from the spectrum (Figure 1b) of radicals remaining after heating up to room temperature of a PVDF sample irradiated at -196 °C. In Figure 1e, there is a doublet of quintets from the

R_1 radical with HFC constants: $a_{\alpha}\text{F} = 11.0$ mT and $a_{\beta}\text{H} = 2.6$ mT. Thus, the EPR spectrum of a PVDF sample heated up to room temperature after irradiation at -196 °C contains the spectra of R_1 radicals and polyenyl radicals.

The characteristic lines of the EPR spectrum of the “terminal” radicals $\sim\text{CH}_2\text{C}^*\text{F}_2$ and $\sim\text{CF}_2\text{C}^*\text{H}_2$ that could be formed during C-C bond breaking were not observed in the spectrum of irradiated PVDF. Their absence could be due to the “cage effect” of radical pairs, leading to mutual recombination of such radicals in the cage or their disproportionation in the cage with the formation of a terminal unsaturated bond. In addition, for high molecular weight polymers, the radicals produced by cleavage of H or F from a terminal $\sim\text{CH}_3$ or $\sim\text{CF}_3$ will be of low intensity due to the low concentration of terminal groups. Thus, the formation of alkyl and polyenyl radicals is the dominant process of PVDF radiolysis.

The appearance of polyenyl radicals in irradiated PVDF can be the result of a number of successive radiation-induced chemical processes. The probability of the polyenyl radical formation increases with the radiolysis temperature and is associated with an increase in the probability of the formation of isolated or conjugated C=C double bonds. In general, before, during, or after the formation of unsaturated bonds in PVDF, hydrogen or fluorine atoms are detached from the polymer molecule. As more hydrogen and fluorine atoms are removed, if the sites from which they removed from are close to an already generated radical site, then formation of polyenyl radicals can occur as observed in the EPR spectra of the irradiated PVDF.

Figure 1 (a–e) shows the EPR spectra of PVDF samples irradiated in vacuum. If the polymer was irradiated in air, then a broad asymmetric line is recorded in the EPR spectrum at -196 °C, which is characteristic of randomly oriented and rigidly fixed peroxide radicals (Figure 1f). [35] A similar spectrum of the peroxide radicals is also recorded if air was introduced into an ampoule with PVDF initially irradiated in vacuum. Obviously, the formation of peroxide radicals is the result of the oxidation of primary macroradicals stabilized in the irradiated polymer.

2.2. XPS spectrum of γ -irradiated PVDF

The effect of irradiation on the chemical composition of PVDF was investigated by XPS. Figure 2a shows a survey XPS spectrum of un-irradiated PVDF. In addition to the carbon (C 1s) and fluorine (F 1s) peaks, oxygen (O 1s) and nitrogen (N 1s) peaks were also recorded. A Na 1s peak was found in the irradiated material, this is likely a trace contaminant introduced during sample preparation and processing and should not be regarded as scientifically important. The recorded C 1s

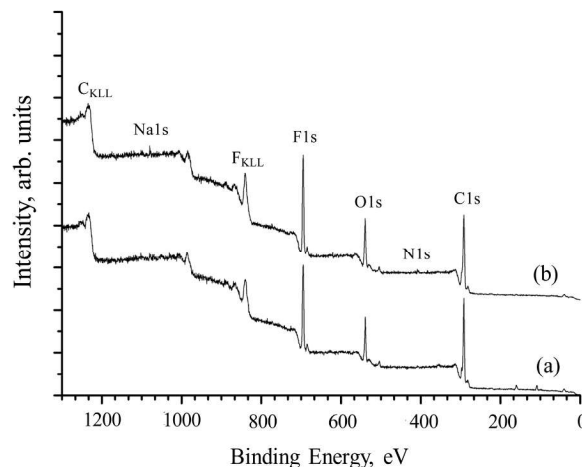


Figure 2. Survey XPS spectra of (a) initial PVDF and (b) the PVDF irradiated with γ -rays at a dose 100 kGy.

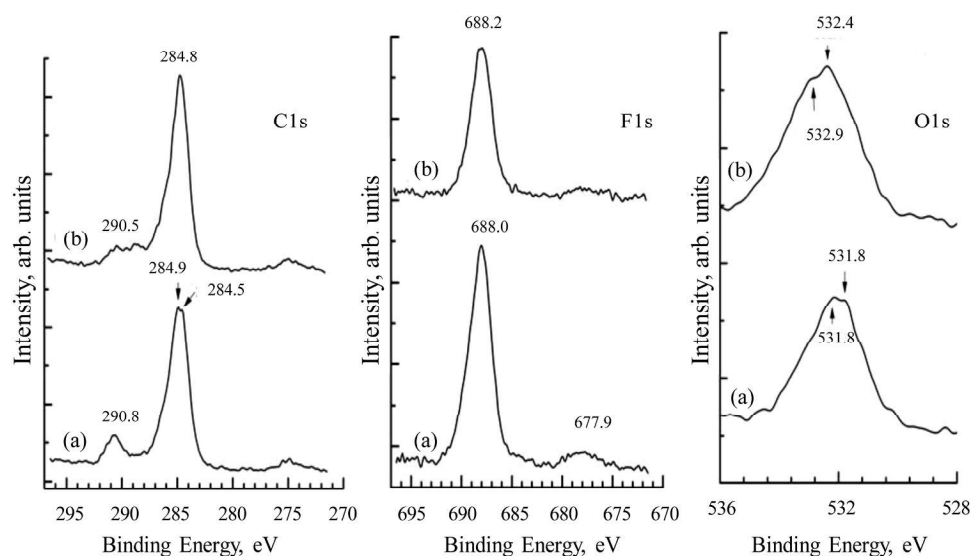


Figure 3. Extended C1s, F1s and O1s XPS spectra of (a) initial PVDF and (b) the PVDF irradiated with γ -rays at a dose 100 kGy.

peak can be decomposed into C-C (284.9 eV) and C-F (290.8 eV), [Figure 3](#). The C 1s line with a binding energy (E_b) equal to 290.8 eV corresponds to carbon atoms of the $>CF_2$ groups. [\[36\]](#) The F 1s spectrum exhibits an intense C-F peak (688.0 eV) and a low-intensity broad peak centered at 677.9 eV. The binding energy of 688.0 eV is typical for F 1s in PVDF and corresponds to a C-F bond in CF_2 . [\[37\]](#) The recorded O 1s line with $E_b = 532.2$ eV is characteristic of molecularly chemisorbed oxygen (532.2 eV). In the C 1s spectrum of the irradiated polymer, a weak peak appears in the range of 287.8–288.0 eV characteristic of carbonyl $>C=O$ groups. [\[11,38\]](#) The N 1s peak is likely caused by slight atmosphere inside the XPS system during measurement.

The position of peaks in the XPS spectrum does not change after γ -irradiation of the PVDF ([Table 2](#)). A comparative analysis of the spectra of the C 1s, F 1s and O 1s lines in the initial ([Figure 3a](#)) and irradiated PVDF, [Figure 3b](#), indicates a change in their relative intensities as a result of irradiation. After γ -irradiation, the intensities of the C 1s and O 1s peaks increased and the intensity of the F 1s peak decreased. This suggests carbonization of the near-surface layer of the irradiated PVDF is occurring which is associated with radiation-chemical transformations with release of HF. HF release leads to formation of unsaturated bonds during the radiolysis of PVDF. The increase in the O 1s peak is most likely the result of the oxidation reaction of the free radicals stabilizing on the surface of irradiated polymer by reacting with atmospheric O_2 , due to air exposure, to form peroxide sites. Thus, γ -irradiation decreases the fraction of fluorine by 6.8 atomic% and increases the amount of carbon and oxygen by 3.9 atomic% and 3.7 atomic %, respectively ([Table 2](#)). In the irradiated PVDF sample, the ratio of the content of fluorine and carbon $[F/C] = 0.16$ is significantly lower than the ratio of these elements on the surface of the initial polymer $[F/C] = 0.27$. Irradiation with γ -rays leads to a decrease in the number of fluorine relative to the starting material.

2.3. Thermal stability of the irradiated PVDF

The curves of the differential thermal analysis (DTA) before (curve 1) and after (curve 2) γ -irradiation of PVDF with a dose of 100 kGy are shown in [Figure 4](#). The DTA curve of the un-irradiated polymer shows a broad melting peak in the temperature range from 145 °C to 195 °C with two minimum points at 167 °C and 169 °C and a shoulder at 176 °C. The observed minimum points and shoulder are related to different crystalline forms of PVDF. The existence of at least four (α , β , γ , δ) crystalline modifications of PVDF has been reported. [\[39\]](#) The minimum point in the melting peak of 167 °C on the DTA curve of the polymer is in

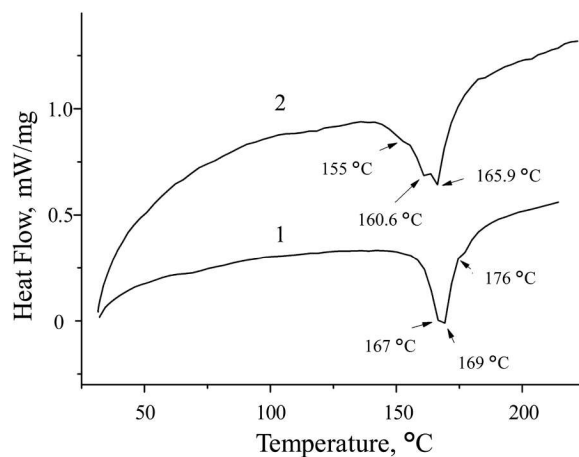


Figure 4. The temperature curves of DTA for PVDF before (1) and after γ -irradiation with a dose of 100 kGy (2).

Table 2

Elemental analysis of PVDF before and after γ -irradiation, from XPS.

Dose, kGy		C 1s	F 1s	O 1s	N 1s
0	E_b , eV	290.8(CF_2) 284.9(CC) 284.5(CC)	688.0(CF_2) 677.9	531.8 532.2	407.3
	atomic %	68.3	18.5	12.1	1.1
	E_b , eV	290.5(CF_2) 284.8(CC)	688.0(CF_2) 688.2(CF_2)	532.4 532.9	408.6
100	atomic %	71.2	11.7	15.8	1.3

agreement with the melting point of 167.4°C previously reported for PVDF. [39]

The endothermic melting peak of irradiated PVDF with a dose of 100 kGy has the same broad peak from 135°C to 182°C as the melting peak of the initial polymer, but it is shifted by about 10°C to lower temperature. There are three minima at 155°C, 160.6°C, and 165.9°C on the DTA curve of irradiated PVDF. They are also shifted to lower temperature as compared to those in the DTA of the un-irradiated polymer. This decrease in the melting temperature of PVDF due to increasing the irradiation dose is consistent with previous reports. [40]

The temperatures of devitrification of a low-temperature amorphous block (-22°C), of melting of two crystalline blocks (at 17°C and 27°C), and of the onset of molecular mobility in two higher temperature amorphous blocks (49°C and 113°C) in PVDF were determined by thermomechanical spectrometry. [41] The final phase transition on the thermomechanical analysis curve is molecular flow of PVDF at 164°C. Comparison of the DTA curves in Figure 4 with the curves of thermomechanical analysis of initial and irradiated PVDF [41] showed that the polymer melting peaks recorded on the DTA are in agreement with those for the temperatures of molecular flow determined by thermomechanical analysis. The data obtained by thermomechanical analysis [41] and the DTA shown in Figure 4 indicate the absence of a completely cross-linked structure in γ -irradiated PVDF with a dose of 100 kGy.

2.4. Mass spectrometry of gaseous products

The results of the mass spectrometry of the gaseous products resulting from the heating of the initial and γ -irradiated PVDF to 220°C are given in Table 3. The order of decrease of the quantity of the released products in a mixture of products (m/z (gross formula)) are: $m/z = 20$ (HF) $\gg m/z = 28$ (C_2H_4) $\approx m/z = 19$ (F) $> m/z = 38$ (F_2) $> m/z = 1$ (H) $> m/z = 16$ (CH_4) $> m/z = 14$ (CH_2) $\geq m/z = 2$ (H_2). The results in Table 3 show that the composition of gaseous products released during heating of the initial and irradiated polymer is similar. The presence of a large amount of HF, F, F_2 , and H as products, and a low yield of products with the composition $C_xF_yH_z$ indicates the absence of noticeable thermal destruction of the PVDF backbone. This is due to the low heating temperature of the samples (only up to 220°C). This temperature is much

Table 3

Tentative assignments for gas products of PVDF samples before and after γ -irradiation and heating to 220 °C.

Fragment	m/z	0 kGy	100 kGy
H	1	22.22	16.67
H ₂	2	7.41	2.78
CH ₂	14	7.41	8.33
CH ₄	16	11.11	11.11
F	19	114.81	127.78
HF	20	233.33	288.89
C ₂ H ₄	28	114.81	136.11
F ₂	38	62.96	50
C ₃ H ₃ ^b	39	114.81	111.11
Ar ^a	40	100	100
C ₂ H ₆ ³ F ^b	49	7.41	
C ₃ F ₂ H ₆	80		2.78
C ₂ F ₃ ^c	81		5.56
C ₂ F ₃ H ₃	84		2.78
C ₂ F ₃ H ₄	85	3.7	5.56 ^d
CF ₃ OH ₂ ^b	87		2.78
C ₃ H ₄ F ₄	116	7.41	5.56
C ₄ F ₅ H ₂ ^e	145		2.78
C ₄ F ₅ H ₄ ^f	147	3.7	5.56

^a Background peak

^b Tentative assignment.

^c An additional possibility is C₃F₂H₇

^d Could also contain CF₃O after irradiation

^e An additional possibility is C₄F₄OH₅

^f An additional possibility is C₄F₄OH₇

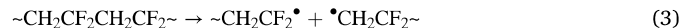
lower than the temperature of the onset of effective thermal destruction of PVDF at 360°C. [39,40]. Thus, HF is the main product of the thermal destruction of PVDF on heating to 220°C, as in the pyrolysis of PVDF. [20] γ -irradiation of PVDF promotes its thermal degradation and increases the HF content in the gaseous products released on heating.

HF was a significant product from polymer transformation during radiolysis by a relatively small dose of γ -irradiation or heating of PVDF up to the melting temperature. HF was also released when the irradiated polymer is stored at room temperature. Visual observation of the storage container showed noticeable traces of a white film on the surface of the vessel due to the release of HF after 2 to 3 days of storage of irradiated PVDF. The deposit increased over time. Thus, according to the available data, the process of HF release during storage of irradiated PVDF does not slow down with time. Additional experiments are planned to address this issue. As a result, an easily removable white deposit forms on the surface of glassware used for storing irradiated PVDF. It dramatically reduces the transparency of the glass and a roughness appears, consistent with the effect of hydrofluoric acid on the glass surface.

2.5. Electronic Structure Calculations and Mechanistic Considerations

We first benchmarked the energetics at the G3(MP2) level for the simple model reactions given in Table 4 as compared to reliable experimental results from the Active Thermochemical Tables (ATcT). [42,43,44] The calculated energies are within 4 kJ/mol of the experimental values with the latter having errors less than ± 4 kJ/mol.

The reaction energies calculated at the G3(MP2) level for models of the reactions for radiolysis of PVDF are given in Table 5. We use CH₃CH₂CF₂CH₂CF₂CH₃ as our model for PVDF. The C-F and C-H bond dissociation energies (BDEs) are larger than the C-C BDE given by reaction (3). Use of a larger model for the chain (reaction (3a)) did not substantially affect the C-C BDE.



The reactions with the lowest endothermicities, reactions (3) and (3a), were not observed experimentally as γ -radiolysis predominantly breaks C-H and C-F bonds rather than intrachain C-C bonds which quickly recombine due to the cage effect. [45] The cage effect is that the radicals generated by breaking a C-C bond do not have time to escape the region they are in due to the size of the chains and C-C recombination occurs. The cleaved H and F atoms can abstract adjacent hydrogen or fluorine atoms from both radical or neutral macromolecules leading to the formation of HF and a C=C bond, eliminating the radical center. Reactions (4) and (5) are highly exergonic



but less so than the energy needed to break the bonds given by reactions (1) and (2). The formation of double bonds can also occur by direct elimination of HF from PVDF, bypassing the stages of formation of macroradicals R_I and R_{II} as given by reaction (6). Note that summing reactions (1)



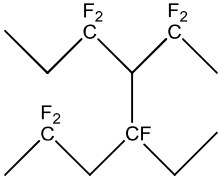
Table 4

G3(MP2) Benchmarks of Model Reactions in kJ/mol at 25°C.

Reaction	ΔH calc	ΔH expt
CH ₄ + F [•] → C [•] H ₃ + HF	-135.2	-131.0
CH ₃ F + H [•] → C [•] H ₃ + HF	-112.5	-108.8
HF → H [•] + F [•]	570.8	569.9
CH ₄ → C [•] H ₃ + H [•]	435.7	438.9
CH ₃ F → C [•] H ₃ + F [•]	458.3	461.5
CH ₃ CH ₂ F → CH ₂ =CH ₂ + HF	48.6	52.9
CH ₃ CHF ₂ → CH ₂ =CHF + HF	85.8	85.8

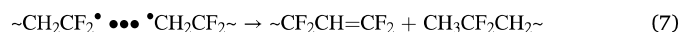
Table 5

Reaction Energetics at the G3(MP2) Level at 25°C in kJ/mol for Mechanism Development.

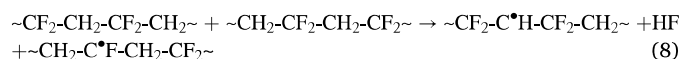
Reaction #	Model Reaction	ΔH	ΔG
1	CH ₃ CH ₂ CF ₂ CH ₂ CF ₂ CH ₃ → CH ₃ CH ₂ C [•] FCH ₂ CF ₂ CH ₃ + F [•]	500.4	454.9
2	CH ₃ CH ₂ CF ₂ CH ₂ CF ₂ CH ₃ → CH ₃ CH ₂ CF ₂ C [•] HCF ₂ CH ₃ + H [•]	426.1	387.0
3	CH ₃ CH ₂ CF ₂ CH ₂ CF ₂ CH ₃ → CH ₃ CH ₂ C [•] F ₂ + C [•] H ₂ CF ₂ CH ₃	388.2	327.1
3a	CH ₃ CF ₂ CH ₂ CF ₂ CH ₂ CF ₂ CH ₃ → CH ₃ CF ₂ CH ₂ C [•] F ₂ + C [•] H ₂ CF ₂ CH ₂ CH ₃	381.8	318.6
4	CH ₃ CH ₂ C [•] FCH ₂ CF ₂ CH ₃ + F [•] → CH ₃ CH ₂ CF=CHCF ₂ CH ₃ + HF	-416.3	-417.8
5	CH ₃ CH ₂ CF ₂ C [•] HCF ₂ CH ₃ + H [•] → CH ₃ CH ₂ CF=CHCF ₂ CH ₃ + HF	-342.0	-349.8
6	CH ₃ CF ₂ CH ₂ CF ₂ CH ₂ CH ₃ → CH ₃ CF ₂ CH=CFCH ₂ CH ₃ + HF	84.1	37.2
7	CH ₃ CF ₂ CH ₂ C [•] F ₂ + C [•] H ₂ CF ₂ CH ₂ CH ₃ → CH ₃ CF ₂ CH=CF ₂ + CH ₃ CF ₂ CH ₂ CH ₃	-276.2	-269.4
8	CH ₃ CF ₂ CH ₂ CF ₂ CH ₂ CH ₃ → CH ₃ CH ₂ CF ₂ CH ₂ CF ₂ CH ₃ → CH ₃ CF ₂ C [•] HCF ₂ CH ₂ CH ₃ + HF + CH ₃ CH ₂ C [•] FCH ₂ CF ₂ CH ₃	355.6	298.6
9	CH ₃ CF ₂ CH ₂ CF ₂ CH ₂ CF ₂ CH ₃ → CH ₃ CF ₂ CH=CF ₂ + CH ₃ CF ₂ CH ₂ CH ₃	105.6	49.2
10	CH ₃ CH ₂ C [•] FCH ₂ CF ₂ CH ₃ + CH ₃ CH ₂ CF ₂ C [•] HCF ₂ CH ₃ →	-347.3	-268.7
	→		
			
11	CH ₃ CH ₂ CF ₂ CH ₂ C [•] F ₂ → CH ₃ CH ₂ CF ₂ C [•] H ₂ + ¹ CF ₂	236.3	184.6
12	CH ₃ CH ₂ CF ₂ C [•] H ₂ → CH ₃ CH ₂ C [•] F ₂ + ³ CH ₂	424.7	376.2
13	CH ₃ CF ₂ CH ₂ CF ₂ C [•] H ₂ → CH ₃ CF ₂ CH ₂ C [•] F ₂ + ³ CH ₂	417.5	368.3
14	CH ₃ CF ₂ CH ₂ C [•] F ₂ → CH ₃ CF ₂ C [•] H ₂ + ¹ CF ₂	235.8	184.1

and (4) or reactions (2) and (5) gives reaction (6). The overall loss of HF from CH₃CH₂CF₂CH₂CF₂CH₃ is endergonic, but would produce approx. 0.05% dehydrogenated product in thermal equilibrium at 25°C. This of course would not include the initial energy from the γ-irradiation. This energy would cause the release of a possibly non-negligible amount of HF which needs to be considered for real world applications. The energy barrier for the unimolecular loss of HF at 25°C is 249.9 kJ/mol for ΔH and 248.7 kJ/mol for ΔG.

The appearance of unsaturation in the irradiated PVDF macromolecule corresponds to the release of HF. An exception to this is the formation of terminal unsaturated bonds in PVDF during the radiolytic cleavage of the polymer C-C bonds. At the beginning of this process, terminal radicals are formed in the "cage" of the radical pair as given by reaction (3). A subsequent attack of the ~CH₂-C[•]F₂ radical on the C-H-bond of the radical ~CF₂-C[•]H₂ in the cage leads to the formation of a terminal unsaturated bond as shown by reaction (7):



Intermolecular cleavage of HF in PVDF with the formation of two free radicals is also possible (reaction (8)) but this reaction is highly endergonic.

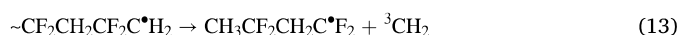
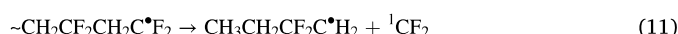
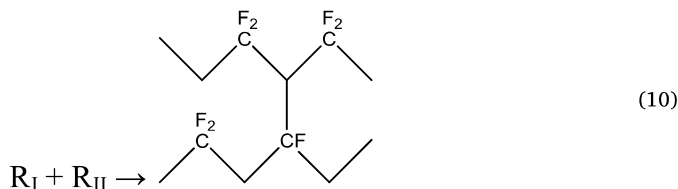


Another possible reaction is that a C-H bond is broken under the influence of γ-irradiation but does not leave the cage so that the resulting H atom abstracts a F atom from the neighboring macromolecule. This cleavage reaction (9) would produce approximately 0.004%

decomposed product at thermal equilibrium at 25°C. This decomposition reaction is much less destructive to surrounding materials than reaction (6) as no HF is produced.



Other possible reactions include the possibility of the γ-irradiation generated radicals reacting across chains leading to cross-linking. Radicals R_I and R_{II} could cross-link as shown by Reaction (10) in a highly exoergic process although geometric constraints limit such processes. As shown by our experimental work, cross-linking is unlikely. Another possibility is for the chains to unzip as shown by reactions (11) to (14).



We note it is relatively easy to lose a terminal CF₂ group with a singlet ground state but much more difficult to lose a terminal CH₂ group with a triplet ground state. Thus, the chains are not likely to unzip by more than one CF₂ group on radical formation by the above reactions for the head-to-tail, normal, configuration.

The formation and accumulation of unsaturated bonds during the radiolysis of PVDF is also consistent with the gradual change of the initial white color of the polymer, first to yellow, and then to brown and black with an increase in the radiation dose. This is due to the accumulation of various polyenyl and conjugated C=C bond-based chromophores in the structure of the radiolyzed PVDF. At the same time, effective release of HF is a distinctive feature of PVDF radiolysis. This is due to the uniform distribution of hydrogen and fluorine atoms along the PVDF chain. This also explains the release of HF during the pyrolysis of PVDF. [20]

The calculated EPR hyperfine coupling constants at the DFT level are given in Table 6. Radical 1 is a model for R_I and the calculated α fluorine HFC is within 3 mT of the experimental value. The HFC for the β hydrogens is much smaller. In contrast, radical 2, the model for R_{II}, has a very small HFC for the α hydrogen and a value near 5 and 8 mT for the β fluorine. There are not large changes when the terminal radicals have two fluorines (3, 5, 6) or two hydrogens (4, 7) in comparison to the radical centers with only a single H or F. As noted above, the HFC's for the polyene radicals become smaller as the polyene moiety has more conjugation. Fluorocarbon centered polyene radicals are predicted to have moderately high α fluorine HFC's, 12 and 9 mT dependent on model size and number of double bonds, and relatively small β hydrogen HFC's that are less than 2 mT. The magnitude of HFC difference with respect to the number of double bonds is greater for the α fluorine than for the β hydrogen in the fluorocarbon centered polyene radicals. The HFC's for hydrocarbon centered polyene radicals are small for the α hydrogen but the β fluorine are near 6 or 4 mT dependent upon increasing chain length and conjugated double bonds.

2.6. Acute toxicity of irradiated PVDF. Determination of LD₅₀

Hydrogen fluoride is highly toxic. Its one-time maximum permissible concentration (0.02 mg/m³) is 250 times less than the maximum one-time exposure of carbon monoxide. This prompted an investigation of the effect of radiation on the toxicity of irradiated PVDF. The

Table 6

Computational EPR hyperfine parameters (mT), $\parallel$ indicates parallel and $\perp$ indicates perpendicular components of hyperfine coupling. H indicates that the hyperfine parameters are for hydrogen and F indicates that the parameters are for fluorine.

Molecule		$a_{\parallel\alpha}$	$a_{\perp\alpha}$	$a_{\parallel\beta(1)}$	$a_{\perp\beta(1)}$	$a_{\parallel\beta(2)}$	$a_{\perp\beta(2)}$	$a_{\parallel\beta(3)}$	$a_{\perp\beta(3)}$
$\text{CH}_3\text{CH}_2\text{C}^*\text{FCH}_2\text{CF}_2\text{CH}_3$	1	20.5 (F)	-1.3 (F)	1.8 (H)	1.4 (H)	2.3 (H)	1.8 (H)		
$\text{CH}_3\text{CH}_2\text{CF}_2\text{C}^*\text{HCF}_2\text{CH}_3$	2	-0.8 (H)	-3.0 (H)	7.8 (F)	1.5 (F)	5.0 (F)	1.3 (F)		
$\text{CH}_3\text{CF}_2\text{CH}_2\text{C}^*\text{F}_2$	3	23.0 (F)	0.4 (F)	0.9 (H)	0.2 (H)				
$\text{CH}_3\text{CH}_2\text{CF}_2\text{C}^*\text{H}_2$	4	-0.8 (H)	-2.9 (H)	9.1 (F)	2.1 (F)				
$\text{CH}_3\text{CH}_2\text{CF}_2\text{CH}_2\text{C}^*\text{F}_2$	5	23.0 (F)	0.4 (F)	0.9 (H)	0.2 (H)				
$\text{CH}_3\text{CH}_2\text{C}^*\text{F}_2$	6	22.9 (F)	1.7 (F)	0.8 (H)	0.1 (H)				
$\text{CH}_3\text{CF}_2\text{CH}_2\text{CF}_2\text{C}^*\text{H}_2$	7	-0.7 (H)	-2.9 (H)	8.4 (F)	1.9 (F)				
$\text{CH}_3\text{CF}_2\text{C}^*\text{H}_2$	8	-0.8 (H)	-2.9 (H)	9.3 (F)	2.0 (F)				
C^*H_3	9	-0.8 (H)	-3.0 (H)						
$\text{CH}_3\text{C}^*\text{FCH}=\text{CFCH}_3$	10	12.0 (F)	-1.5 (F)	1.7 (H)	1.4 (H)	0.6 (H)	0.2 (H)		
$\text{CH}_3\text{CH}_2\text{C}^*\text{FCH}=\text{CFCH}_3$	11	12.0 (F)	-1.5 (F)	1.2 (H)	0.8 (H)	0.6 (H)	0.2 (H)	1.7 (H)	1.4 (H)
$\text{CH}_3\text{CH}_2\text{C}^*\text{FCH}=\text{CFCH}=\text{CFCH}_3$	12	9.4 (F)	-1.2 (F)	0.5 (H)	0.2 (H)	0.8 (H)	0.6 (H)	1.2 (H)	1.0 (H)
$\text{CF}_3\text{C}^*\text{FCF}=\text{CFCH}_3$	13	15.2 (F)	-2.2 (F)	3.3 (F)	0.6 (F)	0.6 (F)	-2.2 (F)		
$\text{CH}_3\text{CF}_2\text{C}^*\text{HCF}=\text{CHCH}_3$	14	-0.5 (H)	-1.8 (H)	1.9 (H)	1.5 (H)	0.5 (F)	-1.9 (F)	6.1 (F)	1.4 (F)
$\text{CH}_3\text{CF}_2\text{C}^*\text{HCF}=\text{CHCF}=\text{CHCH}_3$	15	-0.4 (H)	-1.3 (H)	0.5 (F)	-1.7 (F)	4.3 (F)	0.9 (F)	1.4 (H)	1.2 (H)
F^* ^a		7.4 (F)							
H^* ^a		47.4 (H)							

^a Isotropic hyperfine parameter (mT)

dependence of acute toxicity on the dose of γ -irradiation was studied at various doses of preliminary irradiation of PVDF. The results of the experiments carried out with a single intragastric administration at a dose of 2000 mg/kg for 1 to 14 days for 6 animals per group (Supporting Information) showed that no mice died due to intragastric administration of PVDF. Thus, the given dose did not lead to lethality. The dose of 2000 mg/kg could not be exceeded due to the impossibility of intragastric administration of higher doses of PVDF to animals. The similarity in toxicity between the initial and irradiated PVDF could be due to any HF produced during irradiation leaving the sample prior to intragastric injection. Although this result demonstrates that consumption of irradiated PVDF is not acutely toxic in mice it does not determine the toxicity of exposure to PVDF during irradiation and decomposition, or prolonged exposure.

2.7. Clinical picture of toxicity after the administration of PVDF

During the first day after administration, the animals receiving PVDF showed lethargy, with decreased food and water consumption. In the subsequent period, the general condition and behavior of the animals of all experimental groups returned to normal. There were no differences in these indicators between the experimental and control groups. Data on the effect of the PVDF samples on the body weight of experimental animals are shown in Table 7. There is an increase in the body weight of mice in both the experimental and control groups. There were no significant differences in the change in body weight in the experimental group as compared to the control group.

After 14 days of administration, the animals were euthanized and a macroscopic description of their internal organs was performed. As a result of autopsy and subsequent macroscopic examination of the internal organs, no differences were found between the animals receiving PVDF intragastrically and the control animals. As a result of the studies, irradiated PVDF can be considered to be a moderately low-toxic substance with at least a class 4 toxicity according to the classification of

Hodge and Sterner [46] and GOST 32644-2014. [47]

3. Conclusions

Low-temperature (-196°C) radiolysis of PVDF leads to the formation and accumulation of alkyl radicals formed by removing of the fluorine atom from the polymer chain. The EPR spectrum of a polymer irradiated at room temperature contains mainly polyenyl radicals. The EPR spectrum of paramagnetic centers accumulated during the radiolysis of PVDF changes during storage of the irradiated sample at room temperature as a result of dehydrofluorination of the irradiated polymer macromolecules.

The position and number of the XPS peaks for carbon (C 1s), fluorine (F 1s), oxygen (O 1s) and nitrogen (N 1s) do not change after γ -irradiation of PVDF. The intensities of the carbon and oxygen peaks increase in the radiolyzed polymer, whereas the intensity of the fluorine peak decreases. As a result, the ratio of fluorine and carbon content $[\text{F/C}] = 0.16$ is significantly lower in irradiated PVDF than their ratio on the surface of the initial polymer $[\text{F/C}] = 0.27$. Carbonization of radiolyzed PVDF leading to an increase in the percent of carbon content on the surface and correlates with release of HF. The increase of oxygen content is the result of oxidation of the free radicals formed during the radiolysis of the polymer. The carbonyl ($>\text{C}=\text{O}$) group peak appears in the O 1s spectrum of the irradiated polymer.

A broad PVDF melting peak with two minima at 167°C and 196°C and a shoulder at 176°C was observed in the DTA curve of the polymer. They are related to two different crystalline modifications of PVDF. Three minima are observed in the melting peak of the γ -irradiated polymer and are shifted towards low temperatures at 155 °C, 160.6 °C and 165.9 °C. This decrease in melting point with increased irradiation lowers the maximum use temperature of γ -irradiated PVDF. The DTA and thermomechanical spectrometry data indicate the absence of a crosslinked structure in the PVDF irradiated with a dose of 100 kGy, as irradiated samples retain the ability to melt and flow.

Table 7

Changes in the body weight, g, of BDF1 hybrid mice during the study of acute toxicity of PPDF samples at intragastric administration with a dose of 2000 mg/kg.

Dose of irradiation, kGy	Body weight of animals after administration of the drug for a day:					
	0	1	2	3	7	14
0	25.25±0.51	25.08±0.42	25.27±0.81	25.57±0.77	25.84±0.89	26.05±0.81
50	23.42±0.12	23.31±0.72	23.52±0.63	23.80±0.82	24.13±1.02	24.27±0.79
150	24.12±0.43	24.21±0.77	24.30±0.74	24.40±0.94	24.71±0.55	25.07±0.21
300	26.41±0.61	26.20±0.52	26.32±0.77	26.37±0.69	26.72±0.43	27.02±0.36
500	24.64±0.89	24.61±0.75	24.66±0.80	24.71±0.75	24.99±0.59	25.45±0.97
Control	25.88±0.26	25.78±0.35	25.86±0.54	25.94±0.64	26.19±0.59	26.81±0.87

The presence of a large amount of gaseous HF, F, F₂, H and a low yield of products with the composition C_xF_yH_z during heating indicates the absence of noticeable thermal destruction of the both initial and γ -irradiated polymer backbone. The main product of the PVDF thermal decomposition at heating up to 220 °C is HF.

Irradiation of PVDF with a relatively small dose of γ radiation or heating of the polymer to the melting point of its crystalline phase shows that the products of PVDF destruction are dominated by formation of HF. Storage of irradiated PVDF at room temperature is also accompanied by the evolution of HF. As in the case of storage of proton-irradiated samples of PVDF, an easily removable white deposit formed on the surface of the glassware used for storing irradiated PVDF. This reduces the transparency of the glass and a roughness of the glass appears, consistent with the effect of HF on a glass surface.

Composite, correlated G3(MP2) molecular orbital theory level calculations were used to develop a mechanism for PVDF decomposition. Although intramolecular C-C bond cleavage is the least endothermic, C-H and C-F cleavage dominates experimentally due to the cage effect promoting recombination of bulky intramolecular C-C bond cleavage products. Polymer backbone unsaturation can occur via multiple pathways including abstraction of H or F from the polymer backbone by free F or H, respectively (reactions (4) and (5)), direct elimination of HF (reaction (6)), and backbone C-C chain cleavage paired with H abstraction of a F (reaction (9)). Cross-linking of the polymer backbone is thermodynamically feasible (reaction (10)), but unlikely due to the need for the polymer change to undergo large amplitude motion.

At a single intragastric injection at a dose of 2000 mg/kg of PVDF irradiated with doses of radiation of 500, 1500, 3000 and 5000 kGy to hybrid mice of the BDF1 line, the acute toxicity is not affected at this dose, therefore a value of LD₅₀ could not be obtained. Thus, γ -irradiated PVDF has class 4 toxicity according to the classification of Hodge and Sterner.

An unambiguous answer to the question "how dangerous is γ -irradiated PVDF, if it entered the body?" requires additional studies to determine the clinical toxicity. Further studies are planned to test this. Additional studies are also required to determine the shelf-life of irradiated PVDF. Future work will address the kinetics of HF release from PVDF and irradiated PVDF.

4. Experimental methods

The PVDF plates and powder were purchased from McMaster-Carr Supply Company (Atlanta, Georgia, USA). The molecular mass and the molecular topological structure of the plate were previously determined by the thermomechanical spectroscopy method. [48] The total molecular mass determined by averaging the block-by-block average weight is MW = 149,600 amu. The molecular mass of the powder was not determined. Preliminary experiments with PVDF powder from Aldrich (N. Teutonia Avenue Milwaukee, Wisconsin, USA) with a MW = 534000 amu gave show similar results.

The experimental characterization of PVDF samples by EPR/XPS/DTA was carried out immediately after irradiation of the samples with ⁶⁰Co rays. The acuity toxicity studies used freshly irradiated PVDF samples.

4.1. γ -irradiation of the PVDF samples

The radiolysis of PVDF with ⁶⁰Co γ -rays was carried out using the facility of the UNU "Gammatok- 100" IPCP RAS. The dose rate of γ -radiation was 3 Gy/s.

4.2. EPR spectroscopy

EPR spectra were recorded on a Varian E-12 radio spectrometer. For the EPR study of γ -irradiated polymer, the PVDF sample was first evacuated to a residual pressure of 0.13 Pa, and then at -196 °C or 27 °C,

was irradiated with ⁶⁰Co γ -rays in ampoules made of "Luch" glass.

4.3. X-ray photoelectron spectroscopy

X-ray photoelectron spectroscopy (XPS) spectra were obtained using a JEOL 7000 FE scanning electron microscope.

4.4. Thermal analysis

A standard synchronous thermal analyzer STA 409C Luxx from NETZSCH (Germany), combined with a QMS 403C Aeolos quadrupole mass spectrometer, was used for qualitative measurements of thermal effects (DSC) in a series of temperature programmed experiments. The measurements were carried out in an argon atmosphere. To control the temperature, a Pt/Pt-Rh S-type thermocouple was used. The temperature dependence of the thermocouple sensitivity was taken into account by calibrating the melting points of 6 pure reference metals. The quadrupole mass spectrometer was connected to the thermal analyzer by means of a flexible quartz capillary, the temperature of which was maintained at 300 °C. This increased temperature prevented possible condensation of the reaction products and ensured complete transport to the detector. The device provides analysis of more than 60 lines according to their mass numbers with m/e < 300. The ionizing voltage was 70 V.

4.5. Computational Methods

Molecular geometries were optimized using density functional theory (DFT) with the B3LYP functional [49,50] and the DZVP2 basis set. [51] Frequency calculations were performed to ensure that the geometry was an energy minimum or transition state. The DFT optimized geometries for minima and transition states were used as the initial geometries for the composite, correlated G3(MP2) molecular orbital theory level calculations. [52] The B3LYP/DZVP2 optimized structures were used to predict the EPR hyperfine couplings for radical species. Following our previous work [53], the HFC calculations were performed with the B3LYP functional and a valence triple- ζ basis set with polarization functions (VTZP) from Ahlrichs. [54] The $a_{||}$ and $a_{\perp}$ were calculated for each atom following equation (15) and (16) respectively,

$$a_{||} = A_{iso} + B_{cc} \quad (15)$$

$$a_{\perp} = A_{iso} + (B_{aa} + B_{bb})/2 \quad (16)$$

where A_{iso} is the isotropic Fermi contact coupling, and B_{aa} , B_{bb} , and B_{cc} are the anisotropic spin dipole couplings. All calculations were performed using the Gaussian16 program. [55]

4.6. Acute toxicity

All research work with laboratory animals was carried out in accordance with generally accepted ethical standards for the treatment of animals, which comply with the rules adopted by the European Convention for the Protection of Vertebrate Animals Used for Experimental and other Scientific Purposes (ETS 123) Strasbourg, 1986).

The toxicity of γ -irradiated PVDF was studied after its single intragastric administration to male BDF1 mice weighing 23 to 26 g. Clinically healthy animals were used in the experiment. They were kept under the same conditions of keeping and feeding. Initial and γ -irradiated PVDF were suspended in 1% starch solution for intragastric administration to animals. The individual volume of the administered dose of the polymer solution in starch for each animal was calculated based on the body weight and the dose of the test substance.

At the same time, the mice were injected with no more than 0.5 ml of the suspension following the recommendations given in the "Guidelines for conducting preclinical studies of drugs". [46,47]

An atraumatic probe of appropriate dimensions was used depending on the type of animal and the size of the stomach of the animals to carry out the manipulation of intragastric administration. The animals were deprived of food, but not water, overnight before the administration. After the fasting period, the animals were weighed and the dose was calculated based on the body weight data; then the test sample was administered to the animals.

The animals were constantly monitored with recording the time of the onset of the first clinical signs of intoxication after the introduction of the test samples. The samples containing un-irradiated or irradiated PVDF were injected into mice intragastrically at the maximum possible dose of 2000 mg/kg.

The state of the animals was monitored and the clinical picture of intoxication was recorded for 4 hours after injection of the samples. The body weight of the animals was determined within 14 days after injection of the PVDF in comparison with control animals that received only a single equivalent volume of 1% starch. After the finish of the experiments, the mice were euthanized in a CO₂ chamber and were sent for dissection and pathomorphological examination of internal organs.

CRedit authorship contribution statement

Sadulla R. Allayarov: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Matthew P. Confer:** Data curation, Formal analysis, Investigation, Validation, Visualization, Writing – original draft, Writing – review & editing. **Sergei V. Demidov:** Data curation, Formal analysis, Investigation, Validation, Visualization, Writing – original draft, Writing – review & editing. **Uguljan Yu. Allayarova:** Data curation, Formal analysis, Investigation, Validation, Visualization, Writing – original draft, Writing – review & editing. **Denis V. Mishenko:** Data curation, Formal analysis, Investigation, Validation, Visualization, Writing – original draft, Writing – review & editing. **Elena N. Klimanova:** Data curation, Formal analysis, Investigation, Validation, Visualization, Writing – original draft, Writing – review & editing. **David A. Dixon:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare no competing financial interest. The experimental work was performed at the Institute of Problems of Chemical Physics of the Russian Academy of Sciences, Chernogolovka. The computational work was performed at The University of Alabama. All authors contributed to the data analysis and to writing the manuscript.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.jfluchem.2021.109885](https://doi.org/10.1016/j.jfluchem.2021.109885).

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Article

In Vitro Cell Interactions on PVDF Films: Effects of Surface Morphology and Polar Phase Transition

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Abstract: In recent years, several studies have validated the use of piezoelectric materials for in situ biological stimulation, opening new interesting insights for bio-electric therapies. In this work, we investigate the morphological properties of polyvinylidene fluoride (PVDF) in the form of microstructured films after temperature-driven phase transition. The work aims to investigate the correlations between morphology at micrometric (i.e., spherulite size) and sub-micrometric (i.e., phase crystallinity) scale and in vitro cell response to validate their use as bio-functional interfaces for cellular studies. Morphological analyses (SEM, AFM) enabled evidence of the peculiar spherulite-like structure and the dependence of surface properties (i.e., intra-/interdomain roughness) upon process conditions (i.e., temperature). Meanwhile, chemical (i.e., FTIR) and thermal (i.e., DSC) analyses highlighted an influence of casting temperature and polymer solution on apolar to polar phases transition, thus affecting in vitro cell response. Accordingly, in vitro tests confirmed the relationship between micro/sub-microstructural properties and hMSC response in terms of adhesion and viability, thus suggesting a promising use of PVDF films to model, in perspective, in vitro functionalities of cells under electrical stimuli upon mechanical solicitation.

Keywords: morphology; AFM; in vitro response; hMSC; piezoelectric materials



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1. Introduction

Smart functional biomaterials include all the materials able to support in vitro cell activities over the exposure of bioactive/biocompatible signals, thanks to the integration of additive functionalities strictly related to peculiar microscopic properties (i.e., electrical, magnetic, optical) able to directly or indirectly influence in vitro cell functions [1,2]. In the last years, the fabrication of biointerfaces that do not work only as passive support for cells is dramatically increasing, due to the need to discover innovative materials able to actively instruct “*ex novo*” the formation of the native extracellular matrix by triggering/stimulating specific intracellular cues [3].

In this view, recent studies have confirmed that electro-conductive/electro-responsive materials—alone or in combination with other dielectric ones—can efficiently participate to in vitro cell activities, by corroborating the effect of morphological (i.e., pore sizes, roughness) and/or biochemical signals (i.e., peptides, adhesive factors) usually imparted to modulate the surface and bulk properties at the interface with cells [4]. In this context, electroresponsive polymers—including current responsive and voltage responsive polymers—

currently represent a great promise for the fabrication of nanostructured platforms with highly tunable properties for different applications (i.e., molecular targeting [5], cell instructive interfaces [6,7], and biosensors [8]). Piezoelectric polymers such as polyvinylidene fluoride (PVDF), able to generate a voltage under mechanical stimulation/macroscopic deformation without the support of electrodes or other external sources [9], currently represent a straightforward but efficacious route to deliver electrical cues directly to cells in vitro [10]. Indeed, the peculiar semicrystalline microscopic structure of the PVDF, including five distinct crystallite polymorphs depending upon the conformation of the repeated monomer unit $(-\text{CH}_2\text{CF}_2-)_n$, can confer some unique properties to the substrates, including piezo-, pyro-, and ferroelectric properties [11]. In particular, β -phases with all the dipoles aligned in the same direction normal to the chain axis tend to promote the largest spontaneous polarization, thus determining strong ferroelectric and piezoelectric behavior [12] that concur to particularize the in vitro response. For instance, it has been proved that piezoelectric scaffolds can enhance neurite extension, neural differentiation and neurite outgrowth, thus supporting the regeneration of in vivo peripheral nerve [13]. Furthermore, PVDF has been successfully used as bioactive coating to modify titanium surfaces for orthopedic implants. In this case, it has been demonstrated that polarization of PVDF thin layers can promote a more remarkable adhesion and proliferation of osteoblasts and osteogenic differentiation of rBMSCs compared to a nude titanium surface [14,15]. According to previous experimental evidence, recent studies have shown that PVDF-based substrates with different morphological features had different influences on cell adhesion, proliferation and differentiation due to their surface roughness properties [3].

This work aims to further investigate these correlations by proposing a simple method to fabricate PVDF films to induce the transition from apolar to polar phases by thermal treatments of PVDF solutions at different concentrations, without any support of poling processes. Herein, we will perform a systematic study of morphological and thermal properties as a function of the process conditions used, in order to identify and correlate their effect on molecular phase polarization and, ultimately, in vitro cell response.

2. Materials and Methods

2.1. Materials and Film Preparation

Poly(vinylidene fluoride) (PVDF) (average $M_n \sim 71,000$) and analytical grade N,N-dimethyl acetamide (DMAc) were acquired from Sigma Aldrich (Milan, Italy). Briefly, 2.5 mL of PVDF solution in DMAc—50 or 200 mg/mL as concentration—was cast on to a glass plate at different temperature conditions (40 °C and 80 °C), for the preparation of different films, respectively labeled as 5% and 20%. Firstly, a metal ground—i.e., aluminum circular foil with a 30 mm diameter—was included to promote an efficient heat transfer to the solution, during the casting process. Secondly, the system was placed into a water bath to assure a more uniform distribution of temperatures along the sample volume. A casting time of 6 h was selected for all the samples to assure a complete solvent evaporation.

2.2. Morphological Analysis

PVDF films were investigated by scanning electron microscopy equipped with a field emission source (FESEM—Quanta200, FEI, Eindhoven, The Netherlands), working at a 10 kV accelerating voltage. Specimens were treated via gold–palladium sputter coating before the analysis. Atomic force microscopy (AFM) was adopted to quantitatively investigate the morphology of the PVDF films and the effect of solution characteristics and process parameters. Imaging was performed in tapping mode, in air and at room temperature, with a Dimension Icon instrument (Bruker Corporation, Kennewick, WA, USA). An RTESPA-150 silicone probe with a nominal tip radius of 8 nm, a typical spring constant of ~ 5 N/m and a frequency of ~ 150 kHz was used for the characterization. Images were recorded at $50 \times 50 \mu\text{m}^2$, $25 \times 25 \mu\text{m}^2$ and $3 \times 3 \mu\text{m}^2$ sizes with 512×512 lines per image, and a scan rate of 0.9 Hz. The cross-section analysis of the NanoScope Analysis software was adopted to assess the profile of the specimens in several locations. The

roughness parameter root-mean-square height of the surface (R_q) was calculated using the same software and, in order to get a statistical analysis, the measurements were repeated several times on different $1 \times 1 \mu\text{m}^2$ region of interest boxes. Results were reported as mean value $\pm$ standard deviation (SD).

2.3. Chemical and Physical Analyses

Thermal properties (i.e., crystallinity) of films were evaluated by differential scanning calorimetry (DSC) using a DSC Q1000 (TA Instruments, New Castle, DE, USA). An amount of approximately 10–15 mg was sealed in a nonhermetic aluminum pan under a nitrogen atmosphere. The scans were performed, under gaseous nitrogen flow, from 25 °C up to 600 °C at 10 °C/min. Neat PVDF pellets—i.e., no thermal treatments—were used as negative control (CTR) in this study. Physical transitions of PVDF were observed via Fourier transform infrared spectroscopy (FTIR). FTIR spectra were collected in the attenuated total reflection (ATR) mode using a single reflection ATR accessory (UATR from Perkin-Elmer, Newark, NJ, USA). This unit was equipped with a diamond crystal as internal reflection element (IRE) and two ZnSe crystals as transfer elements. The IRE had horizontal geometry, and an angle of incidence of 45°. The optimum wavenumber range for the present configuration was 4000–650 cm^{-1} . The ATR accessory was equipped with a pressure transducer on the crystal tip to ensure reproducible and uniform sample-to-IRE contact. Measurements were taken by a Spectrum 100 interferometer (Perkin-Elmer), equipped with a wide-band deuterated triglycine sulfate (DTGS) detector and a Ge on KBr beam splitter. The frequency scale was internally calibrated to 0.01 cm^{-1} using a He–Ne reference laser. From 32 to 128 scans at a resolution of 4 cm^{-1} were averaged to improve the signal-to-noise ratio.

2.4. In Vitro Studies

In vitro biological assays were performed using a human mesenchymal stem cell line from LONZA (hMSC, PT-2501). hMSC were cultured in 75 cm^2 cell culture flask in Eagle's alpha minimum essential medium (α -MEM) supplemented with 10% fetal bovine serum, antibiotic solution (streptomycin 100 $\mu\text{g}/\text{mL}$ and penicillin 100 U/mL, Sigma Chem. Co., Milan, Italy) and 2 mM L-glutamin. The cells were incubated at 37 °C in a humidified atmosphere with 5% CO_2 and 95% air. Four to six hMSC passages were used for all the experimental procedures. Prior to in vitro biological assays, PVDF films were cut into a round shape, 8 mm as diameter, placed in 96 cell culture plates and sterilized by immersion in 70% of ethanol (v/v) with antibiotic solution (streptomycin 100 $\mu\text{g}/\text{mL}$ and penicillin 100 U/mL), rinsed with phosphate-buffered saline (PBS) three times and air-dried. For the evaluation of cell adhesion, hMSC cells (1×10^4 cells/mL) were seeded onto PVDF films and incubated for 4 and 24 h in α -MEM culture medium at 37 °C. After a prescribed time, the PVDF films were rinsed three times with phosphate buffered saline (PBS) to remove nonadherent cells. The adherent cells were fixed with 4% paraformaldehyde for 10 min and fixed cells were incubated with 0.1% Toluidine blue for 3 h was carefully washed in distilled water to remove excess of toluidine dye. The dye was extracted with 0.1% of sodium dodecyl sulfate (SDS) and the optical absorption was quantified by spectrophotometry at 600 nm with a Wallac Victor3 1420 (PerkinElmer, Boston, MA, USA). Cells in conventional polystyrene 24-well culture plates were used as a control. Cell viability of hMSC onto PVDF films was investigated in triplicate by the MTT assay at two, four, and six days of culture. This assay is based on the ability of mitochondrial dehydrogenases of living cells to oxidize a tetrazolium salt (3-[4, 5-dimethylthiazolyl-2-y]-2, 5-diphenyltetrazolium bromide), to an insoluble blue formazan product. The concentration of the blue formazan product is directly proportional to the number of metabolically active cells. hMSC seeded onto PVDF films were washed with PBS and incubated with fresh cultured medium containing 0.5 mg/mL of MTT for 4 h at 37 °C in the dark. Then, the supernatant was removed, and dimethyl sulfoxide (DMSO) was added to each well. After 60 min of slow shaking, the absorbance was quantified by spectrophotometry at 570 nm

with a plate reader. The culture medium during the experimental time was changed every day with new media. Conventional polystyrene 24-well culture plates were used as a control. In order to evaluate morphology and cell spreading, hMSCs were investigated by confocal laser scanning microscopy (LSM 510, Carl Zeiss, Berlin, Germany). Briefly, hMSCs were incubated with Cell Tracker™ Green CMFDA in phenol red-free medium at 37 °C for 30 min; subsequently, hMSC were washed with PBS and incubated for 1 h in complete medium. After labeling the culture, hMSC were detached from the plate using trypsin and seeded onto PVDF films at 1×10^4 cells/mL and incubated for 24 h. After the incubation time, nonadherent cells were removed by rinsing carefully three times with PBS and, then, cell–material interactions were visualized by confocal microscopy.

3. Results and Discussion

Organic piezoelectric biomaterials currently offer several benefits over inorganic piezoelectric materials, because they include a high biocompatibility, excellent flexibility, environmental friendliness, and a high level of processability [16]. Among them, PVDF identifies one of the most interesting candidates for use in biomedical field, due to its high dielectric constant and piezo-, pyro- and ferroelectric properties [17]. At the microscale structural level, it is characterized by different crystalline phases with different orientation and dipole packing—namely α , ϵ (apolar) and β , γ , δ (polar),—that can be appropriately balanced in order to impart unique piezoelectric properties [18]. Moreover, PVDF polymorphs can be converted by applying external physical forces—i.e., temperature, pressure, mechanical stretching—thus enabling to finely modify microstructural (i.e., crystallization) and macrostructural (i.e., roughness) properties, as widely reported in the literature [19,20].

In this work, we investigated the transition from apolar to polar phases driven by thermal treatments of PVDF solutions at different concentrations, without any support of poling processes [21].

Thermal transition is coupled to a change in surface morphology strictly dependent upon temperature conditions and polymer concentration used. This is clearly reported in Figure 1, which includes SEM images of PVDF films under different preparation conditions that confirm a relevant effect of process parameters (i.e., polymer concentration, casting temperature) on the surface morphology. In all the cases, a peculiar microstructure was recognized, including spherulite units that cover all the surface, increasing in size with the casting temperature and decreasing as solution concentration increases.

These results are confirmed by AFM analyses (Figures 2 and 3). Figure 2 shows the height profile images for the different PVDF films produced in this study, and the relative profiles. It is interesting to note that the AFM analysis (i.e., interdomain measurements) confirms the spherulitic morphology highlighted by the SEM images, with the size of the spherulites increasing with the cast temperature and decreasing with solution concentration.

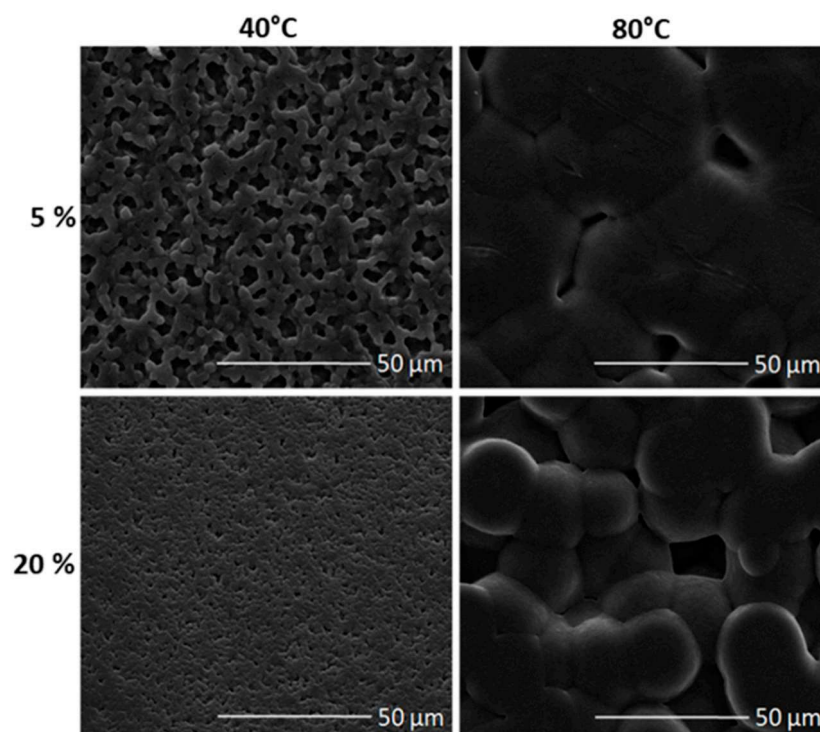


Figure 1. Qualitative analysis of surface morphology of PVDF films: SEM images of samples from polymer solutions with different concentration (i.e., 5 and 20%) and treated by different casting temperature (i.e., 40 and 80 °C).

AFM images at higher magnification (i.e., intradomain measurements), shown in Figure 3, reveal that the spherulitic domains present a nm-rough surface, with roughness (root-mean-square height values, R_q) ranging from 8.5 ± 1.7 nm to 65.1 ± 10.9 (see Table 1). Noteworthy was that R_q increased with temperature only in the case of a less concentrated solution (5%). Indeed, in the case of 20% solution, high viscosity of the PVDF solution may tend to limit short range mass transport phenomena driven by temperature, thus inhibiting the formation of surface roughness at the nanoscale.

Table 1. Root-mean-square height of the surface in terms of intra-/interspherulitic domains.

	Rq Intra-Domain * (nm)		Rq Inter-Domain ** (µm)	
	5%	20%	5%	20%
40 °C	14 ± 3	13 ± 2	0.9 ± 0.1	0.42 ± 0.07
80 °C	65 ± 11	9 ± 2	1.5 ± 0.1	1.6 ± 0.1

* Evaluated from the average on $n \times 1 \mu\text{m}^2$ ROI boxes. ** Evaluated on $25 \times 25 \mu\text{m}^2$ ROI boxes.

Further, we investigated how these morphological differences can be associated with changes in phase transition with effects on the piezoelectric properties of the film. At the first stage, differential scanning calorimetry was used for this purpose. In Figure 4, DSC thermograms showed endothermic peaks that correspond to the melting of α and β phases, falling into a temperature range from 167 °C to 172 °C, in agreement with previous studies [22].

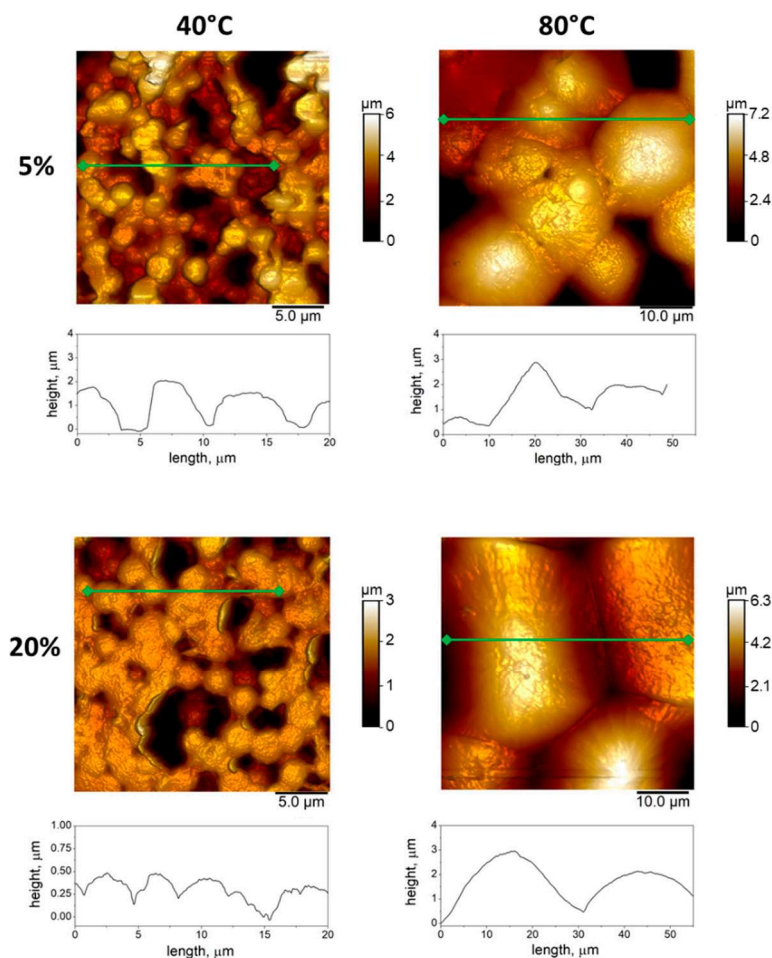


Figure 2. Quantitative analysis of surface morphology via AFM: images collected from samples with different polymer concentration (i.e., 5 and 20%) and treated by different casting temperature (i.e., 40 and 80 °C). Below the images, the profiles at the micrometric scale corresponding to the green cross-section lines were reported.

α phases are formed by the crystallization occurring during the casting process commonly induced via solvent evaporation. In the presence of temperature, β phases characterized by all-trans planar zig-zag conformation generally occur, due to the presence of additive dipole moments triggered by thermal vibrational modes that induce locally a spontaneous polarization of crystals [22]. In this study, results highlighted that the temperature-treated films (80 °C) are characterized by higher crystallinity as confirmed by higher heat of fusion—ranging from 58.4 to 60.6 J g^{−1} as a function of the polymer concentration—with respect to the control (i.e., 52.4 J g^{−1}). Similar effects were recognized also for low casting temperatures—i.e., 40 °C (Figure S1). Noteworthy was the presence of double peaks that suggested a different attitude of the PVDF solution to form crystalline phases. A unique peak was observed only in the case of high polymer concentration (20%), where the formation of multiple crystalline phases may be hindered to a reduction in polymer chains mobility occurred during the casting process [23].

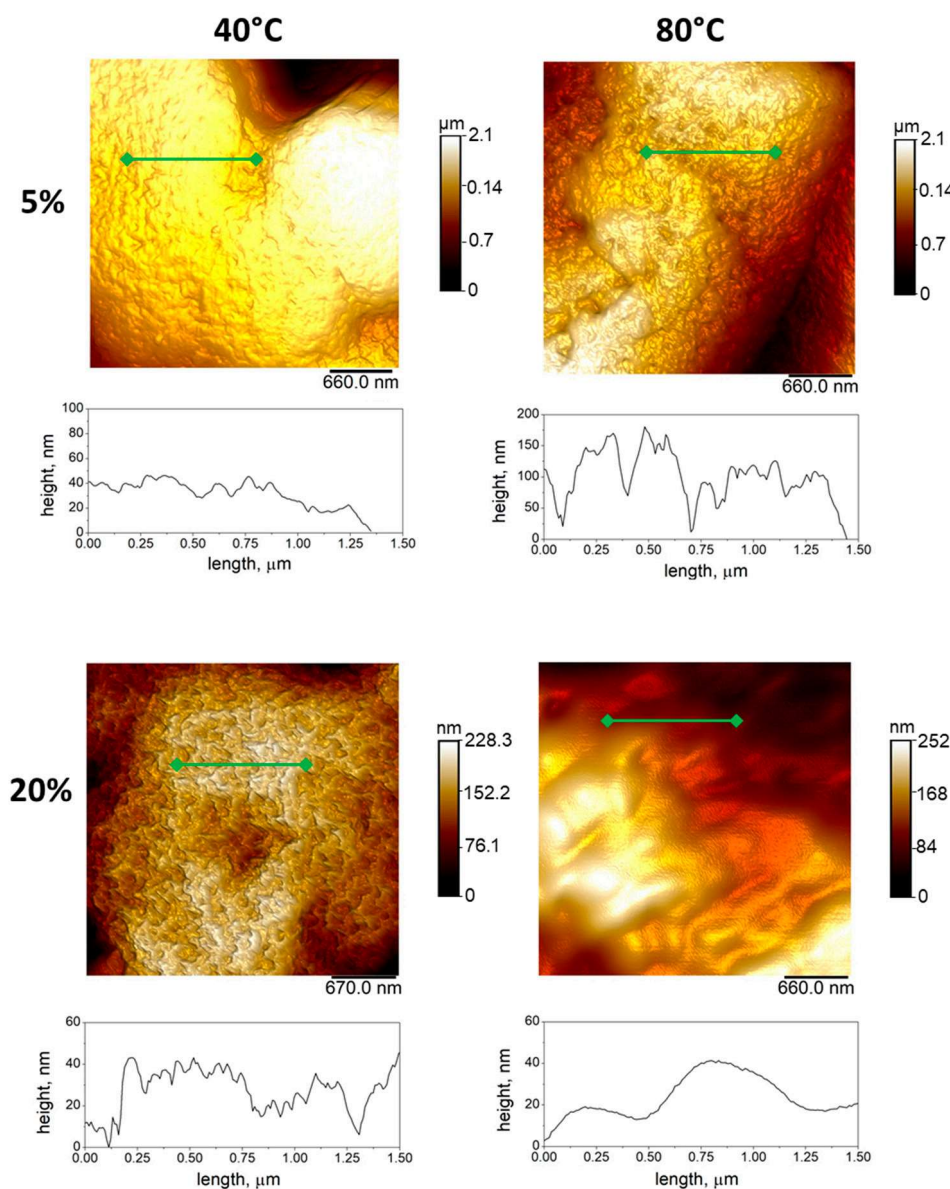


Figure 3. Quantitative analysis of surface morphology via AFM: images collected from samples with different polymer concentration (i.e., 5 and 20%) and different casting temperature (i.e., 40 and 80 °C). Below the images, profiles at the sub-micrometric scale corresponding to the green cross-section lines were reported.

In order to further investigate microscopic properties of crystalline phases, infrared spectroscopy techniques were used. It is well known that an overlapping of neighboring fluorine atoms occurs in all-trans PVDF, because the diameter of the fluorine atom (0.270 nm) is slightly larger than the space provided by an all-trans carbon chain (0.256 nm). To diminish this overlap, CF₂ groups are tilted to the right and left, relative to their original conformation. This deflection of CF₂ groups converts the all-trans form into TGTĠ (α form) or TTTGTTTĠ (γ form). Hence, the α -phase is more easily formed than the β -phase in normal circumstances [24]. Accordingly, ATR-FTIR analyses were performed to investigate the effect of process temperature—i.e., cast temperature—on the phase transition mechanisms (Figure 5). In particular, the IR spectrum of PVDF is very sensitive to ordering, both in terms of the overall amount of crystalline phase (crystallinity degree) and with respect to phase structure (α , γ and β polymorphic forms). According to previous works [25], there are several signatures that identify the different crystalline modifications. These are located at 410, 489, 532, 614, 763, 795, 854, 975, 1149, 1209, 1383 and 1423 cm^{-1} for the

α -phase, at 445, 473 and 1275 cm^{-1} for the γ -phase and at 431, 482, 811 and 1234 cm^{-1} for the β -phase. The spectra represented in Figure 5 indicated that the PVDF sample (black trace) contains only the α -phase. Both spectra (blue and red traces, respectively) are essentially coincident: β and γ -phase are largely predominant respect to α -phase. Shoulders at 1275 and 445 cm^{-1} reveal the presence of a minor fraction of β -phase. No relevant differences in the characteristic peaks of polar phases were also detected in the case of PVDF films (5%) (Figure S2).

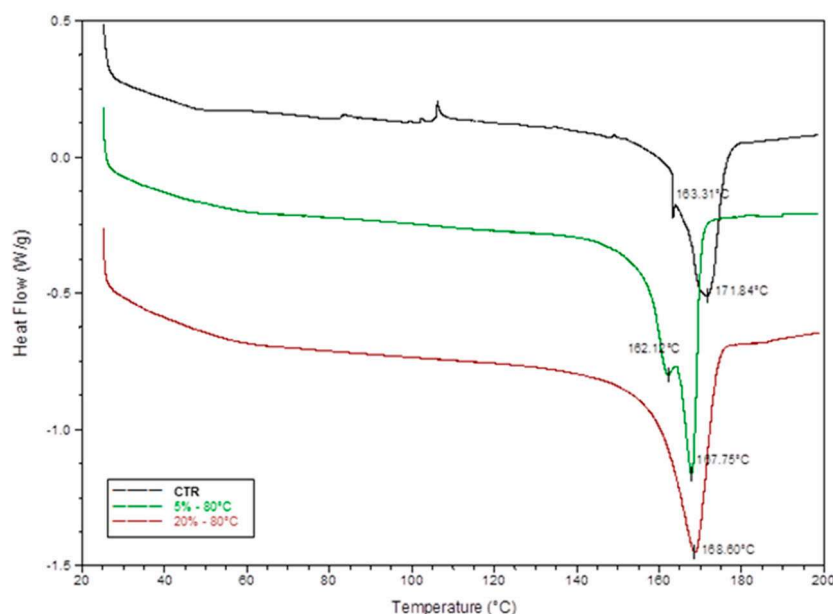


Figure 4. DSC thermograms of samples casted at 80 °C from PVDF solution at 5 and 20% and for pure PVDF pellets used as control.

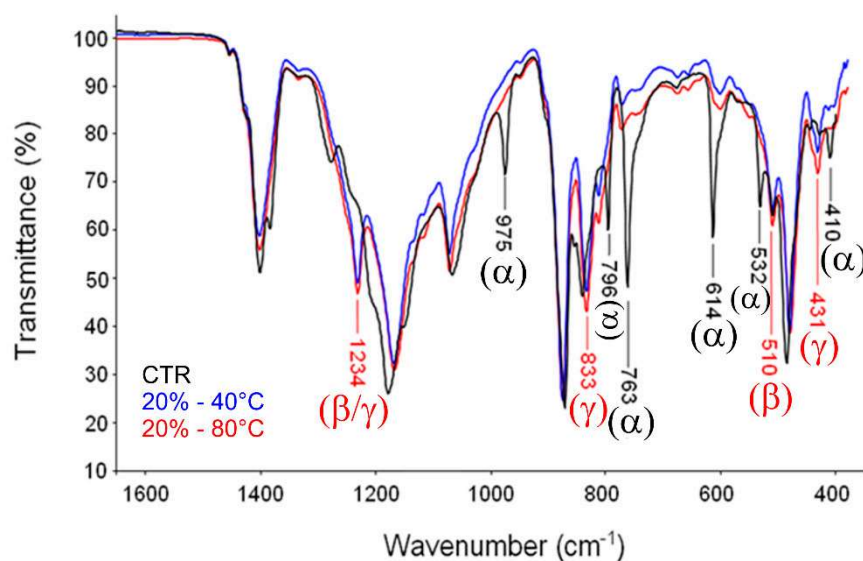


Figure 5. ATR spectra of PVDF films (20%) casted under different temperature conditions (40–80 °C). CTR refers to neat PVDF pellets used as control.

In order to validate the correlation between micro- (i.e., crystallinity, polar phase fraction) and macroscopic properties (roughness, spherulite size) of PVDF interfaces, *in vitro* tests were performed to investigate the correlations between phase transition and cell response. Figure 6A shows the *in vitro* response of hMSC on PVDF films in terms of adhesion, after 4 h and 24 h of cell culture. These results confirm that PVDF films

cast at 80 °C, support cell adhesion better than 40 °C cast ones. Moreover, a positive effect on cell adhesion is recognized in the case of (20%) films independently upon the process temperature either at 4 and 24 h, in comparison with (5%) films. This is due to the contribution of the size effect of spherulitic interdomains (see Table 1), that confirms the strict correlation between surface roughness and cell interactions, in agreement with previous experimental evidence in the literature [26]. Accordingly, the morphology of hMSC cells was observed after 24 h in culture by fluorescence microscopy. As reported in Figure 6B, no significant differences were detected among cells, regarding cell body elongation and fibroblastic morphology. In this context, the effect of polymer concentration and casting temperature on cell viability was quantitatively evaluated via MTT assay after 2, 4, and 6 days of cell culture, by measuring the optical absorbance at 570 nm (Figure 6B). A significant increase of hMSC viability was recorded in all the PVDF films that showed higher levels of MTT conversion and spreading affinity (Figure 6C) in the case of films cast at 80 °C, independently upon the PVDF concentration used. It means that the characteristic size of spherulite-like units—at micrometric scale—obtained at higher temperatures (80 °C) tend to promote higher metabolic activities of cells on the PVDF film surface, rather than 40 °C cast ones. Furthermore, MTT data present a good statistical significance ($p < 0.05$) among different groups. Noteworthy, all the results also confirm that PVDF films, which include polar phases, showed a more efficient biological response, in terms of adhesion and hMSC viability, in agreement with previous evidences reported in literature. In perspective, this peculiar effect, due to the synergistic combination of morphological and piezoelectrical signals, could be successfully addressed to keep in vitro functionalities of tissues such as bone with intrinsic piezoelectric properties [27], in order to design electro-active models that mimic the complex microenvironment of bone under the application of in vivo-like biomechanical stimuli.

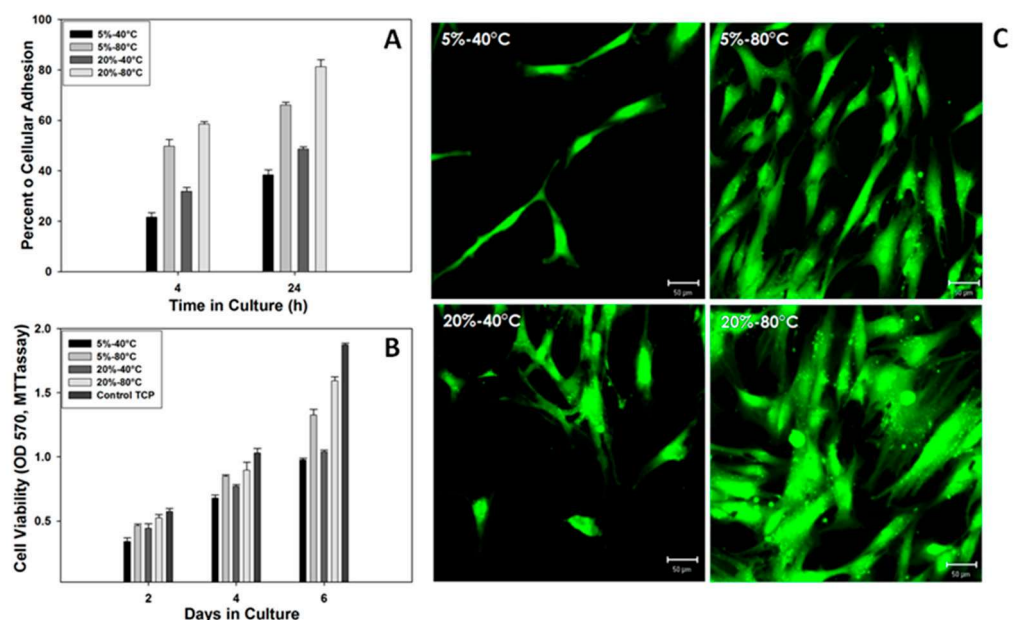


Figure 6. hMSC in vitro culture: (A) adhesion, (B) viability tests and (C) morphology of cell bodies via confocal microscopy.

4. Conclusions

In this work, we have investigated morphological properties of microstructured surfaces and correlations between phase transition and in vitro cell response in order to validate the use of PVDF films as bio-functional interfaces for in vitro studies. Different spherulite-like morphologies and polar phase transitions in PVDF films have been imparted by switching casting temperature and polymer concentration. All the results revealed a more pronounced trans conformation of chains, as the polymer concentration (20%) and

temperature (80 °C) increased. These peculiar morphological properties strongly influence the biological response of hMSC, affecting film biocompatibility in terms of adhesion and cell viability. In summary, micro-structured films with globular surface patterns and polar phases distribution could be really promising for the design of in vitro models to reproduce peculiar piezoelectric properties of the bone microenvironment.

Supplementary Materials: The following are available online at <https://www.mdpi.com/article/10.3390/ma14185232/s1>, Figure S1: DSC thermograms of samples (20%) casted at different temperatures (40 °C, 80 °C). Neat PVDF pellets were used as 407 control (CTR). Figure S2: PVDF films cast from 5% solution under different temperature conditions (40 °C, 80 °C). Asterisks denote 401 peaks characteristic of the phase.

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