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Solvent solutions: comparing extraction methods for edible oils and proteins in a changing regulatory landscape. Part 2: Hazards control[☆]

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Abstract – Safety is a critical consideration in the oil mill industry, particularly in the context of solvent extraction processes. This study focuses on the safety concerns associated with various solvents used in oil extraction, highlighting the potential risks to workers and end consumers, as well as environmental impacts. The analysis reveals that alcohols, such as ethanol and isopropanol, generally offer better safety profiles compared to hexane, despite presenting higher risks in terms of ATEX (explosive atmosphere) considerations at ambient temperature. These alcohols have higher electrical conductivity, which reduces the risk of electrostatic charge accumulation and subsequent ignition. However, methanol stands out as particularly hazardous due to its wide explosivity range and low minimum ignition energy. Ketones, including acetone and methyl ethyl ketone (MEK), and ethyl acetate also show relatively favourable safety characteristics. These solvents exhibit good electrical conductivity and lower toxicity levels, making them safer alternatives to hexane. Ethyl acetate and MEK are particularly noted for their compatibility with existing safety protocols and equipment. On the other hand, methanol, hexane, and dichloromethane (DCM) rank poorly in multi-criteria safety comparisons. Methanol, DCM and hexanes are presenting specific toxicities making these solvents less desirable from a safety perspective. 2-Methyloxolane (2-MeOx) occupies an intermediate position, with some improvements over hexane but challenges related to its low water miscibility and potential for peroxide formation. The study concludes that while no single solvent is superior across all safety criteria, alcohols and certain ketones could present promising alternatives to hexane if safety was the dominant criteria of selection. In an holistic approach, the possible improvements in safety brought by these solvent must be balanced by their impacts on other criteria like energy consumption, products quality, and economic affordability.

Keywords: Safety / Explosivity / Toxicity / Solvents / Extraction

Résumé – La sécurité est une question cruciale dans l'industrie de la trituration, particulièrement dans le contexte des procédés d'extraction par solvant. Cette étude se concentre sur les préoccupations de sécurité associées aux solvants pouvant être utilisés pour l'extraction d'huile. Elle compare les risques potentiels pour les travailleurs et les consommateurs finaux, ainsi que les impacts environnementaux. L'analyse révèle que les alcools, tels que l'éthanol et l'isopropanol, offrent généralement de meilleurs profils de sécurité par rapport à l'hexane, malgré des risques plus élevés en termes d'atmosphère explosive à température ambiante dans les espaces clos. Ces alcools ont une conductivité électrique plus élevée, ce qui réduit le risque d'accumulation decharges électrostatiques et d'inflammation subséquente. Cependant, le méthanol se distingue comme particulièrement dangereux en raison de sa large plage d'explosivité et de sa faible énergie minimale d'inflammation. Les cétones, notamment l'acétone et le méthyléthylcétone (MEK), ainsi que l'acétate d'éthyle présentent également des caractéristiques de sécurité relativement favorables. Ces solvants présentent une bonne conductivité électrique et des niveaux de toxicité plus faibles, que pour

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[☆] Contribution to the Topical Issue: "Extraction solvents / Solvants d'extraction".

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l'hexane. L'acétate d'éthyle et le MEK se distinguent pour leur compatibilité avec les systèmes existants. Le méthanol, l'hexane et le dichlorométhane (DCM) se classent mal dans les comparaisons de sécurité multicritères en raison de leur toxicité pour l'homme et les milieux aquatiques. Le 2-méthyloxolane occupe une position intermédiaire, avec une moindre toxicité que l'hexane, mais des défis liés à son potentiel de formation de peroxydes et sa mauvaise compatibilité avec la plupart des élastomères appellent desprécautions supplémentaires. Globalement, l'éthanol, l'isopropanol et les cétones seraient plus sûrs mais cette amélioration de la sécurité a pour corolaire une miscibilité avec l'eau qui pose de multiples problèmes pour le process.

Mots-clés : Sécurité / Explosivité / Toxicité / Solvants / Extraction

Highlights

Ethanol and isopropanol generally offer improved safety profiles, despite an increased potential for ATEX (explosive atmosphere) risks within extractors. Ketones and ethyl acetate demonstrate favourable characteristics. Methanol, hexane, and dichloromethane are the least safe solvents. 2-Methyloxolane occupies an intermediate position in terms of safety.

1 Introduction

Safety is paramount in the operation of oil mills using solvent extraction, as these facilities handle large quantities of flammable and potentially toxic substances. The choice of solvent not only affects extraction efficiency and product quality but also has significant implications for worker safety, environmental impact, and consumer health. The primary risks in oil mill operations stem from the flammability of solvents, which can create explosive atmospheres under certain conditions. Hexane, the most commonly used solvent, has a low flash point and can easily form flammable vapors. This necessitates stringent safety measures, including proper ventilation, explosion-proof electrical equipment, and rigorous handling procedures. Occupational safety is a critical concern, as workers may be exposed to solvent vapors during routine operations or in case of leaks. Prolonged exposure can lead to various health issues, ranging from respiratory irritation to more severe neurological effects, depending on the solvent used. Therefore, understanding the toxicological profiles of different solvents is crucial for implementing appropriate safety protocols and selecting personal protective equipment. Consumer safety is another key consideration, particularly regarding solvent residues in the final products. While refining processes typically reduce these residues to very low levels in edible oils, there is ongoing scrutiny of potential long-term effects of trace amounts. In oilseed meals used for animal feed, higher residue levels may be present, necessitating careful monitoring to ensure compliance with regulatory limits and to safeguard the food chain. This article, as part of a larger work on solvent extraction in the oil mill industry, focuses specifically on hazard control aspects. It builds upon the physical properties discussed in Part 1 and sets the stage for subsequent sections on processing considerations and product quality. The following sections will examine:

- Explosivity and explosion prevention.
- Electrical safety considerations.
- Toxicological profiles of various solvents.
- Environmental hazards and emissions control.
- Material compatibility and leak prevention.
- Fire extinction methods for different solvents.
- Occupational exposure limits and detection methods.

By comprehensively analyzing these aspects for a range of potential solvents, including hexane and its alternatives, this article aims to provide a thorough understanding of the safety challenges and considerations in oil mill operations.

2 Fire and explosion prevention in solvent extraction processes

Hexane, according to FEDIOL (2006), is a relatively volatile liquid with a flash point below ambient temperature which can readily form flammable (explosive) atmosphere in open vessels. It is also of low electrical conductivity (Tab. 1) and immiscible with water therefore it can accumulate electrostatic charges generated by interfacial friction while flowing through pipes. The phenomenon known as flow electrification is more pronounced in biphasic systems because the interface between the two liquids provides a larger area for charge separation and accumulation. The data for electrical conductivity collected in Table 1 can vary a lot from one source to another. This is partially explained by the conditions of the measure and the purity of the solvents, especially in function of the water content. But in some cases, the exactitude of the data may raise doubts, for example the value for hexane given by the source [16] which is 4 orders of magnitude greater the three first data. It is the same with Rapinel *et al.* (2020) where the data with a gap of 3 orders of magnitude look like an error of unit. This does not question the value for 2-MEOx given by the same authors, as it was confirmed by the EcoXtract company. In the case of methanol, we also observe a large gap between the two available data. It seems that the most hydrophobic solvents, those which are less miscible with water (*i.e.*, DCM, EA, and 2-MeOx), have lower conductivity and therefore the highest potential to accumulate electrostatic charges, though to a lesser extent than hexane. Ketones and alcohols present electrical conductivity comparable that of water (5.5×10^6 pS/m). Considering that they will be used most of the time in mixture with some water and impurities, these solvents are significantly decreasing the hazard of ignition by sparks generated by electrostatic electricity.

Table 1. Minimum ignition energy, maximum experimental flame gap, and electrical conductivity of the solvents.

	Minimum ignition energy (mJ)	Maximum experimental safe gap (mm)	Electrical conductivity (pS/m)	Temperature classification (T-class)
Hexane	0.24 FEDIOL. (2006)	0.93 FEDIOL. (2006)	$1\cdot10^{-5}$ FEDIOL. (2006)	T3 – T4
	0.29 HazCalc Online		$1\cdot10^{-5}$ Rigby, A. (2019)	
			$1\cdot10^{-5}$ NFPA (2007)	
			24 ESIG. (2013)	
			$1\cdot10^{-2}$ Rapinel *et al.* (2020)	
Methanol	0.14 HazCalc Online	0.92 IEC. (2024)	$7\cdot10^{4}$ [Barthel *et al.* (1995)	T2
			$4.4\cdot10^{7}$ NFPA (2007)	
Ethanol	0.28 IEC. (2013)	0.89 IECEx. (2024)	$1\cdot10^{8}$ Seitz, *et al.* (2014)	T2
		0.89 TPC. (2024)	$1.3\cdot10^{5}$ Rigby, A. (2019)	
			$1.3\cdot10^{5}$ NFPA (2007)	
IPA	0.65 Chem-Lab nv. (2023)	0.9 NFPA. (2021)	$3.5\cdot10^{8}$ Chem-Lab nv. (2023)	T2
			$3.5\cdot10^{8}$ NFPA (2007)	
			$3.5\cdot10^{8}$ Rigby, A. (2019)	
Acetone	0.55 IEC. (2013)	1.02 TPC. (2024)	$2\cdot10^{7}$ [Shell Chemicals (2016)	T1 – T2
	1.15 HazCalc Online		$6\cdot10^{6}$ NFPA (2007)	
MEK	0.27 IEC. (2013)	0.92 TPC. (2024)	$2\cdot10^{7}$ Shell Chemicals. (2016, a)	T2
	0.53 HazCalc Online		$1\cdot10^{7}$ NFPA (2007)	
Ethyl acetate	0.46 Carl Roth GmbH. (2023)	0.99 TPC. (2024)	$2\cdot10^{4}$ Shell Chemicals Europe B.V. (2005)	T2
	1.42 HazCalc Online		$2\cdot10^{6}$ ESIG. (2013)	
			$5\cdot10^{4}$ NFPA (2007)	
DCM	9300 IEC. (2013)	> 0.9 TPC. (2024)	$4\cdot10^{3}$ Rigby, A. (2019)	T1
			$4\cdot10^{3}$ NFPA (2007)	
2-MeOx	0.20 EcoXtract, personal communication	0.88 EcoXtract, personal communication	$8\cdot10^{3}$ Rapinel *et al.* (2020)	T3

Another aspect to consider is the classification of electrical equipment that can operate safely in atmosphere where the solvent is likely to be present. The two main parameters to take into account are the self-ignition temperature and the maximum distance a flame can travel. The first one affects the temperature class of the devices, *i.e.* the maximum temperature that an apparatus can reach. The classification is made according to the self-ignition temperature of the solvents and in practice, a 10–20% safety margin is observed between the ignition temperature and the rated nameplate (IEC, 2017). Table 1 gives the classes in which each solvent falls. In no case would a change of solvent necessitate a change of motor class, since T3 or T4 class motors authorized for hexane would still be usable with lower class solvents. In the event of replacement, lower-class motors may be less expensive.

The maximum experimental safe gap (MESG) is a standardized measurement used to classify flammable gases and vapours for the design of electrical equipment in hazardous areas and flame arrestor devices. This information is used differently according to the kind of area where the electrical equipment are used. In hazardous locations (mines), the classification made according to the National Electric Code (NEC) defines 4 groups: A: MSEG 0.25 mm (acetylene), B: MSEG $\leq$0.45 mm (except acetylene); C: 0.45 mm $<$ MSEG $\leq$ 0.75 mm; D MSEG $>$ 0.75. In the IEC/ATEX system, for equipment used in more usual locations like oil mills, 3 classes are defined: C for MSEG $<$ 0.5 mm (hydrogen); B (ethylene) when 0.5 $<$ MSEG $<$ 0.9 and A (propane) when MSEG $>$ 0.9. Although hexane falls in the class A, most of the oil mill are using class B or C equipment. A revamping toward methanol, ethanol, IPA and 2-MeOx will

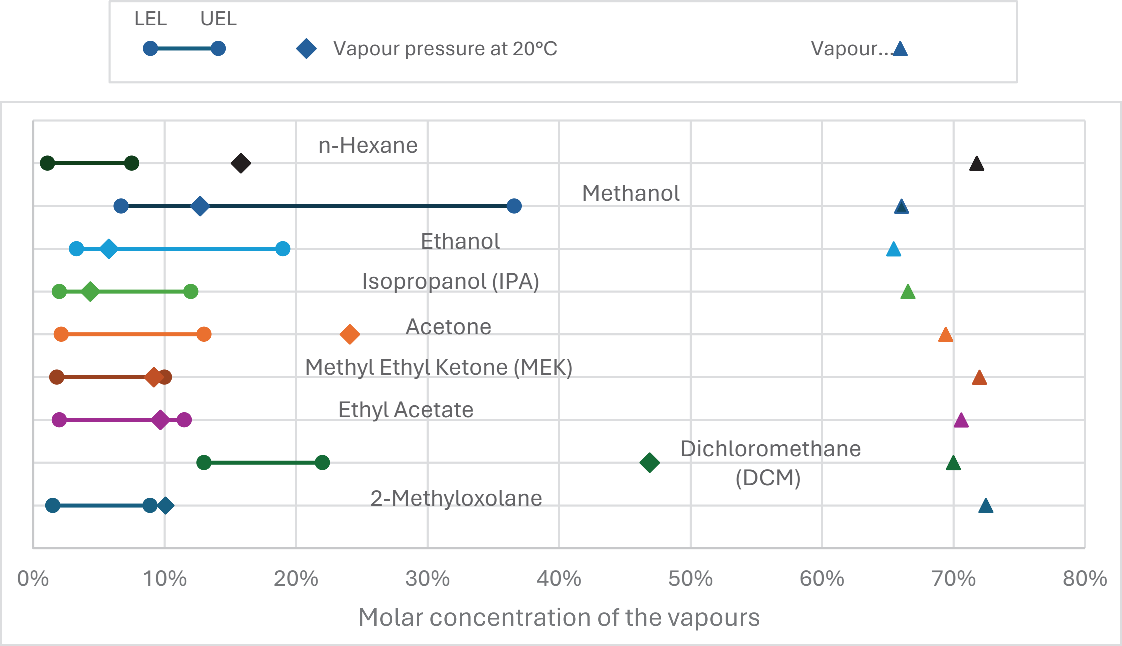


Fig. 1. Diagram presenting the explosivity domains of the solvents, the molar concentration of the solvent at 20°C and at the boiling point (BP) temperature minus 10 °C. LEL: lower limit of explosivity; UEL upper limit of explosivity.

require a change of electrical class from A to B for the electrical devices present in the plant not already in more stringent classes.

2.1 Comparison of the explosivity domains at ambient and working temperatures

Figure 1 compares the domains of explosivity of the solvents with their vapour pressures at 20 °C and at the temperature of the extraction.

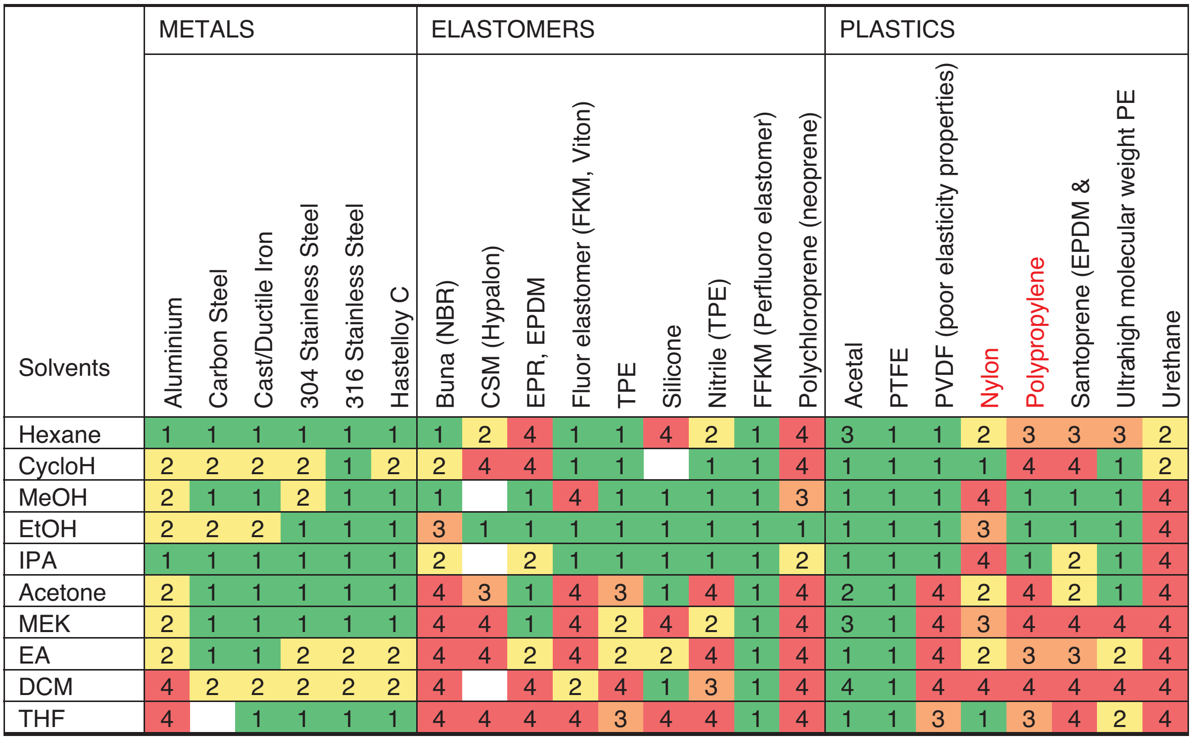
Regarding the safety of the solvent at room temperature, hexane, acetone and DCM with their high volatility are, in closed vessels, above the upper limit of explosivity. This makes the handling of the solvent after recycling safer than in the case of the other solvent where explosive atmospheres are present in the skies of the vessels where these solvents are present. In open area, however, hexane presents a high level of hazard due to its relatively low MIE in combination with very low electrical conductivity and water immiscibility which is favourable to the accumulation of electrostatic charges.

In the recommendations edited by Fediol (2006), a mean to preserve safety during the startup of the extractor requires that the temperature reaches 38 °C before starting any mechanical operation. This temperature corresponds to a partial pressure of the hexane vapour that is 4.5 times over the UEL. Such a level is intended to make sure that all the volumes in the apparatus are well saturated by the hexane vapours because the vapours are heavier than the air.

Methanol is the solvent with the largest domain of explosivity, which combined with the lowest MIE, makes this solvent the most hazardous of the list. It is also reactive in presence of aluminium or magnesium salts and able to generate hydrogen creating potentially additional explosion hazard. Ethanol has a rather low volatility which limits its rate of evaporation at ambient temperatures but in closed vessels, an ATEX is constantly present in the air above the liquid. With a UEL at 19%, going out of the domain of explosivity requires temperature above 42 °C. IPA would be safer than ethanol with a lower volatility and a domain of explosivity not going beyond 12% but ATEX will also be present in closed vessel up to 37 °C. This drawback is compensated by a higher MIE and electrical conductivity limiting the risk of ignition. The high volatility of acetone makes the air above vessels at ambient temperatures far above the domain of explosivity. The other characteristics of acetone (MIE, MESG, autoignition temperature and conductivity) make this solvent safer than hexane in closed vessel although its volatility in open air combined with its larger domain of explosivity are leading to the reverse conclusion in case of spillage. MEK, EA and 2MeOx are sharing similar volatilities, domain of explosivity, and likelihood of ATEX at ambient temperatures, even though at 20 °C, 2-MeOx is out when EA and MEK are in. What differentiates these solvents is the electrical conductivity, which is lower for 2-MeOx than EA by at least one order of magnitude if we retain the references [12,17]. MEK like alcohols and acetone presents a much higher conductivity and contrary to EA and 2-MeOx, MEK has little likelihood to be biphasic in regular operation.

All solvents except DCM are flammable and can cause explosive atmospheres (ATEX). It should therefore be remembered that, while there are differences in terms of hazard, none of the non-DCM solvents is exempt from this danger. An example is the reduction in the risk of static electricity accumulation by switching from hexane to IPA, which is offset by the presence of ATEX that do not exist with

Table 2. Compatibility between solvents and metals, elastomers and plastics.



Solvents	METALS						ELASTOMERS									PLASTICS							
	Aluminium	Carbon Steel	Cast/Ductile Iron	304 Stainless Steel	316 Stainless Steel	Hastelloy C	Buna (NBR)	CSM (Hypalon)	EPR, EPDM	Fluor elastomer (FKM, Viton)	TPE	Silicone	Nitrile (TPE)	FFKM (Perfluoro elastomer)	Polychloroprene (neoprene)	Acetal	PTFE	PVDF (poor elasticity properties)	Nylon	Polypropylene	Santoprene (EPDM &	Ultrahigh molecular weight PE	Urethane
Hexane	1	1	1	1	1	1	1	2	4	1	1	4	2	1	4	3	1	1	2	3	3	3	2
CycloH	2	2	2	2	1	2	2	4	4	1	1		1	1	4	1	1	1	1	4	4	1	2
MeOH	2	1	1	2	1	1	1		1	4	1	1	1	1	3	1	1	1	4	1	1	1	4
EtOH	2	2	2	1	1	1	3	1	1	1	1	1	1	1	1	1	1	1	3	1	1	1	4
IPA	1	1	1	1	1	1	2		2	1	1	1	1	1	2	1	1	1	4	1	2	1	4
Acetone	2	1	1	1	1	1	4	3	1	4	3	1	4	1	4	2	1	4	2	4	2	1	4
MEK	2	1	1	1	1	1	4	4	1	4	2	4	2	1	4	3	1	4	3	4	4	4	4
EA	2	1	1	2	2	2	4	4	2	4	2	2	4	1	4	1	1	4	2	3	3	2	4
DCM	4	2	2	2	2	2	4		4	2	4	1	3	1	4	4	1	4	4	4	4	4	4
THF	4		1	1	1	1	4	4	4	4	3	4	4	1	4	1	1	3	1	3	4	2	4

1: excellent, 2: good, 3: fair to poor, 4 not recommended. Sources: Graco inc. (n.d.); Parker H. corp. (n.d.)

hexane at ambient temperature in equipment where the aforementioned solvents are present.

2.2 Prevention of peroxidation in the storage of 2-Methyloxolane

A significant safety concern associated with 2-MeOx is its propensity to form peroxides during storage. Peroxides are highly reactive compounds that can accumulate over time, especially when the solvent is exposed to air and light. This accumulation poses a substantial risk because peroxides can crystallize and form shock-sensitive explosive crystals, which can detonate under mechanical impact or friction. The danger of peroxide formation in 2-MeOx necessitates stringent safety measures to mitigate the risk of explosion. Regular monitoring of peroxide levels is essential, and the solvent should be stored in tightly sealed containers, preferably under an inert atmosphere to minimize exposure to oxygen. Additionally, the use of stabilizers or antioxidants, can inhibit peroxide formation and enhance storage safety. In industrial settings, it is crucial to implement protocols for the safe handling and disposal of 2-MeOx, including procedures for peroxide testing and neutralization. Equipment used with 2-MeOx should be designed to minimize friction and impact to prevent accidental detonation of accumulated peroxides. Proper training for personnel on the hazards of peroxide formation and the safe handling of peroxide-forming solvents is also imperative to ensure a safe working environment. During oilseed processing, contact with biological matrices containing natural antioxidants and passage through recycling stages where temperatures reach levels that allow peroxides to decompose are factors that prevent the accumulation of peroxides (Rapinel *et al.*, 2020).

2.3 Leak prevention: seals, gaskets, and other compatibility issues between solvents and materials

Table 2 shows the compatibility between the main solvents and a range of materials including metals, elastomers, and plastics. Elastomers are of great importance for the prevention of leaks and solvent emissions. Their elasticity is essential to enable the materials to conform closely to the shape of the bearing surfaces between the various parts of machines containing solvents. Hexanes are relatively easy to manage in regard to this issue of material compatibility, NBR rubber, FKM and certain nitrile rubbers have good resistance, and their costs are fairly low. Alcohols present the largest range of compatibility. Only methanol has incompatibilities with FKM and neoprene, while EtOH and IPA can be in contact with all elastomers except NBR. With other solvents, the list of compatible elastomers is much shorter. Ketones are faring well with EPDM, and FFKM. Acetone is compatible with silicone while MEK could be in contact with TPE and nitrile. Ethyle acetate has a relatively good compatibility with EPDM, TPE

Table 3. Classification and labelling of the solvent according to ECHA/REACH documentation.

Solvent		Hexane	Iso-Hx	Cycl Hex	MeOH	EtOH	IPA	Acetone	MEK	EA	DCM	2-MeOx
CAS RN		110-54-3	107-83-5	110-82-74	67-56-1	64-17-5	67-63-0	67-64-1	78-93-3	141-78-6	75-09-2	96-47-9
Occupational Exposure Limit (ppm)		20			200	-	-	500	200	200	100	
France VLE /8h (ppm, molar)		20	500	200	200	1000	(400 CT)	500	200	200	50	
Germany (MAK)		50	500		200	200	200	500				
Flammable		🟧	🟧	🟧	🟧	🟧	🟧	🟧	🟧	🟧		🟧
Acute toxicity					🟧							
Health hazard		🟧	🟧	🟧	🟧	🟨					🟧	
Nocive or irrit.		🟧	🟧	🟧		🟨	🟧	🟧	🟧	🟧	🟨	🟧
Envion. hazard		🟧	🟧	🟧								
Corrosive												🟧
Properties of concern		Repro-toxic *				Cancer **					Cancer + endoc***	
LD 50 oral (g/kg)		0.024-0.049	0.0158	5	1.19-	1.18 - 15.0	5.84	5.8	2-6	10.19	2	0.3
Flam. Liq. 2	H225	✓	✓	✓	2.77	✓	✓	✓	✓	✓		R
Acute Tox. 3	H301				✓							
Acute Tox. 4	H302					R					n	R
Asp. Tox. 1	H304	✓	✓	✓								
Acute Tox. 3	H311				✓							
Skin Irritant 2	H315	✓	✓	✓		n					R	R
Eye dam. 1	H318											R
Eye Irritant 2	H319	R	n			R	✓	✓	✓	✓	R	n
Acute Tox. 3	H331				✓							
STOT SE 3	H335		n				n		n		n	n
STOT SE 3	H336	✓	✓	✓			✓	✓	✓	✓	R	n
Mutagen 2	H341										n	
Carcinog B1en.	H350					R						
Carcinogen. 2	H351				n						✓	
Reprotoxic 2	H361f	✓										
STOT SE 1	H370				✓	R						
STOT SE 2	H371					R		n				
STOT RE 1	H372	n ✓										
STOT RE 2	H373	✓									n	
Aquatic Ac. 1	H400		n	✓								
Aquatic Chr 1	H410		n	✓								
Aquatic Ch 2	H411	✓	✓									

(*) suspected to be toxic to reproduction; (**) Some submitters consider as carcinogenic; (***) Suspected carcinogenic & under assessment for endocrine disruption.
The symbol "✓" is present when the danger is recognized in the "harmonised classification and labelling" approved by the EU; R when the danger is identified by a large number of companies filling a reach registration; "n" is for dangers notified by a few suppliers to ECHA.
REACH: Registration, Evaluation, Authorisation and Restriction of Chemicals.

and silicone, but only FFKM is excellent for this solvent. DCM may be in contact with silicone, FFKM and FKM. The compatibility of 2-MeOx with elastomers is not available in current compatibility tables, but it is generally considered as equivalent to THF (Rapinel, 2020). Only FFKM is considered compatible which an expensive solution. An alternative to FFKM is the use of rubber coated with PTFE. PTFE is not an elastomer and lack of elasticity to ensure fair sealing, but it can protect more soft materials.

FKM, FFKM and PTFE are per- and polyfluoroalkyl substances, *i.e.* molecules where fluor has been used on carbon skeleton to make it more resistant to high temperatures or chemical reactions. These materials are widely used in various industries due to their desirable properties. However, some PFAS chemicals have been found to have negative environmental and health impacts, leading to increased scrutiny and regulatory efforts to restrict their use. FFKM, and FKM elastomers, and PTFE may contain PFAS chemicals used as processing aids during production. The proposed PFAS regulations in the EU aim to ban the use of PFAS chemicals, as they are considered persistent environmental pollutants. This could impact the supply and availability of FFKM, FKM, and PTFE materials, as they are commonly used in various industries (ECHA, 2024).

2.4 Olfactive detection of the solvents in the perspective of leak detection and explosion prevention

The olfactive threshold of hexane detection is ~130 ppm, that means that a human can detect the presence of the vapours at a concentration about 0.013% in the air, far below the lower limit of explosivity which is 1.1%. Although these thresholds vary from one individual to another and olfactive detection cannot be considered a safe detection method, every solvent on the list is likely to be detected by olfaction at concentrations lower than the LEL. On this aspect 2-MeOx is the most detectable because of a very low detection threshold.

2.5 Fire extinction considerations for solvents in oil mill processing

Different solvents require specific fire extinction approaches due to their unique physical and chemical properties. Hexane, being highly volatile with a flash point below ambient temperature, poses a significant fire risk. Its low electrical conductivity and immiscibility with water make water-based firefighting methods ineffective and potentially dangerous due to the risk of spreading the fire. Foam-based fire suppression systems are more appropriate for hexane fires, with dry chemical powder as a backup option (Fediol, 2006). Methanol presents unique challenges due to its invisible flames and wide range of flammability. Standard foam is ineffective against methanol fires, necessitating the use of alcohol-resistant foams. Water can be used to dilute methanol, but this requires large quantities and careful application to avoid spreading the fire (Methanex corp., 2020). Ethanol and isopropanol (IPA), like methanol, require alcohol-resistant foams for effective fire suppression. Their lower volatility compared to hexane reduces the risk of vapor formation at ambient temperatures, but in closed vessels, an explosive atmosphere is still a concern. Water can be used for cooling and dilution, but foam is preferred for direct fire attack (Alcool and Tobacco, 2021). Acetone, with its high volatility and large domain of explosivity, requires careful handling in fire situations. Alcohol-resistant foam is the preferred extinguishing agent, with dry chemical powder as an alternative. Water spray can be used for cooling containers but may be ineffective for fire extinction due to acetone's low flash point (OSHA, 2019). MEK (Methyl Ethyl Ketone), ethyl acetate, and 2-MeOx have similar volatilities and explosivity domains. For these solvents, alcohol-resistant foam is generally the most effective extinguishing agent. Dry chemical powder can also be used, especially for smaller fires. Water spray may be employed for cooling containers but is not recommended for direct fire extinction (NFPA, 2018). DCM (Dichloromethane), while less flammable, can decompose in fire to produce toxic gases including phosgene and hydrogen chloride. This necessitates the use of self-contained breathing apparatus for firefighters. Water spray or fog can be used to cool containers and disperse vapours, but foam or dry chemical agents are preferred for direct fire suppression (EPA, 2000).

3 Toxicology and environmental hazards

Table 3 recapitulates the main information related to the safety of the solvents included in this comparison.

3.1 Occupational exposure limits

Table 1 in the section 1 of this article (physical properties) gives the odour thresholds for the solvents. Occupational exposure limits are not always available in the European documentation, so the France and Germany figures have been represented for 8 hours exposure when available. For IPA in France, only a short-term value was available (CT). In light of this, n-hexane presents the lowest limit at 20 ppm, a condition which require thorough verification since olfactory detection for this solvent starts at 130 ppm. DCM, with 50 ppm in France and 100 ppm in Europe is also a risky solvent from this perspective since its olfactory detection starts between 200 and 300 ppm. Cyclo-hexane, MeOH, IPA, MEK, and EA have the same limit value at 200 ppm which is generally close to the odour detection threshold. Isohexane and acetone have a 500 ppm exposure limit well above the olfactive detection threshold. There is no consensus on ethanol limits, with German limit at 200 ppm versus 1000 ppm in France.

Table 4 recapitulates the hazard sentences placed in front of the ECHA's substance information datasheet. The first column reproduces the warnings for which a harmonised classification and labelling exists, the second column indicates the properties of concern, and the last column, the warnings given by many suppliers but not subject to harmonised classification. Only two solvents are presenting consensual properties of concern: n-hexane for its potential toxicity to reproduction and DCM for suspicion of

Table 4. Harmonised hazard classification and labelling of ECHA, properties of concern, and additional mentions from declaring companies.

Solvent	Harmonised C&L	Properties of concern	Additional mentions
n-Hexane	May be fatal if swallowed and enters airways, is toxic to aquatic life with long lasting effects, is a highly flammable liquid and vapour, is suspected of damaging fertility, may cause damage to organs through prolonged or repeated exposure, causes skin irritation and may cause drowsiness or dizziness.	Suspected to be toxic to reproduction	Causes damage to organs through prolonged or repeated exposure and is suspected of damaging fertility or the unborn child
iso-Hexane			
cyclo-Hexane			
Methanol	Toxic if swallowed, is toxic in contact with skin, is toxic if inhaled, causes damage to organs and is a highly flammable liquid and vapour.		
Ethanol		Some submitters consider as carcinogenic	Causes damage to organs, is toxic if swallowed, may cause cancer, is toxic in contact with skin, is toxic if inhaled, causes serious eye damage and causes skin irritation
Propan-2ol	Causes serious eye irritation and may cause drowsiness or dizziness.		
Acetone			
MEK			
Ethyl acetate			
DCM	Suspected of causing cancer	Suspected to be carcinogenic Under assessment as endocrine disrupting	Causes serious eye irritation, causes skin irritation and may cause drowsiness or dizziness.
2-MeOx	Harmful if swallowed, causes serious eye damage and causes skin irritation		

carcinogenicity and endocrine disruption. Ethanol has also a carcinogenicity related to its consumption but of a lesser concern when the substance is used as solvent.

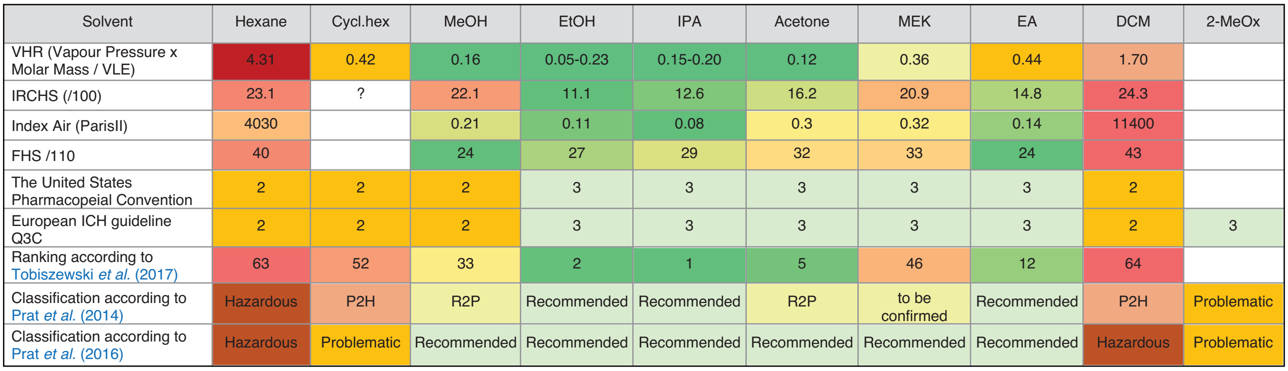
3.2 Pictograms

Regarding the pictograms which aims at signalling the presence of hazards to users in harmonised of ECHA (European Chemicals Agency) classification and labelling (HEC&L), except DCM, all the solvent must explicitly avert on their flammability. MEOH is the only solvent bearing the skull and crossbones pictogram for acute toxicity. The pictogram for health hazard is present for hexanes, MeOH and DCM. In the case of ethanol, the harmonized C&L does not include this pictogram, but some suppliers are using it. The pictogram for "nocive or irritant" is present for almost all solvent except for methanol. Its presence is not harmonized in the case of EtOH and DCM. Hexanes are the only solvent to bear the pictogram for environment hazard and 2-MeOx is the only solvent with the corrosive sign.

3.3 Toxicity and corrosiveness

Statement codes for oral toxicity H300 to 302 are grading the substances in 3 categories: fatal, toxic and harmful. The only solvent with a H301 classification is MeOH. EtOH and MeOx are categorized H302 by certain suppliers but not in the HEC&L. Hexanes are bearing the H304 statement which means "May be fatal if swallowed and enters airways » which is also a strong level of dangerousness. MeOH bears the H311 statement which concern the medium level of dermal acute toxicity (toxic). H315 statement is for skin irritant of the second category (on two) and applies for hexanes in HEC&L and for DCM and MeOx for large number of supplier and EtOH for a lower number of suppliers. Codes H318 and H319 are for eyes damages by order of gravity. Except for cyclohexane and MeOH, all the solvents are concerned. MeOx bears the highest grade but not in HEC&L, as EtOH and DCM for the H319 code. H331 regards the toxicity by inhalation and correspond to the second and last level of classification. It concerns only MeOH. Code H335 and H336 are warning for respectively "respiratory irritation" and "drowsiness or dizziness". H335 is employed by a minority of suppliers for iso-hexane, IPA, MEK, DCM and 2-MeOx but H336 is concerning almost all the solvent except MeOH and EtOH and maybe less justified for 2-MeOx. With a minor number of suppliers, DCM bears the H341 code for suspicion of causing genetic defect. EtOH is a known carcinogen in human consuming alcohol. For this reason, a large number of suppliers use the warning code H350 although it wouldn't be a real concern if ethanol was used as a solvent because it wouldn't change significantly the degree of exposition of the general population. Ethanol is present at low concentration in a large number of fermented foodstuffs like sauerkraut, kimchi or sourdough bread as in numerous fruit juices. It is also present in dairy cows feedstuffs like maize or grass silages or

Table 5. Classification / scoring of the solvents according to various methodologies.



Solvent	Hexane	Cycl.hex	MeOH	EtOH	IPA	Acetone	MEK	EA	DCM	2-MeOx
VHR (Vapour Pressure x Molar Mass / VLE)	4.31	0.42	0.16	0.05-0.23	0.15-0.20	0.12	0.36	0.44	1.70	
IRCHS (/100)	23.1	?	22.1	11.1	12.6	16.2	20.9	14.8	24.3	
Index Air (ParisII)	4030		0.21	0.11	0.08	0.3	0.32	0.14	11400	
FHS /110	40		24	27	29	32	33	24	43	
The United States Pharmacopeial Convention	2	2	2	3	3	3	3	3	2	
European ICH guideline Q3C	2	2	2	3	3	3	3	3	2	3
Ranking according to Tobiszewski *et al.* (2017)	63	52	33	2	1	5	46	12	64	
Classification according to Prat *et al.* (2014)	Hazardous	P2H	R2P	Recommended	Recommended	R2P	to be confirmed	Recommended	P2H	Problematic
Classification according to Prat *et al.* (2016)	Hazardous	Problematic	Recommended	Recommended	Recommended	Recommended	Recommended	Recommended	Hazardous	Problematic

distillers grains. DCM bears the code H351 in HEC&L which means that it is suspect of causing cancer. The International Agency for Research on Cancer (IARC) has classified dichloromethane as a Group 2A carcinogen – "probably carcinogenic to humans". Some suppliers have also used the H351 for methanol but it seems less justified.

H361f, n-Hexane has been classified by the European Commission as a Category 2 reproductive toxicant due to the potential risk of impaired fertility. The metabolite 2,5-hexanedione, formed from n-hexane metabolism, is believed to be responsible for the testicular toxicity and effects on male fertility. In developmental toxicity studies in rats, n-hexane exposure during pregnancy caused a reduction in foetal body weights and an increase in early and late foetal resorptions, indicating potential developmental toxicity (Anses, 2013). While the International Agency for Research on Cancer (IARC) has not classified n-hexane for carcinogenicity, the EPA has determined that n-hexane is not classifiable as to its human carcinogenicity (Group D). However, n-hexane has been identified as a potential reproductive hazard, with the New Jersey Department of Health stating it can cause reproductive damage (NCfBI, 2022; NJDH, 2016).

Codes H370 and H371 are warning of hazard for specific organs in case of single exposure, H370 being for the highest harmfulness. Only MeOH enters in the H370 codification according to HEC&L, but EtOH is also bearing this warning code with a large number of suppliers when is not the H371 code. Acetone is sometimes also bearing this warning code.

Codes H372 and H373 state a toxicity after repeated exposure. Only hexane has received such a classification for the second hazard category in HEC&L. This codification is due to evidence from animal studies showing n-hexane can cause damage to certain organs, particularly the nervous system, upon repeated or prolonged exposure. DCM sometimes bears this warning code because repeated exposure could harm the respiratory system. Regarding hexane, a 1994 opinion of the Scientific Committee for Food of the European Commission (the ancestor of the EFSA) based on a toxicity study carried out by TNO (1989) validated a 'no adverse-effects' concentration value of 40 mg/kg body weight for a technical hexane containing 58 % of n-hexane. The amount of hexane critical for a 60 kg human (200 times less than NOEL) would be 12 mg/day, which translated in proteins products with 10 ppm of residues makes more than one kg per day. Knowing that refined oils are holding less than 1 ppm of hexane residues, hexane residues are not considered as contaminant of concern and available publication on contaminants in oils and fats are not mentioning hexane (van Duijn, 2014; Lacoste, 2014). Van Duijn (2016) says that hexane, like gasoline is removed during the drying of oil prior to bleaching and did not mention the solvent in other part of an article dedicated to the fate of contaminants during the refining. In France, the oilseeds sector has instituted a national plan of surveillance which gather all the analysis results communicated by the companies on the basis of voluntariness which concerns the contaminants for which analysis are regularly made. This database does not receive analysis concerning hexane (Dauguet and Lacoste, 2013). But if the hexane residues in food products seems under control, it remains possible to raise questions about the possible consequences of residues left in the meals used to feed farm animals, particularly with regard to the possibility of the solvent passing through fats for which it has a great affinity, but to our knowledge, there are not available studies on the topic.

Codes H400 is for acute aquatic organisms toxicity category 1. Cyclohexane is concerned since it is highly toxic to aquatic life. It enters also in the H410 codification for it can cause long-term effects in aquatic environment. N-hexane and iso-hexane enters in the second category for long-term toxicity for aquatic life and are codified H411.

3.4 Ranking and classification by other instances than ECHA

Table 5 recapitulates different approaches aiming at comparing the harmfulness of chemical substances. In order to provide a synthetic indicator of dangerousness, several authors belonging to the chemical industry and pharmacy proposed a classification of the solvents based on the available information about their various effects on safety at the workplace, on the health and on the environment. One of the simplest methods has been proposed by Popendorf (1984) and consist in assessing **the vapours hazard ratio** (VHR) which is the vapour pressure at ambient temperature divided by the occupational exposure limits (OEL). This method is helpful since OEL alone are not reflecting the likelihood of reaching the OELs. In our case, extraction solvents require a relatively high volatility to remain recoverable at temperatures compatible with the preservation of oil and meals quality, so volatilities variations are not very large, and the results are reflecting mainly their OEL. By this indicator, we could distinguish 3 groups of dangerousness: the first group includes n-hexane and DCM which could be considered the most hazardous; the second includes cyclohexane, EA, and 2-MeOX; and the last group includes iso-hexane, MeOH, EtOH, IPA, and acetone with VHR below 0.3. This indicator is limited to the assessment of the substances' toxicity by inhalation and therefore doesn't take into account other toxicity routes (oral, skin) and environmental impacts.

According to Debia *et al.* (2011), **Paris II software** was developed by the U.S. Environmental Protection Agency (U.S. EPA) to help industrialist finding substitute for polluting solvents while keeping the properties of use. This software built an air index taking in account the solvent volatility and its toxicity, the latter being characterized through eight impact scores about human toxicity (oral, dermal, by inhalation), aquatic, and terrestrial toxicity, photochemical, acidification, ozone depletion, and global warming impacts. The software is presently unavailable, as its commercialization having been stopped. However, it is still possible to have access the scores given by this method, although 2MeOx and Isopropanol scores were not available. The scores were also poor for n-hexane and DCM, but with a clear distinction between these solvents, DCM being considered much more hazardous. Acetone had a worse score than methanol while EtOH, IPA and EA are the group with better appreciation.

Another comparison score is the Indiana Relative Chemical Hazard Score (**IRCHS**). It was developed by the Indiana Clean Manufacturing Technology Institute (CMTI) of Purdue University to evaluate impacts of chemicals on workers and the environment (Debia *et al.*, 2011). The score combines environmental hazard value and occupational hazard value. The two values are normalized to a maximum of 100 and have the same weight in the final score. The scoring about the environment is based on U.S. regulations and consider impacts on air, land and water as well as ozone with weighting respectively of 1, 1, 1, and 0.5. The scoring for occupational risks gathers data about toxicity and data about hazards like flammability, reactivity, corrosivity, the later having twice the weight of toxicity. Consequently, compared to the pervious scores, the IRCHS places much greater emphasis on workplace safety features than the earlier indices. As a result, this score significantly lowers the rank of MeOH whose score is close to those on n-hexane and DCM. The least harmful solvents according to this method are EtOH and IPA, EA is slightly worse followed by acetone.

P2OASys is another method developed by the Toxics Use Reduction Institute (TURI) at the University of Massachusetts Lowell. Its aim is to help companies assess the potential impact on the environment, workers and public health of the substances they are likely to use. The system considers 11 categories with a total of 61 criteria: acute toxicity, chronic toxicity, physical hazards, pollution of aquatic environments, persistence/bioaccumulation, air pollution, disposal hazards, chemical hazards, use of energy and resources, product hazards, and exposure potential (Debia *et al.*, 2011). A partial score is assigned by P2OASys to each criterion within a category, and a score from 2 to 10 is calculated for each category based on the two highest partial scores in that category. The **FHS** (up to 110) is calculated by adding the 11 scores. This method gives a slightly worse score to DCM than to n-hexane both of which remain far from the others solvents. The lowest grade are given to Methanol and EA (24), with EtOH, IPA and acetone getting respectively 27, 29 and 32.

U.S. and Europe pharmaceutical industries have set up a classification of residuals solvents in drugs into three class: class 1 for solvent to be avoided, class 2 for solvent to be limited, and class 3 for solvent with low toxic potential. Both the U.S. and E.U. give the same class to the solvent in our scope, all hexanes, MeOH and DCM are falling in class 2 while the other alcohols (EtOH, IPA), EA and acetone are falling in class 3.

Tobiszewski *et al.* (2017) have also proposed a novel procedure for assessing the environmental risk associated to solvent emissions. Its specificity is to take into account the potential distribution of solvents between media (air, water, soil, sediment), so it gives different weightings to the impacts according to media where the pollutant is the most likely to be found. For example, EtOH is more likely to go in water, while hexane mainly goes into the air. Consequently, EtOH's effects in air and hexane's effects in water are minimized. As a result, the method ranked IPA as the least damaging solvent among a list of 78 solvents. EtOH was second and acetone 5th. EA was 12th, MeOH 33rd, cylco-hexane 52nd, n-hexane 63rd and DCM 64th.

The Innovative Medicine Initiative **IMI-Chem21** was a public private partnership between six large pharmaceutical companies in Europe, ten university and five small to medium enterprises with the goal of developing more sustainable solutions in biological and chemical methodologies. It was organised in six work packages, the first of which was dedicated to finding targets for the other WPs and included the task of analysing the different available solvent selection guides to propose a more consensual classification. The existing guides were set up by Astra Zeneca, The American Chemical Society's Green Chemistry Institute (ACS CGI), GSK, Pfizer and Sanofi. Each individual guide prioritized hazards according to the risk perceived by its creators but, the analysis showed that for a substantial number of substances the categorization yielded comparable results. EtOH, IPA and EA were classified in the "recommended" list, MeOx in the "problematic" category and hexane in the category "hazardous". MeOH and acetone were sometimes classified as recommended, sometimes as problematic while, DCM and cyclohexane were classified between problematic and hazardous. This classification was then refined and reconsidered for an alignment with the Global Harmonized System (GHS) and European regulations. A methodology based on a simple combination of criteria was developed resulting in the CHEM21 selection guide of solvents. This final classification eliminated the 'in between" classes and led to reclassifying MeOH and acetone in the "recommended" category. For the solvent between problematic and hazardous, DCM was directed to the hazardous category while cyclo-hexane toward the problematic one.

Discussing this classification, Byrne *et al.*, 2016 concluded that although the selections guides are decided by various subjective considerations from mere compliance with regulation to wider concerns for environmental impacts, they tend to converge. He claims that "there is no need for more general-purpose solvent selection guides of the familiar format because they are no longer providing any significant advancement in this field". According to Byrne, this methodology clearly separates the considerations about the greenness of the solvents from their technological value. The guides give preference about level of dangerousness of the solvent but are not designed to advise on their fitness for the various uses. Since low water miscibility and latent heat of vaporisation are desirables traits in the case of oilseeds extraction, this leads toward generally less green solutions in terms of worker exposure and environmental impacts.

4 Conclusion

The comprehensive analysis of hazard control aspects for various solvents used in the oil mill industry reveals a complex landscape of safety considerations, with some clear trends emerging: Alcohols (ethanol and isopropanol) demonstrate overall better safety profiles despite some increased ATEX (explosive atmosphere) risks. Their higher electrical conductivity, lower toxicity, and better environmental compatibility make them attractive alternatives to hexane. Methanol, hexanes, and dichloromethane (DCM) consistently rank poorly in multi-criteria comparisons. Their higher toxicity, environmental concerns, and in the case of hexanes and DCM, lower electrical conductivity, make them less desirable from a safety perspective. Ketones (acetone and methyl ethyl ketone) and ethyl acetate show relatively favorable safety profiles, with good electrical conductivity and lower toxicity compared to hexane. 2-Methyloxolane (2-MeOx) occupies a middle ground, offering some improvements over hexane but presenting challenges due to its low water miscibility and potential for electrostatic charge accumulation.

Key findings include:

- Explosivity and flammability risks vary significantly among solvents, with alcohols presenting a wider range of explosive limits but generally better overall safety characteristics.
- Electrical conductivity differences greatly impact the risk of ignition, with alcohols and ketones showing significant advantages over hexane and other non-polar solvents.
- Toxicological profiles and occupational exposure limits favor alcohols, ketones, and ethyl acetate over hexane, methanol, and DCM.
- Environmental impacts and VOC emissions tend to be lower for more polar solvents like alcohols and ketones.

The transition to alternative solvents in the oil mill industry requires careful consideration of these safety aspects alongside efficiency and regulatory compliance. While no single solvent emerges as a clear superior choice across all criteria, the analysis suggests that ethanol, isopropanol, acetone, methyl ethyl ketone, and ethyl acetate offer promising alternatives to hexane from a safety perspective. Future research and development efforts should focus on optimizing safety protocols for these alternative solvents and potentially exploring novel extraction technologies that could mitigate some of the hazards associated with traditional solvent-based processes. Additionally, further investigation into improving the safety profile of 2-MeOx could be beneficial, given its favourable extraction properties. As regulatory pressures on hexane use continue to evolve, the oil mill industry must carefully weigh these safety considerations against other operational factors to determine the most suitable path forward for sustainable and safe extraction processes.

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