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Green Solvents for Liquid–Liquid Extraction: Recent Advances and Future Trends †

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Abstract: Using environmentally friendly solvents for liquid–liquid extraction offers a promising avenue for promoting sustainability in various industries. Green solvents, including ionic liquids, deep eutectic solvents, supercritical fluids, and bio-based solvents, offer several advantages compared to the traditional solvents of the present time. These solvents possess low toxicity, biodegradability, and reduced environmental impact, making them highly desirable for liquid–liquid extraction processes. Through careful adjustments in composition and physicochemical properties, these solvents can be customized to achieve efficient and selective extraction of desired compounds. Additionally, recent advances in green solvents often contribute to improved energy efficiency, reduced waste production, and the potential for developing novel products with unique characteristics. By embracing green solvents for liquid–liquid extraction, industries can actively contribute to sustainable development, minimize environmental harm, and support the transition towards an eco-friendlier future.

Keywords: green chemistry; green solvent; liquid–liquid extraction; ionic liquids; deep eutectic fluids; bio-based solvent; supercritical solvent

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1. Introduction

Liquid–liquid extraction (LLE) is one of the best-known separation methods due to its outstanding qualities, such as ease of use, high efficiency, and high selectivity. Another common term for liquid–liquid extraction is "Solvent Extraction" [1] process that involves taking liquids, mixing them, and being able to separate them "when the liquid settles". Often, one part is water, while the other can be an organic solvent.

However, one of the primary downsides of liquid–liquid extraction (LLE) is using cost-prohibitive toxic and non-renewable solvents, resulting in several environmental problems. The application of commonly used solvents like toluene, dichloromethane, chloroform, and DMF is restricted in many countries due to an increase in potentially hazardous cases [2]. The adverse effects of utilizing undesirable solvents can be avoided by using green solvents.

The concept of "green" solvents indicates the desire to reduce the environmental impact brought on by using solvents in chemical production or extraction processes [3]. In addition, many other factors are taken into account when determining whether a solvent qualifies as green, including health and safety concerns, indirect effects from production, use, and disposal, such as the depletion of non-renewable resources, potential solvent recycling, and energy consumption in their synthesis, recycling, and waste treatment. Given this, several solvents used during the extraction process may be called "green solvents". Other than water, the primary green solvents include various ionic liquids (such as deep eutectic solvents), organic-based solvents, and CO_2, frequently used under supercritical conditions (SC-CO_2).

The advancement of green solvents and their application in separation processes are imperative due to climate change and the necessity of developing environmentally friendly extraction processes. Thus, this paper aims to cover and evaluate the recent advanced green solvents for liquid–liquid extraction (LLE), their characterization, and efficiency.

2. Traditional Solvents and Environmental Concerns

Several solvents are commonly utilized in extraction processes: hydrocarbons (such as toluene or xylene, aliphatics, etc.), esters (such as ethyl, methyl, or butyl acetates), alcohols (such as methanol and isopropanol), halogenated (such as methylene chloride), ketones (such as acetone, methyl ethyl ketone, or cyclohexanone), etc. They have an alternative origin, mostly coming from olefins (mostly ethylene and propylene) or crude oil.

These traditional solvents are well-established, readily available, and more affordable than other raw materials used in different formulas. They frequently have extremely high solvency powers, evaporate quickly, and satisfy all standards for the final product.

2.1. Hydrocarbons

Hydrocarbons are the most commonly used extraction solvents and provide the best results [4]. A few years ago, hydrocarbons in the chemical industry and extraction methods tended towards specialization and were used for almost everything.

Released hydrocarbons into the environment are a substantial source of contaminated soil and water. In addition to the effects of burned hydrocarbons, escaping unburned hydrocarbons is even more harmful. Engine exhaust evaporates oil and gasoline and contains toxic, carcinogenic substances. Heavier forms have the potential to contaminate soil and groundwater. Special hydrocarbons are in demand today due to their improved emissions, which are either less inflammatory or safer for people. These improvements can improve compliance with existing regulations while maximizing the performance of these alternative solvents.

2.2. Esters

Esters are a valuable solvent for chemical processes, including extractions. Ester solvents typically have polarity and strong hydrogen bonding. They can dissolve various organic substances, especially those derived from living things or conditions that might promote corrosion damage on metallic surfaces. They are frequently used instead of volatile, highly controlled solvents to remove impurities from metallic items since they are non-toxic, non-volatile, and biodegradable. The environmental impacts of utilizing ester solvents (such as ethyl, methyl, or butyl acetates) and other effects are moderate to low, and aquatic organisms are hazardous.

2.3. Alcohols

Alcohol (such as methanol, isopropanol, and ethanol) is widely chosen as an extraction solvent due to its less toxic nature, and several experiments have been carried out to determine the solvent concentration, solvent/solid ratio, and extraction time to maximize the efficiency of this solvent.

The utilization of alcohol as a solvent has numerous advantages, including the potential to significantly reduce environmental effects, such as the emission of greenhouse gases, as well as its status as a GRAS solvent, low flammability, and as a renewable product created by biotechnological processes [5].

Additionally, alcohol enables the extraction of both oil- and water-soluble components. Because they are dispersed with both phases and function as mediators, it considerably increases water solubility in organic layers. Emulsions are frequently formed as a result of this.

2.4. Ketones

Ketones are chemically stable, low-density, and have an extensive solvent effect. Due to their ability to dissolve various synthetic and natural resins and their being at least partially soluble in water, they are ideally suited to low-viscosity and high-solid formulations. Acetone, methyl ethyl ketone, and cyclohexanone are examples of ketones that can create larger but still low-level concentrations in the air around the source. It is expected to be confined to the region where it is discharged. Since it does not adhere to the soil very effectively, the ketone that enters the earth may pass through the ground and reach groundwater (bore water).

3. Types of Green Solvents for Liquid–Liquid Extraction

Using organic solvents contributed immensely to pollution, causing more damage to public health and the environment through the years. Today, people are rallying to go green and clean. Many studies focus on searching for the most sustainable alternative solvent to minimize the harmful substances present in traditional solvents [6]. This is rooted in green chemistry principles, which aim to reduce pollution's effects by regulating its source point. It promotes limiting the production of hazardous substances by various chemical methods. Thus, chemical products and processes are now designed to be safer and non-toxic.

Green solvents are alternatives derived from raw materials, such as crops, and then modified to create less harmful environmental impacts. They are prominently used in the present time as they are proven to be environmentally friendly and economically effective [7–9]. However, there is no such thing as the perfect green solvent. Despite its claims to be better than the traditional ones, it is imperative to be critical in choosing the most suitable solvent for a specific industrial application. Several considerations should be considered, such as solubility, polarity, volatility, flammability, boiling point, and cost.

3.1. Water as Solvent

The term "universal solvent" was coined for water because of its ability to form a solution with almost any substance [10]. Its molecular structure has both positive and negative sides, so it effectively binds with other molecules of the opposite charge [11]. Aside from being the so-called solvent for all, it is also highly regarded as the greenest solvent as it possesses the following qualities: abundant, natural, low-cost, ubiquitous, and ready for use [7,11,12].

The unique characteristics of water make it distinct from any other solvent. The high heat capacity of water allows it to absorb heat from its surroundings and then dissipate it as a cooling effect under extreme exothermic conditions. As a desirable heat buffer, it maintains a persistent state by resisting change. In terms of acting as a solvent, it improved the chemoselectivity and regioselectivity of solutions while increasing the rate of the chemical reaction [13]. Moreover, water is also known to have a high dielectric constant. The dielectric constant expresses how quickly an electric field can polarize a material compared to a vacuum. This stems from the alignment of dipoles in its hydrogen bond, making it a high-polar solvent. However, at elevated pressures and temperatures, the polarity of water decreases as expected, causing the hydrogen bond network to fail. As a result, organic compound solubility increases substantially more than would be estimated based only on changes in water temperature [14].

Supercritical or subcritical water is widely used in industry, especially in extraction, hydrolysis, and gasification processes. Compared with ordinary liquids at room temperature, supercritical water exhibits different properties, such as dielectric constant and reduced polarity, similar to organic solvents [15]. The reversibility of this property makes it an excellent solvent suitable for both reactions and extractions of nonpolar organics. In addition, the difference between supercritical and subcritical water is the strength of H^+

and OH^- ions due to the development of water decomposition, which gives strong acidity and alkalinity simultaneously. Therefore, some reactions that require strong acids or bases can be carried out in supercritical or subcritical water under moderate conditions, reducing waste generation.

3.2. Ionic Liquids

Over the past decades, ionic liquids have been considered the emerging innovative fluids for the separation process. These compounds that contain ions with a melting point that is not higher than 100 °C have drawn the attention of researchers due to their practical applications [16]. Because of their unique chemical composition, ILs are liquid at room temperature. The negative and positive ions (anions and cations) comprising the liquid should be chosen carefully to break the crystalline solid phase.

Solvents called ionic liquids (ILs) are capable of various enticing interactions. These interactions include strong and specific forces like hydrogen bonds, halogen bonds, dipole-dipole interactions, magnetic dipole interactions, electron pair donor/acceptor interactions, and weak and non-specific forces, including van der Waals, solvophobic, and dispersion forces. Local configurations inside the bulk and close to interfaces can be precisely altered thanks to the many strong intermolecular interactions in ILs [17]. The presence of diverse and potent intermolecular forces in ILs allows for precise adjustments in local arrangements within the bulk and near interfaces. The amphiphilic nature of many IL ions serves as a basis for ordering similar to ionic surfactant systems. However, it is unclear whether or not interactions between ions lead to strong bonding. Additionally, the melting point of ILs is poor due to the dense and asymmetrical structure of the component ions. This is also why it is combined in various mixtures to optimize their thermophysical qualities.

The various possible applications of ILs have drawn the attention of scientists and researchers. It was called a "solvent of the future" back in 2003. Many definitely saw it as a replacement for the usual solvents used in chemical processes [18]. Even so, several issues were found regarding the use of ILs. It is costly, economically inconvenient, and hard to dispose of, and the solvent itself can be relatively toxic, which may cause undesirable environmental changes. Regardless of the many setbacks of this type of solvent, it is still proven to improve green processes via increased catalyst recovery and solvent reuse. Sustainability and recyclability are still imposed through the process, promoting "green chemistry" [19].

3.3. Supercritical Fluids

Liquids in a supercritical state exhibit characteristics similar to those of both liquids and gases. While maintaining liquid-like density, the viscosity of a supercritical fluid is comparable to that of typical gases. Additionally, the diffusivity of supercritical fluids is significantly higher than that of regular liquids [20]. Phase behavior plays a vital role in determining the efficiency of supercritical liquids. In an isobaric system, for example, the solubility of the solute in a solution increases with increasing temperature. However, at different pressure ranges, the solute becomes less soluble [19].

A supercritical solvent could be any solvent if it acts in its critical state. The two most known solvents of this type are supercritical water and carbon dioxide (CO_2). Their eco-friendly properties make them the most used solvent among others. CO_2 is capable of dissolving compounds that are either polar or nonpolar. For compounds with low molecular weights that are less volatile and more polar, it effectively separates such substances [21]. While it is true that CO_2 is a greenhouse gas, it could still be brought to life without causing harm to nature if properly extracted, processed, and returned to the environment.

In general, industrial operations using supercritical fluids (SCFs) provide a cost-effective, environmentally friendly, and sustainable approach, giving the chance to create new products with qualities tailored to customer needs [21]. One of the major benefits of SCFs is the simplicity with which fundamental thermophysical parameters like diffusivity, viscosity, density, and dielectric constant may be changed. This can be carried out by merely changing the operating pressure and/or temperature. In addition, SCFs have good heat transfer characteristics. Unlike current methods that utilize hazardous materials or emit strong greenhouse gases, they can be used as heat transfer fluids without having a substantial adverse environmental impact.

3.4. Deep Eutectic Fluids

Because of the drawbacks of ionic liquids (ILs), the new type of solvent is the deep eutectic fluids. It was first introduced in 2001 and obtained its name in 2003. It was considered one of the most innovative products ever made in history, leading to massive advancements in all industries [22]. Due to their many similar properties to ILs, such as high thermal stability, low vapor pressure, and volatility, DESs are sometimes known to be a classification of IL. When comparing ILs to DESs, DESs have the benefit of being easier to synthesize since they only require mixing, and no further purifications are needed.

Additionally, because synthetic raw materials are inexpensive, DESs have a low production cost. On the other hand, the high viscosity and solid state of DESs at room temperature may be a little bit of an issue. However, the physicochemical features of DESs can be tailored by carefully selecting the suitable hydrogen bond acceptor and donor. Nevertheless, it remains better than the former because of DESs [23–25].

3.5. Bio-Based Solvents

A bio-based solvent is generated from renewable biomass, such as plants or plant wastes. These solvents are considered more environmentally benign and sustainable than traditional solvents obtained from fossil fuels since they provide low toxicity, biodegradability, and a lower carbon footprint [26]. These are widely used for numerous applications, including chemical synthesis, extraction procedures, and cleaning formulations [27,28].

Overall, solvent selection remains a critical action in determining the efficiency of a process. Several factors must be considered, such as the type of solution, the properties of both the solute and solvent, their compatibility, their economic stand, and many more. Despite the many available solvents in the present time, one has to know that choosing sustainability comes with many sacrifices but rewarding consequences.

4. Recent Advances in Green Solvents for Liquid–Liquid Extraction

Over the last few years, significant advancements have been made in liquid–liquid extraction, including using green solvents as an alternative to conventional organic solvents, as concerns grow about the environmental and health impacts associated with traditional solvents used for extraction. According to the Green Analytical Processes (GAC), a solvent must have a lesser environmental, health, and economic impact to be considered a 'green solvent0'. This principle was introduced in the late 20th century and has since expanded into different applications, including extraction. Developing these green solvents is considered the most popular facet of green chemistry [29].

Various green solvents and their performance in the extraction process of different compounds are being explored today. ILs are one of the most noteworthy green solvents, as they sparked great interest among researchers due to their effectiveness in extracting bio-derived solvents such as polyphenols from *Polygonum cuspidatum* [30], tocols from crude palm oil [31], and bioactive phenolic compounds from the leaves of *Vitis vinifera* [32] for biopharmaceuticals, as plants contain a wide variety of compounds such as primary and secondary metabolites. These metabolites are extracted and studied, and one of the most adapted methods for this process is liquid–liquid extraction, formerly using toxic organic solvents, but recently, green solvents have been utilized due to the number of advantages they offer in the extraction of solvents from plants. ILs were found to have the ability to interact selectively with particular analytes. It can interact with polar or nonpolar compounds and prevent solvent loss since its vapor pressure is deemed negligible at room temperature [33]. However, a study found that the use of this solvent resulted in an inverse relationship between yield and concentration. This questions the economic feasibility of the method utilized; hence, the need for further investigation of the whole process, especially the extract and raffinate phases, as noted by the author [30]. The effectiveness and efficiency of ILs in the separation and recovery of earth elements using liquid–liquid extraction was also tested by extracting auric chloride [34], yttrium [35], and other rare earth elements [36,37]. Metal separation can be enhanced by using hydrophilic ionic liquids as builders or complexing agents [38]. With all the advantages mentioned above, other publications reported that ILs were found to be more expensive to synthesize and that there was a lack of studies regarding the effect on the environment considering the toxicity and life span of the solvent [39,40]. As articles and studies emerge about ILs, some are still questioning the 'greenness' of this solvent because of its poor ability to biodegrade, as well as its sustainability and biocompatibility [41].

With the constraints and disadvantages of ILS comes the DES, an ILs analog that also serves as an alternative to traditional solvents and ILs. DESs are a cheaper alternative for separating aromatics through liquid–liquid extraction with a higher selectivity and distribution ratio and an extraction efficiency of up to 82.83% in a single cycle. In comparison, five cycles would yield a 99.8% recovery [42]. DESs are used as an extractant for bioactive compounds from agricultural by-products and other natural sources. According to studies, DESs were found to have very low toxicity compared to conventional solvents, making them suitable for pharmaceutical and food processing industries [43]. In 2020, a method called dispersive liquid–liquid microextraction was established using a hydrophobic DES for folic acid to be analyzed in wheat flour samples.

The solvent was prepared by mixing methyltrioctylammonium chloride, which is the hydrogen bond acceptor, and amyl alcohol, which is the hydrogen donor. Small amounts of folic acid could be extracted accurately, quickly, and cheaply. This method also draws out the need for solvent removal, the need to use a strong acid or base, and low waste generation [44]. Detoxification of the wastewater from olive oil processing was carried out by liquid–liquid extraction using NaDES. The wastewater, which contained phenol, a highly toxic compound for humans, was extracted using different solvent concentrations. It separated the phenol from the solution while maintaining the water's neutral pH, proving its effectiveness. However, there were still gray areas and conjectures within the study regarding the pH dependence that requires further investigation before proving that the detoxification method is food-safe [45]. DESs were also used to extract pyrethroids from tea and fruit juices. Pyrethroids are organic compounds derived from chrysanthemum flowers in low concentrations. Pyrethroids are widely used in pest control and agriculture, hence the need for efficient extraction. They synthesized new DESs immiscible in water using hexafluoroisopropanol and L-carnitine/betaine. The results showed that 1:2 mol/mol of L-carnitine and HFIP provided the shortest extraction time, high recovery, and less consumption of the organic solvent, and proved that the DLLME with DES as a base was a highly efficient and reliable method in the extraction of pyrethroids from fruit juices and tea [46]. In 2015, DESs comprised of decanoic acid and ammonium salts were used in the extraction of volatile organic fatty acids from aqueous solutions [47], which was later followed by the removal of alkali and metal ions from water using hydrophobic DESs with decanoic acid-lidocaine as the base. It was found that the increase in the length of the carbon chain resulted in a higher efficiency, proving how efficient DESs are compared to conventional extractants [48].

Among the existing studies about green solvents in liquid–liquid extraction, the two most common methods are the aqueous biphasic system, aqueous two-phase systems (ATPS), and DLLE, or dispersive liquid–liquid extraction. ATPS is a technique in liquid–liquid fractionation known for its success in separating earth metals, sewage treatment, drug residues in food in veterinary practice, and many more [49]. Liquid biphasic systems that are ILs-based showed feasible and efficient techniques in separation for the extraction of different biomolecules derived from complex crude extracts [50], which is backed up by a study that analyzed the partitioning of proteins from ILs-based LBS comprised of citrate salts and lolilyte 221 PG, which was discovered to be a complex yet feasible extraction depending on the pH, ionic strength, nature of the targeted biomolecules, and the concentration of components that are phase-forming [51]. The ILs-based DLLME method is another method of liquid–liquid extraction. It is a known environmentally friendly sample preparation technique because of how simple, fast, and efficient this method is, as it consumes minimal amounts of reagents and solvents. Introduced in 2006 [52], this method has gained popularity in various fields such as engineering, medicine, agriculture, and pharmacology, among others. Despite its simplicity, it is known to be highly efficient in extraction; however, some faults were still pointed out by researchers, noting that there are restrictions regarding the extraction solvent and the requisites associated with the dispersive solvent [53]. Ionic liquids, up to this day, are still considered an effective microextraction technique, including DLLME.

5. Technological Advances and Process Optimization

In recent years, there have been notable technological advancements and process optimization strategies to enhance the efficiency of liquid–liquid extraction using green solvents. Traditional liquid–liquid extraction processes often rely on organic solvents that pose environmental and health risks. However, the development of green solvents, characterized by their sustainability and reduced ecological impact, has revolutionized the field. Technological innovations, such as novel solvent systems, advanced equipment, and optimization strategies to improve liquid–liquid extraction processes' efficiency, selectivity, and environmental sustainability, have accompanied this paradigm shift.

Green solvents have gained significant attention due to their environmentally friendly nature and potential for sustainable extraction processes. Several technological advances have emerged to enhance the efficiency and effectiveness of liquid–liquid extraction using green solvents.

One notable advancement is the development of novel green solvents tailored specifically for liquid–liquid extraction. Traditional solvents, such as chlorinated solvents and aromatic hydrocarbons, replace greener alternatives like ILs, SCFs, DESs, and bio-based solvents. These green solvents possess unique properties, such as low volatility, high selectivity, and biodegradability, making them suitable for various extraction applications. These solvents, such as those used in agricultural crops, are derived from raw materials and subsequently modified to reduce their environmental impact. They are widely used due to their proven sustainability and economic viability [7–9]. However, selecting an appropriate solvent for a given industrial application requires considering solubility, polarity, volatility, flammability, boiling point, and cost.

Furthermore, innovations in equipment and instrumentation have contributed to the optimization of liquid–liquid extraction processes. Microfluidic devices and continuous flow systems offer enhanced control over process parameters, including temperature, flow rates, and phase ratios [54]. These advancements improve efficiency, reduce solvent consumption, and precisely extract target compounds.

Process optimization strategies are another area of technological development currently being explored. The choice of solvent significantly influences the liquid–liquid extraction process, and there is a growing trend toward developing environmentally sound solvents that are optimized to enhance the compatibility between solute and solvent and improve the separation efficiency [55,56]. Optimization techniques, such as response surface methodology [57] and experimental design, facilitate the identification of optimal process conditions that lead to efficient extraction. Furthermore, the integration of hybrid techniques, including membrane extraction [58], supercritical fluid extraction [59], and reactive extraction [60], along with liquid–liquid extraction employing green solvents, serves to improve the efficiency and selectivity of the extraction process.

Modeling and simulation tools have also advanced, enabling predictive modeling of liquid–liquid extraction processes using green solvents. These tools assist in designing and optimizing extraction systems, facilitating process scale-up, and reducing experimental efforts. In [61], the researchers created coarse-grained models for imidazolium-based ILs, utilizing a novel approach to the Martini force field. This model could accurately replicate spatial heterogeneity and global densities across various temperatures. This presents the feasibility of conducting large-scale simulations of experiments involving liquid–liquid extraction.

On the other hand, a study on the interaction between different ionic liquids and the mixture of methyl tert-butyl ether (MTBE) and methanol in the context of MTBE production was conducted [62]. The researchers employed a combination of quantum chemistry and molecular dynamics (MD) simulations to investigate this interaction. The results showed that the MD simulations yielded similar results to the experimental data, indicating that MD simulations can predict extraction performance even without phase equilibrium data.

6. Future Outlook

Identifying future research directions and emerging trends and addressing challenges and limitations is crucial for advancing and broadening the adoption of green solvents in liquid–liquid extraction processes. As researchers continue exploring and optimizing green solvents' use, several vital aspects merit attention for future investigations.

While significant progress has been made in identifying and utilizing green solvents, there is still a need to discover and develop new solvents with enhanced extraction properties. Researchers may explore the synthesis of innovative green solvents and their characterization to expand the available options for liquid–liquid extraction.

Investigating the fundamental interactions between green solvents and target solutes is essential to optimizing liquid–liquid extraction processes. Future research may focus on interpreting the mechanisms of solute extraction, enabling a deeper understanding of how green solvents interact with specific solutes, and guiding the selection of appropriate solvents for different extraction conditions.

Continued efforts may be directed toward optimizing liquid–liquid extraction processes using green solvents. This includes exploring innovative process configurations, such as hybrid systems and intensified techniques, to enhance efficiency, selectivity, and overall performance. Integration with separation techniques other than membrane or supercritical fluid extraction can also lead to synergistic effects and improved extraction efficiency.

Green solvents for liquid–liquid extraction have primarily been studied at the laboratory scale. Future research may focus on scale-up considerations and bridging the gap between laboratory-scale experiments and industrial implementation. Understanding the scalability of green solvent-based extraction processes, addressing potential engineering challenges, and evaluating economic feasibility are vital for their implementation in industrial settings.

As green solvents gain prominence in liquid–liquid extraction, addressing safety considerations and ensuring regulatory compliance is crucial. Researchers may focus on assessing the potential hazards of green solvents, developing safety guidelines, and ensuring that the proposed solvents meet regulatory standards for their intended applications.

Advancing green solvents for liquid–liquid extraction requires collaboration between researchers from various disciplines, including chemistry, chemical engineering, environmental science, and sustainability. Collaboration between academia, industry, and policymakers is critical for knowledge sharing, technological advancements, and overcoming challenges related to implementation and commercialization.

In conclusion, future research in green solvents for liquid–liquid extraction may focus on developing novel green solvents, understanding solvent-solute interactions, optimizing and intensifying extraction processes, addressing scale-up considerations, ensuring safety and regulatory compliance, and fostering interdisciplinary collaboration. By addressing these aspects, researchers can contribute to developing sustainable and efficient liquid–liquid extraction processes using green solvents, enabling their broader application in diverse industrial sectors.

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