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Review

A short review on natural gas hydrate, kinetic hydrate inhibitors and inhibitor synergists☆

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ABSTRACT

Gas hydrate-caused pipeline plugging is an industrial nuisance for petroleum flow assurance that calls for technological innovations. Traditional thermodynamic inhibitors such as glycols and inorganic salts suffer from high dosing, environmental unfriendliness, corrosiveness, and economical burden. The development and use of kinetic hydrate inhibitors (KHIs), mostly polymeric compounds, with their inhibiting effects on hydrate nucleation and growth are considered an effective and economically viable chemical treatment for hydrate prevention. However, the actual performance of a KHI candidate is dependent on various factors including its chemical structure, molecular weight, spatial configuration, effective concentration, pressure and temperature, evaluation methods, use of other additives, etc. This review provides a short but systematic overview of the fundamentals of natural gas hydrates, the prevailing categories of polymeric kinetic hydrate inhibitors with proposed inhibition mechanisms, and the various synergists studied for boosting the KHI performance. Further research endeavors are in need to unveil the KHI working modes under different conditions. The conjunctive use of KHIs and synergists may facilitate the commercial application of effective KHIs to tackle the hydrate plugging problem in the oil and gas flow assurance practices.

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1. Introduction

Natural gas hydrates, down to the molecular level, are clathrate crystalline structures formed of natural gas components such as methane, ethane, propane and water molecules *via* weak intermolecular forces under high pressures and low temperatures [1]. Large amounts of *in-situ* gas hydrates exist in deep ocean and permafrost regions, while approximately 97% could be found in the submarine hydrate sediments [2–5]. Gas hydrates have drawn massive attention from both academy and industry for several reasons. First of all, explicitly, they represent a giant potential energy source for the coming decades, as even the most conservative estimation suggests that the amount of energy locked in hydrate form is twice that of all the other types of fossil fuels on the planet, combined [6]. Secondly, in a more implicit manner, gas hydrates pose challenge to our already fragile climate and environmental system, if large-scale, unexpected release of methane gas from hydrate reservoirs occurs [7–13]. Thirdly, there are quite a few promising engineering applications under research nowadays utilizing gas hydrate as a convenient

technology carrier. These include hydrate-based carbon capture and storage [14–16], seawater desalination [17–19], hydrogen storage [20–22], natural gas storage and transport [23–25] and even innovative air-conditioning systems [26]. When it comes to the realm of flow assurance in the petroleum industry, natural gas hydrates are not welcomed. They are deemed an industrial nuisance as oil and gas pipeline blockages due to hydrate formation may cause unexpected production stop and unbearable economical loss [27–28]. Therefore, the management strategies for the prevention and remediation of natural gas hydrates are challenging and crucial. Even in deep sea hydrate exploration practices, including trial production of natural gas from hydrate reservoirs, we will inevitably face the risk of hydrate reformation in the production pipeline due to the harsh subsea conditions of colder water, higher pressure and lower temperature.

There have been a few different methods for hydrate prevention and remediation in flow assurance. We could reduce the pressure or heat up the flow line to keep the system out of hydrate region. In many cases however, especially in deep sea environments, such methods may not be ideal or economical. Indeed, reducing pressure or supplying heat to treat the formed hydrates may even pose significant safety alarm, if inappropriate depressurization location or inaccurate temperature control is taken. The third common method for hydrate prevention and remediation is chemical treatment. Traditionally, thermodynamic hydrate inhibitors (THIs) such as methanol and mono ethylene glycol,

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and salts like sodium chloride and calcium chloride, are used in large quantities to shift the hydrate equilibrium curve towards hydrate-free region. However, high doses are required for THIs to properly perform. Take methanol or MEG for example, up to 20 wt%–60 wt% could be required for them to effectively behave as hydrate inhibitors. The use of alcohols and salts also faces challenges such as high volatility, the need of large storage capacities and recycling units, the strong corrosion to the pipe walls and not the least, the environmental hostility. In attempts to address these challenges and inconvenience, low dosage hydrate inhibitors (LDHIs) [29,30] have been intensively explored, including the two major categories of kinetic hydrate inhibitors (KHIs) and anti-agglomerants (AAs). They are usually dosed at much lower concentrations (less than 3.0 wt% active components), as compared to the much higher concentration required for THIs to perform. The industrial KHIs are mostly polymeric compounds, preventing hydrate formation by delaying the nucleation and/or growth of hydrate embryos. Typical AAs are surfactants developed to prevent the formed hydrate particles from aggregation, thus able to maintain the multiphase petroleum fluid flow. This work has put its emphasis on KHIs, its inhibition mechanisms, and the various synergists studied in order to boost the KHI performance.

The following sessions briefly review three topics in a consecutive manner: (1) a brief overview of gas hydrate fundamentals with proposed nucleation mechanisms; (2) the major types of KHIs studied nowadays, some of them commercial, and the proposed KHI mechanisms in the literature with evidence and support from experimental and computational studies; and (3) an overview of most studied KHI synergists. In the aim of developing successful offshore hydrate prevention strategies, it is essential to have fundamental understanding into gas hydrates, and conduct effective screening and evaluation of high performance hydrate inhibitors/synergists with exploration of the molecular mechanisms behind.

2. Natural Gas Hydrates

2.1. Hydrate structures and microscopic properties

A basic understanding of the molecular properties of natural gas hydrates in science is a prerequisite for developing high-efficiency hydrate inhibitors for practical applications. Depending on the type and size of the gas molecules, hydrates of natural gas components can manifest different crystalline structures. The most common gas hydrate structures are structures I, II, and H. The unit cell of each structure is illustrated in Fig. 1.

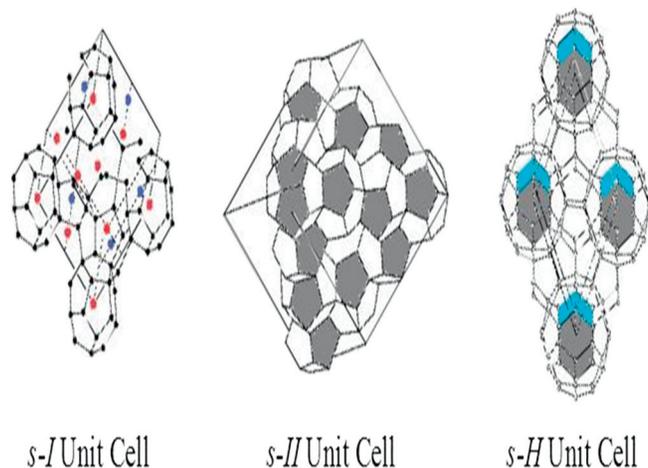


Fig. 1. Unit cells of common gas hydrate structures.

For example: A standard structure II unit cell consists of 16 pentagonal dodecahedron cages (5^{12}) and 8 hexakaidecahedron cages ($5^{12}6^4$); a water cage of $5^{12}6^4$, as the numbers indicate, possesses 12 pentagonal faces and 4 hexagonal faces. The number of water molecules in the unit cells of structures I, II, and H hydrate crystals as shown in Fig. 1 is 46, 136, and 34, respectively [1,28].

There are strict requirements on the size of the guest molecules for them to be properly fit into the water cages. In principle, natural gas molecules with a radius of larger than 1 nm are too giant to be encapsulated by even the largest water cage found in hydrate crystalline structures. To be more precise, gas molecules including methane, ethane, carbon dioxide, and hydrogen sulfide have diameters of 0.42–0.6 nm, and are able to form s-I hydrate. Larger guests including propane or iso-butane with a diameter of 0.6–0.7 nm, form s-II hydrate. Intriguingly, smaller gas molecules including nitrogen and hydrogen with a diameter of less than 0.42 nm also form s-II hydrate. One may wonder why this would happen. A plausible explanation could be that the number of smaller 5^{12} cages in s-II is about three times that in s-I, per unit volume [28]. Therefore, choosing to form s-II instead of s-I for smaller molecules may have contributed to a promoted overall structural stability. There is not always a fixed structure for a specific gas component to fit into. An example could be cyclopentane (C_5H_{10}). Cyclopentane forms either s-I or s-II hydrate, depending on the given conditions [28]. Also, hydrates formed of methane and ethane mixtures, may shift the structure between s-I and s-II, as a function of the varying methane and ethane proportions [31,32]. Still larger gas molecules such as cycloheptane or neohexane with a diameter of 0.7–0.98 nm could only form s-H hydrate, provided that a smaller helper gas such as methane or nitrogen is present to fit in the smaller cavities.

From a molecular mechanics viewpoint, it is worth noticing that hydrate structures are held stable by a set of weak van der Waals forces, *i.e.* the intermolecular repulsive and attractive forces. That is to say, no chemical bonds or other strong forces exist between the gas and water molecules. This differentiates gas hydrates from other crystalline structures (such as inorganic salts) that are chemical compounds *via* covalent bonds. The dominating weak intermolecular force that holds hydrate structures is the London dispersion force [33] existing between molecules without permanent dipoles. It occurs when electrons of two adjacent atoms take positions that induce temporary dipoles for temporary attractions. This is the case for gas hydrates as the guests entrapped in the water cages are typically non-polar natural gas molecules. For example, the dispersion force constitutes up to 87% of the total interactive energy between the molecular pair of methane and water [34]. Fig. 2 is an illustration of the intermolecular dispersion force.

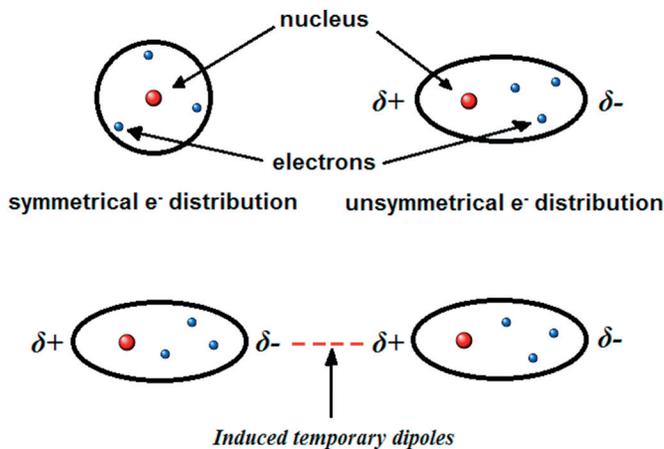


Fig. 2. Illustration of the dominating dispersion force that holds gas hydrate structures stable.

2.2. Hydrate equilibrium and phase diagram in thermodynamics

Fig. 3 is an illustrative graph showing hydrate-free, meta-stable, and hydrate regions in association to thermodynamics. In Fig. 3, the blue line is the hydrate equilibrium curve and the red line is the spinodal curve. The system is superheated in hydrate-free region (e.g. point A), thus no hydrate will form. The metastable region will be crossed at point B. A metastable region refers to a thermodynamic range within which the spontaneous crystallization is improbable unless one adds crystal seeds into the reactor. The free Gibbs energy of a metastable system is unlikely sufficient to produce critical-sized nuclei. The spinodal line stands for the limit of the thermodynamic metastability. Crossing the spinodal line at point C with further increased supersaturation level may lead to spontaneous crystallization, and the probability of nucleation would increase when the system condition approaches point C. Because of the low probability of nucleation with its stochastic nature in the metastable region, it is difficult to quantitatively determine the transition between the metastable region and the labile region to the left of the spinodal line. The hatched region along the spinodal line is an indication of this uncertainty. Nevertheless, plausible experimental and theoretical trials have been conducted in batch and loop experiments to detect phase boundaries for quantifying risk maps for hydrate formation in dispersed oil–water and oil-dominant systems [35,36]. As the stochastic nature of hydrate nucleation suggests, neither the start of an individual nucleation event nor the amount of nuclei that would form within a certain period of time could be predicted.

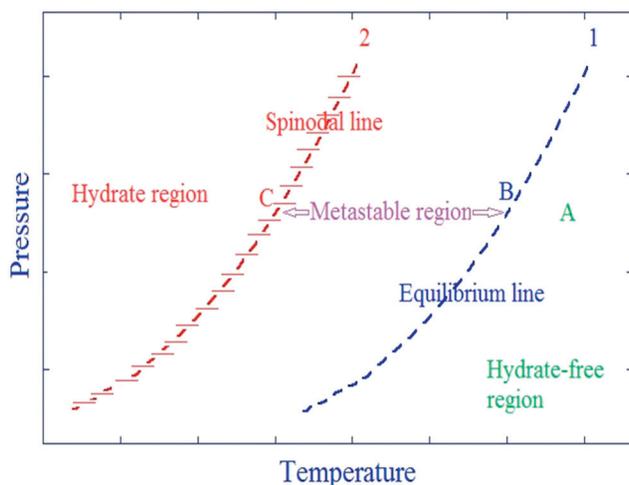


Fig. 3. An illustrative diagram showing hydrate-free, metastable and hydrate regions in thermodynamics.

2.3. Hydrate nucleation mechanism hypotheses

Scientifically wise, the nucleation mechanism of hydrate crystallization is not yet fully understood. Dissolved gas molecules and the surrounding water molecules form metastable clusters or initial embryos that continuously emerge and shrink in the presence of mass and concentration fluctuations. In the end, only part of the nuclei that manage to reach a critical size are able to sustain their growth and guide the system into post-nucleation or growth stage. There is however no strict boundary between hydrate nucleation and the initial growth, as both events take place at the molecular level, hardly practical for precise *in-situ*, real time observations.

Table 1 summarizes the four major hypotheses each with a postulated nucleation process proposed for explaining the molecular mechanism of hydrate nucleation. These include the labile cluster nucleation

Table 1

Major hypotheses proposed in the literature for hydrate nucleation

| Nucleation hypotheses | Controlling factor(s) | Postulated mechanism/process |
|---|------------------------|--|
| 1. Labile cluster nucleation [37,38] | Water | Water + dissolved gas → labile clusters → critical size reached → sustained nucleation |
| 2. Local structuring nucleation [39] | Dissolved gas | Gas re-configuration → perturbation → local structuring → rearrangement into nuclei |
| 3. Gas interfacial nucleation [40,41] | Vapor–liquid interface | Gas transport → liquid surface adsorption → docking → anchoring for nucleation |
| 4. Blob-amorphous clathrate nucleation [42] | Water, dissolved gas | Solution → blobs formation → amorphous clathrate → hydrate crystals |

hypothesis [37,38] by Sloan and his co-workers, the local structuring nucleation hypothesis [39] by Radhakrishnan and Trout, the gas interfacial nucleation hypothesis [40,41] by Long and Kvamme, and the most recent blob-amorphous clathrate nucleation hypothesis [42] by Jacobson *et al.* There is barely a consensus achieved among the hydrate community. Multi-scale experimental investigations with improved monitoring techniques and advanced molecular dynamics (MD) simulations are required to further reveal the molecular mechanisms of hydrate nucleation.

In the consecutive growth stage, catastrophic hydrate growth indicated by a sudden pressure drop and rapid gas consumption is usually observed in laboratory experiments. Unlike hydrate nucleation which is a statistically random process, hydrate growth behavior is more predictable and rather repeatable with experimental measurements.

2.4. Site of hydrate formation

Depending on the specific experimental setup and conditions, lab-scale experiments and MD simulations performed so far have suggested several different locations that initial nucleation and subsequent growth might take place. These could be the vapor–liquid interface, the cell wall, or the bulk liquid phase. With our current knowledge, it can be stated that the initial hydrate nucleation and growth has a higher tendency to occur at the water–hydrocarbon (*i.e.* hydrate former) interface. Several experimental and computational proofs upon this could be found. Long and Sloan [43] with their studies on hydrates of carbon dioxide and natural gas in a sapphire cell found that the hydrate formation was triggered at the water–gas interface. The studies of Fujioka *et al.* [44] on liquid CO₂ hydrate formed in water showed that CO₂ dissolution and hydrate formation were to a large extent controlled by the development of a thin hydrate film at the liquid CO₂–water interface. In addition, the MD simulations performed on methane hydrate formation by Moon *et al.* [45] witnessed hydrate nucleation and initial growth at the methane–water interface. From a mass transfer point of view, it is understandable to have these agreed experimental and computational observations on the location of initial hydrate formation. The solubility of common natural gas components in water is understandably low, so is the water concentration in the surrounding phase of hydrate former. Consequently, a significant concentration gradient for either phase co-exists at the interface between water and the hydrate former. Though less likely to have initial critical nuclei form in the bulk phase, the presence of physical agitation could effectively disturb the system and disperse the initially formed hydrate embryos from the interface into the water phase, therein facilitating hydrate nucleation and growth in the bulk phase as well.

With the above understanding of the microscopic properties, thermodynamics and phase diagram, probable nucleation mechanisms and locations of hydrate formation, it is time to bring in the polymeric kinetic hydrate inhibitors, with a close look at the role they play in hydrate prevention.

3. Kinetic Hydrate Inhibitors

3.1. Types of KHIs

KHIs, mostly high molecular weight polymeric compounds, have been the hotspot in hydrate research in the last few decades [46]. Various KHI candidates have been synthesized and evaluated for their inhibition performance upon gas hydrates, in laboratory scale and in field applications [29,46]. The industry-oriented KHIs are classified into the following three main categories. Derivatives such as copolymers or grafted polymers are often synthesized as well to explore their KHI potentials. They may exist in either liquid or solid form for shelf storage, but need to be dissolved or diluted to a suitable concentration and get into the multiphase fluid system to properly perform.

3.1.1. Poly-N-vinyl lactam polymers

A major type of polymeric KHIs, compounds of this category have typical lactam rings. Examples are five-ring polyvinylpyrrolidone (PVP) [47], six-ring polyvinylpiperidone (PVPip) [48], seven-ring polyvinylcaprolactam (PVCap) [49], and eight-ring polyvinylazacyclooctanone (PVACO) [50]. Among these, PVP and PVCap are commercial products while PVPip and PVACO are not. A common experience is that an increased lactam ring size would enhance the KHI performance [48,50]. Nevertheless, it is worth mentioning that their actual performance is highly sensitive to PT conditions. For instance, at higher driving forces, PVP appears to have no effect during hydrate nucleation, but eventually bring an inhibiting effect on the crystal growth [51,52].

VCap is the most used monomer for producing VCap-based polymers and co-polymers as commercial KHIs. One VCap-based KHI product readily available on the market is the Luvicap series from BASF where PVCap is the effective component dissolved in mono ethylene glycol. Other commercial products include also co-polymers of VP, VCap and other monomers. For example, Inhibex 501 from Ashland is a 1:1 copolymer of VP/VCap; PVP-VA73 is a copolymer of VP/VC; and VC-713 is a copolymer of VP/VCap/DMAM. Table 2 presents these selected, representative examples of KHIs in this category with information of their polymeric structures, molecular weight, and solvent and concentration if in liquid form.

3.1.2. Hyper-branched polyesteramides

Structure of a representative hyper-branched polyesteramide [53] evaluated as a KHI is shown in Fig. 4.

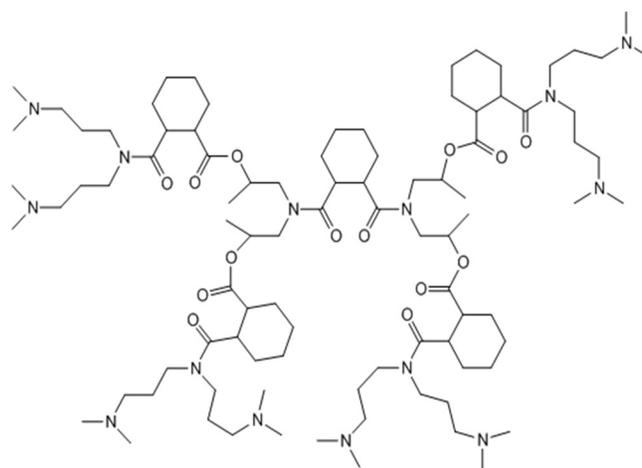


Fig. 4. A hyper-branched poly(esteramide) structure as a KHI candidate.

As shown in Fig. 4, the level of hydrophilicity could be adjusted by modifying the end tips of such structures [46]. It is claimed to have a better performance than the VCap-based polymers on structure-I hydrates [30]. However, since the type of hydrate structure usually formed during oil and gas transport is s-II instead of s-I, the actual field performance of hyper-branched polyesteramide remains unknown and may need to be tested on site.

3.1.3. Isopropylmethacrylamide (IPMA) polymers

This category of polymeric KHIs and their copolymers has also been widely studied. Fig. 5 shows the structure of poly(isopropylmethacrylamide) [54]. IPMA copolymers [55] have improved their tolerance to saline environments with higher cloud points. VCap polymers and polyesteramides with good tolerance to saline are also under continuous development. This is considered a new criteria of KHI design adapted to the corresponding requirements of nowadays petroleum industry.

3.1.4. Other polymeric KHIs

Other polymer-based KHIs include polyalkyloxazolines [56,57] and pyroglutamate polymers, while the latter have been commercialized and used in a few field applications [58,59]. Also, polymaleimides [60], maleic copolymers and alkylamide derivatives [61], polyaspartamides

Table 2

A few selected commercialized poly-N-vinyl lactam polymer and co-polymer samples

| Polymeric KHI | Chemical structure | Molecular weight | Solvent | Concentration |
|------------------------|--------------------|------------------|-------------|---------------|
| PVP (K-15, K-17, etc.) | | 5000–16000 | (powders) | / |
| Luvicap EG | | 2000 | MEG | 40 wt% |
| Inhibex 501 | | 5000–8000 | Butylglycol | 50 wt% |
| PVP-VA73 | | 38000–40000 | (Powders) | / |
| VC-713 | | 82700 | Ethanol | 37.5 wt% |

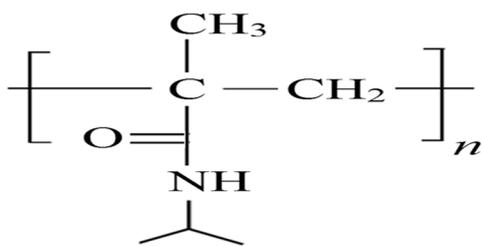


Fig. 5. Structure of an isopropylmethacrylamide (IPMA) polymer as a KHI candidate.

[62–64], polyallylamides [65], proteins, modified starch and starch derivatives [66,67] have been tested as potential KHI candidates. Recently, studies on sodium chloride, a traditional thermodynamic hydrate inhibitor, reported that it could inhibit hydrate formation in porous media [68]. In this study, only the growth rate of hydrate formation was observed to have a decline, and no effect on the nucleation induction time has been demonstrated. It is however important to conduct research on hydrate formation and dissociation in porous media for the uniqueness it has and insights it can provide. One thought behind this is the exploitation of hydrate for natural gas resource that would take place in the hydrate sediments beneath the permafrost or the deep ocean, and the *in-situ* hydrate dissociation due to pressure reduction or injection of inhibitor chemicals.

Another type of KHI candidate that is gaining increasing interest nowadays is the anti-freeze Proteins (AFPs)—also called Ice-structuring Proteins (ISPs), due to their green aspect. KHI candidates of this category are usually extracted from organisms such as fish, insects, or plants surviving in cold environments [69–75]. Walker *et al.* [76] presented an up-to-date review of studies on AFPs as potential, environmentally friendly KHIs.

Comprehensive reviews by Kelland [29–30,46] documented in details the KHI polymer chemistry, molecular structures, functional groups, organic synthesis, and the history of development. Readers of further interest are encouraged to refer to these profound reviews. In principle, the basic idea for developing a potential KHI is to create an appropriate combination of hydrophobic and hydrophilic groups in a way that the water phase could be effectively disturbed while the polymer maintains water soluble. This could be seen as the rule-of-thumb for the design of effective KHIs. The first generation KHI, the polyvinylpyrrolidone (PVP), is an acceptable trial of this. The PVP molecules are synthesized by connecting the hydrophilic amide group that sits on the lactam ring with the hydrophobic carbon chain [47].

The polymeric KHIs could be divided into several categories based on the different functional groups in their chemical structures [30,77]. At the moment, water-soluble polymeric compounds are the prevailing type of KHI extensively studied. They are expected to partly or fully replace methanol, glycol and salts in the oil and gas industry for hydrate prevention. When dissolved in the bulk liquid phase, these polymers could prolong the induction time of hydrate nucleation, reduce the nucleation rate or the initial growth rate, therein preventing hydrate formation in the pipe under a certain level of subcooling for a certain time length. The inhibition performance of a KHI chemistry upon gas hydrate formation, in terms of subcooling suppression, is highly related not only to the polymer structure, spatial configuration, molecular weight or effective concentration, but also to factors including the nucleation mechanism and growth pattern of the specific hydrate forming system, the pressure and temperature conditions of the multiphase mixture, the degree of subcooling, the applied stirring rate and cooling rate, *etc.* [78–83]. From what we see at this moment, early generation KHIs including PVP and PVCap suffer from their general inhibition performance. Meanwhile, the commercial KHIs available on the market including the Inhibex and Luvicap series may see an overestimation of their performance once transferred from laboratory results to petroleum practices. Caution has to be taken that the experimental evaluations

may not be a guarantee for these KHIs to be safely applied in the deep-water oil and gas exploration and transportation. Significant enhancement on the inhibition power *via* synthesis of new polymer chemistry or the use of salts and other smaller molecules as KHI synergists is yet to be explored. More about synergists is provided in Section 4: Use of KHI synergists.

3.2. Proposed KHI mechanism hypotheses

KHI studies in the literature have so far ascribed the performance of KHIs to different mechanisms. There is no consensus yet on the inhibition mechanism in hydrate community, but only hypotheses. The major inhibition mechanism hypotheses proposed for KHIs upon hydrate nucleation and/or growth and relevant experimental/computational evidences are provided in Table 3, with brief explanations to each provided in the followed subsections.

3.2.1. Adsorption–inhibition mechanism hypothesis

The adsorption–inhibition mechanism assumes that the polymeric KHI molecules would adsorb onto the surface of clustering embryos; thus, hydrate nucleation cannot continue. The mechanism is supported by several experimental investigations, among others: studies on the effect of PVP by Posteraro *et al.* [52] on s-I methane hydrate formation; studies on the effects of PVP and PVCap by Sharifi *et al.* [85] on s-II methane-ethane-propane hydrate; and studies on the effects of Gaffix-VC713/Luvicap-EG/PVP/PEO-VCap by Rojas González [86] on s-II hydrate of natural gas mixture. These works suggested that the retarded gas incorporation and hydrate nucleation was probably due to polymer binding to the hydrate lattices.

MD simulations by Anderson *et al.* [88] on methane hydrate formation in the presence of PVP and PVCap also indicated the adsorption–inhibition mechanism. However, it is difficult to quantify how close a specific type of KHI polymer chain stands from or sits onto the hydrate lattices, and how strong the adsorption/binding would be.

3.2.2. Perturbation–inhibition mechanism hypothesis

The perturbation–inhibition mechanism assumes that the dissolved KHI molecules could effectively perturb the water phase to prevent water molecules from gathering and forming complete cages. That is to say, the presence of polymer chains would only allow the emergence of incomplete water cavities which is insufficient to form hydrate nuclei. Support from experiments includes studies on the effects of PVP and PVCap by Varma-Nair *et al.* [95] on s-II methane–propane hydrate formation; studies on effect of PVP by Talaghat [103] on s-I (methane/carbon dioxide) and s-II (propane/isobutane) hydrate formation; and studies on the effect of PVCap by Villano *et al.* [94] on s-II synthetic natural gas (SNG) hydrate. The study of hydrate inhibition from Sa *et al.* [91] by adding trace amount amino acids into the system provides a more recent experimental evidence. Their results suggest that the amino acid molecules dissolved in water could change the water structure, rendering it incompatible for a transition to crystalline hydrate structures. However, without precise *in-situ* observation or monitoring techniques, what is really happening at the molecular level remains unknown.

There are also MD simulations with results in favor of this hypothesis. A representative work is from Kvamme *et al.* [96] where their MD simulations showed that PVP and PVCap in lack of direct contact with the hydrate particles could still trigger the dissociation of s-I and s-II hydrate. This gives a strong indication that the work mode of perturbation–inhibition with polymeric KHIs is highly probable. Less explicitly, the simulation work by Hawtin and Rodger [97] on methane hydrate formation in the presence of an effective KHI component, poly(dimethylaminoethylmethacrylate), PDMAEMA gave inspiring support to the water perturbation mechanism. Their work showed that with helical conformations the polymers at the water–gas interface are more effectively interacting with the water layer. The simulations

Table 3

Major inhibition hypotheses proposed for polymeric KHIs in the literature with evidences. EXP—experimental investigations; MD—molecular dynamics simulations.

| Nr. study | Hydrate former | Hydrate structure | Examined KHIs | Type of evidence | Reference |
|---|---|-------------------|---|------------------|-----------------------------------|
| I. Adsorption-inhibition mechanism (AIM): | | | | | |
| Polymers adsorb on the nucleus surface, preventing it from gaining critical size. | | | | | |
| 1 | C1 | I | PVP | EXP | Posteraro <i>et al.</i> [52] |
| 2 | C1 | I | PVP | EXP | Ivall <i>et al.</i> [84] |
| 3 | C1–C2–C3 | II | PVP/PVCap | EXP | Sharifi <i>et al.</i> [85] |
| 4 | C1–C2–C3–C4–i–C4–C5–neo–C5–i–C5–C6–C7–C8–C9–N ₂ –CO ₂ | II | Gaffix-VC713/Luvicap-EG/PVP/PEO-VCap | EXP | Rojas González [86] |
| 5 | C1–C2 | I–II | PVCap | EXP | Ohno <i>et al.</i> [87] |
| 6 | C1 | I | PVP/PVCap/ <i>N</i> -vinylacetamide (VIMA) | MD | Anderson <i>et al.</i> [88] |
| 7 | C1 | I | PVCap/VC-713 | MD | Kvamme and Åsnes [89] |
| 8 | C1 | I | VP/vinylvalerolactam (Vval)/ <i>L</i> -proline/1-formylpyrrolidine/DMAEMA | MD | Cómez Gualdrón <i>et al.</i> [90] |
| II. Perturbation-inhibition mechanism (PIM): | | | | | |
| Perturbing the water phase, preventing the formation of nuclei therein. | | | | | |
| 9 | CO ₂ | I | Amino acids (alanine/aspartic acid/asparagine/phenylalanine/histidine) | EXP | Sa <i>et al.</i> [91] |
| 10 | C1–C2–C3–C4–i–C4–N ₂ –CO ₂ | II | Alkyl-vinylformamide Polymers | EXP | Kelland <i>et al.</i> [92] |
| 11 | C1 | I | Morpholine | EXP | Park <i>et al.</i> [93] |
| 12 | C1–C2–C3–C4–i–C4–N ₂ –CO ₂ | II | Luvicap 55W/Poly(<i>N,N</i> -dialkylacrylamide)s/poly(<i>N,N</i> -dimethylacrylamide)s (PDMAA)s | EXP | Villano <i>et al.</i> [94] |
| 13 | C1–C3 | II | PVP/PVCap/poly(diethyl acrylamide) (PDEAM)/poly [<i>N</i> -3-sulfo-propyl)- <i>N</i> -methacryloyl-oxyethyl- <i>N,N</i> -dimethyl ammonium betaine] (PSPE) | EXP | Varma-Nair <i>et al.</i> [95] |
| 14 | C1; C3; CFC13 | I; II | PVP/PVCap/Modified PVCap/VC-713 | MD | Kvamme <i>et al.</i> [96] |
| 15 | C1 | I | Poly(dimethylaminoethylmethacrylate (PDMAEMA) | MD | Hawtin and Rodger [97] |
| 16 | C1 | I | PVP/PVP-A/PVP-E | MD | Li <i>et al.</i> [98] |
| III. Crystal growth-inhibition mechanism (CGIM): | | | | | |
| Blocking the growing crystals and covering the surfaces to prevent further crystal growth. | | | | | |
| 17 | C1–C2–N ₂ –CO ₂ | II | PVCap/PVPC/VVA | EXP | Zhao <i>et al.</i> [99] |
| 18 | C1–C3 | II | Industrial KHIs | EXP | Glénat <i>et al.</i> [100] |
| 19 | C1–C2–C3–C4–i–C4–i–C5–N ₂ –CO ₂ | II | PVCap | EXP | McNamee [101] |
| IV. Nucleation site interference-inhibition mechanism (NSIM): | | | | | |
| Covering and interfering with the suitable nucleation sites to prevent nuclei formation from there. | | | | | |
| 20 | C1; C1–C2 | I | Chitosan | EXP | Xu <i>et al.</i> [102] |
| 21 | C1; C1–C2; C1–C3 | I; II | Cationic starches | EXP | Lee <i>et al.</i> [67] |

suggest that the increased interaction can be mostly attributed to the nitrogen groups sitting on the side-chain of the inhibitor molecules. Such observations are in consistent with results from more recent MD simulations by Li *et al.* [98] on the growth inhibition performance of PVP and variant polymers (PVP-A, PVP-E) on methane hydrate. The work by Li *et al.* showed that the binding interactions between the examined KHIs and liquid water molecules largely determines their inhibition performance. More specifically, the strong binding effect of KHIs greatly disrupts the hydrogen bonding connections between the water molecules around the newly forming hydrate nuclei thereby preventing water to form more clathrate cages, without which a nucleus would be unable to reach the critical size for self-sustainable growth. These MD studies together offered insightful knowledge on the interactions among KHI molecules, water molecules and initially growing hydrate nucleus. Simulations of longer time scale (at microseconds level or better) and increased system complexity with a variety of compound spatial configurations would be of great help to further unveil the molecular mechanisms of KHI inhibition and offer practical guides for synthesis and screening of more effective inhibitors.

3.2.3. Crystal growth inhibition mechanism hypothesis

The crystal growth inhibition mechanism takes the adsorption-inhibition mechanism one step further into the stage of hydrate growth. It assumes that the presence of KHIs would inhibit specifically the process between the initially slow and followed fast growth period after hydrate onset [104]. Klomp *et al.* [105] argued that during crystal growth, the chain structures of KHI polymers would fit in and partly

cover the already formed crystal lattices (also called a “lattice fit”). Subsequently, the crystal morphology would be altered and the rate of crystal growth reduced. The larger surface area the polymers manage to cover, the more efficient its performance as a hydrate growth inhibitor will be.

The studies by Zhao *et al.* [99] on the effects of PVCap/PVPC/VVA on s-II hydrate of methane–ethane–N₂–CO₂ mixture seem to have supportive results to crystal growth inhibition. The question is that they also included bentonite in their studies, which was able to suppress hydrate nucleation. It is then difficult to separate the nucleation inhibition effect of bentonite from the nucleation/growth inhibiting effect of the tested KHIs. Glénat *et al.* [100] studied the formation and inhibition of s-II methane–propane hydrate. While they did observe the growth inhibition in the presence of VCap polymers, their hydrate growth experiments could not prove that the crystal growth inhibition is the only answer to the observed results. In a similar manner, there are studies by McNamee [101] on the effect of PVCap on s-II hydrate of synthesized natural gas mixture. The point is that there is no reason to associate this crystal growth inhibition mechanism only to the post-nucleation stage.

3.2.4. Nucleation site interference–inhibition mechanism hypothesis

In addition to the three major hypotheses mentioned above, a less popular mechanism theory for polymeric KHIs proposed in the literature is the nucleation site interference–inhibition mechanism. Support came from Lee *et al.* [67] when they studied cationic starches on s-I hydrates of methane, methane–ethane mixture, and s-II hydrate of methane–propane mixture; and also from Xu *et al.* [102] when they

studied the effect of chitosans on s-I hydrates of methane and methane-ethane mixture. The main idea is that the polymer chains may cover or interfere with the suitable nucleation sites to prevent *in situ* formation of nuclei from there. Strictly speaking, even we assume that is truly how the tested KHIs work, their actual performance would be in doubt, especially in the complicated multiphase fluid flow in the pipeline. In the real systems, the fluid is in contact with the pipe wall and impurities contained in the system, presenting numerous nucleation sites that are impractical to be interfered by polymers achieving a full coverage.

To sum up, the above hypotheses proposed in attempt to clarify the inhibition mechanism of KHIs indicate that we do not possess full knowledge of how KHIs work during hydrate nucleation and growth. It is important to bear in mind that the polymer chains may have an effect on either nucleation or growth stage, and very often they do intervene and delay the two stages simultaneously [106,107]. Interestingly, once hydrates have formed, it is also probable that certain KHIs may enhance the stability of the formed hydrate, causing unusually slow dissociation [108]. KHI performance may depend largely and comprehensively on its type, molecular size, spatial configuration, and physiochemical properties relative to the water, gas, hydrate phases, and the presence of other petroleum chemicals injected in the fluid system. More efforts from both experimental studies and computational simulations are required to enhance our understanding of KHIs and their working mechanisms. Readers conducting systematic KHI studies and performance evaluation are advised to go through several recent reviews by Ke and Kelland [77], and Shahnazar *et al.* [109], where the prevailing experimental methods, monitoring techniques, structures and mechanisms in KHI research are provided and their advantages and disadvantages compared.

4. Use of KHI Synergists

To maximize KHI performance by extending their subcooling suppression power, massive efforts have been directed into search for effective synergists for different KHIs in various hydrate forming systems. The three most studied types of synergists are quaternary ammonium salts, glycol ether compounds, and polyethylene oxide (PEO). Table 4 is a summary of these synergists in the literature, their chemistry, KHIs to assist and the studied hydrate system.

4.1. Ammonium and phosphonium salts

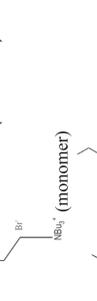
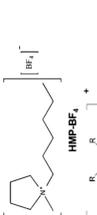
Quaternary ammonium ionic liquid salts (QALs) have been tested widely and known to be synergists for KHI polymers such as PVCap. Kelland and his co-workers have synthesized a series of bromide salts and studied their performance as KHI synergists. Two quaternary ammonium salts with *t*-heptyl groups they synthesized, *i.e.* Tris(*t*-heptyl)PeAB and Tris(*t*-heptyl)PrAB [110] proved to be outstanding crystal growth inhibitors to structure II tetrahydrofuran hydrates. Their observations showed that the THF hydrate growth nearly stopped at an additive concentration of 0.2 wt% and was fully suppressed when Tris(*t*-heptyl)PeAB or Tris(*t*-heptyl)PrAB was dosed at 0.4 wt%. In addition, these two salts showed excellent synergistic effects when blended with PVCap at a concentration of 0.25 wt% to inhibit the formation of structure II natural gas hydrates, with no pressure drop observed in their performed experiments. The results were indeed very optimistic, especially considering the fact that one of the salts, tris(*t*-heptyl)PeAB, has rather limited solubility in water. However, we must be aware that such synergism to PVCap was reported in the presence of a liquid hydrocarbon phase, decane, up to 20% that they purposely added to the high-pressure autoclaves to help dissolve the sparingly soluble tris(*t*-heptyl)PeAB. This was omitted when conducting THF hydrate experiments as tetrahydrofuran itself is a strong organic solvent. Their followed-up work on Tris(*t*-heptyl)PeAB and Tris(*t*-heptyl)PrAB [111] further confirmed the excellent synergy with PVCap in oil-based systems. An important indication from their work is that these sparingly water-soluble but oil-soluble *tert*-heptylated quaternary ammonium salts, when designed with correct

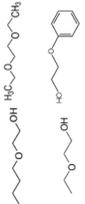
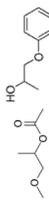
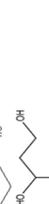
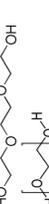
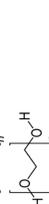
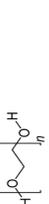
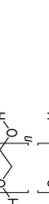
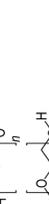
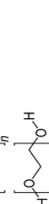
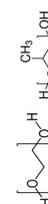
functional groups, can still be good synergists to commercial KHI polymers such as PVCap. Kelland's group also reported tetra(iso-hexyl)-ammonium bromide (TiHexAB) [112], *N*-(4-fluorobutyl)-*N,N*-dipentylpentan-1-aminium bromide [114], poly-tributylammonium ethylacrylate bromide (PTBAEABr) [115] and hexabutylguanidinium bromide [119] as synergists to PVCap to inhibit sII hydrate formation. As in their studies of PTBAEABr, it was found that *B*-vinyl lactam polymers incorporating the synergistic functional group did not outperform the polymer blend with the synergist molecules added. Sefidroodi *et al.* [113] found that tetrabutylammonium bromide (TBAB) and tetrapentylammonium bromide (TPAB) showed obvious synergistic effects to Luvicap EG on sII hydrate. But again, PTBAEABr demonstrated a better synergism than TBAB when blended with PVCap, while the latter is the main effective component in Luvicap EG. From the results in these synergist studies one may postulate that the more hydrophobic bromide salts including TiHexAB, THexAB, TiPAB, and TiHepAB are able to perturb the free water structures more effectively than the less hydrophobic TBAB, and thus hinder the nucleation process to a larger extent. It also suggests that water perturbation could be an equal, if not more important than the surface adsorption mechanism, for the synergist molecules to conjunctively perform with the corresponding KHIs.

Lee *et al.* [117] examined a series of ionic liquids containing tetrafluoroborate (BF_4^-) in conjunctive use with polyvinylcaprolactam and tested the inhibition performance of varied mixtures upon natural gas hydrate formation. The mixed recipes outperformed PVCap when the latter was dosed alone, and one of the best ionic liquid they identified, the 1-hexyl-1-methylpyrrolidinium tetrafluoroborate (HMP- BF_4) exhibited inhibition performance when used alone. They postulated the significant synergetic effect of the tested ILs may arise from their preventing the incorporation process of methane molecules into the smaller 5^{12} cages. No sufficient proof regarding the cage occupancy was provided. MD simulations may help examine whether this hypothesis makes sense. Lee *et al.* [118] extended their research using the same synergist HMP- BF_4 with PVCap by adding 3.5 wt% NaCl brine and mineral oil in the system to mimic the real operating conditions. First of all, it is unclear why they did not take the optimum KHI-synergist recipe (1.0 wt% PVCap + 0.5 wt% HMP- BF_4) identified in their previous work as the starting point in this followed study. They used a less effective recipe of 0.5 wt% PVCap + 0.5 wt% HMP- BF_4 instead. Secondly, they observed an unexpected trend of KHI performance that longer induction times were measured at higher water cuts. They claimed that this was due to a dilution of hydrate nuclei that was previous concentrated in the water droplets in the oil phase and now dispersed in the bulk water phase with increased water cut. The statement seems quite arbitrary. First of all, they have not monitored the nuclei concentrations in the water phase or the trend of its variation with increasing water cut. Moreover, the onset of hydrate nucleation is not merely affected by nuclei concentration, but probably and more importantly, decided by the stationary nucleation rate and the time point when critical-sized nuclei have emerged and crossed over the free energy barrier, which eventually makes the continuous growth of hydrate crystals possible.

Magnusson and Kelland [116] showed that Tetraalkyl-phosphonium-bromide salts such as (*n*-Bu) $_4$ PBr and (*n*-Pe) $_4$ PBr are synergists to Luvicap EG, Luvicap 55 W and Inhibex 713 when applied to sII hydrate. (*n*-Pe) $_4$ PBr demonstrated better synergistic effect than (*n*-Bu) $_4$ PBr and a 29:1 synergist-KHI ratio was found to be optimal. This specific ratio they found poses another question on the structure-performance relationship. That is, would varied KHI-synergist ratios cause the spatial configurations to significantly change with varying grid interactions of polymers and smaller synergist molecules? The work by Lee *et al.* [117] also reported optimum KHI-synergist ratios. The highest performance was observed with PVCap/HMP- BF_4 dosed at 1.0 wt% and 0.5 wt% respectively, while a further increase of the synergist to 1.0 wt% gave slightly worse inhibition power. No clear explanation was given about this. The issue of ideal KHI-synergist ratio might be solved with further, systematic

Table 4
Synergists most studied for the enhancement of KHIs performance

| Synergist | Chemical formula | KHI | Hydrate former | Hydrate structure | Reference |
|---|---|--|---|-------------------|---|
| Tris(<i>t</i> -heptyl)- <i>N</i> -propyl-1-ammonium bromide/Tris(<i>t</i> -heptyl)- <i>N</i> -pentyl-1-ammonium bromide |  | PVCap | Tetrahydrofuran (THF); C1-C2-C3-C4-i-C4-N ₂ -CO ₂ | II | Mady and Kelland [110,111] |
| Tetra(iso-hexyl)- ammonium Bromide |  | PVCap | C1-C2-C3-C4-i-C4-N ₂ -CO ₂ | II | Chua and Kelland [112] |
| Tetraethylammonium bromide (TEAB)/Tetrapentylammonium bromide (TPAB) |  | Luvicap EG | C1-C2-C3-C4-i-C4-N ₂ -CO ₂ | II | Sefidroodi et al. [113] |
| 4-fluorobutyl-dipentylpentan-1-/bis(4-fluorobutyl)-pentylpentan-/tris(4-fluorobutyl) pentan-1-aminium bromides |  | PVCap | THF; C1-C2-C3-C4-i-C4-N ₂ -CO ₂ | II | Mady and Kelland [114] |
| Poly-tributylammonium ethylacrylate bromide (PTBAEABr) |  | PVCap | C1-C2-C3-C4-i-C4-N ₂ -CO ₂ | II | Nakarit et al. [115] |
| Tetraalkyl- phosphonium-bromide salts: (<i>n</i> -Bu) ₄ PBr/(<i>n</i> -Pe) ₄ PBr |  | Luvicap EG/Luvicap 55W/INHIBEX 713 | C1-C2-C3-C4-i-C4-N ₂ -CO ₂ | II | Magnusson and Kelland [116] |
| 1-hexyl-1-methylpyrrolidinium tetrafluoroborate (HMP-BF ₄) |  | PVCap | C1-C2-C3-C4-i-C4-N ₂ -CO ₂ | II | Lee et al. [117,118] |
| Hexaalkylguanidinium bromide |  | PVCap | C1-C2-C3-C4-i-C4-N ₂ -CO ₂ | II | Kelland et al. [119] |
| Ethylene glycol monobutyl ether (EGME) Ethylene glycol monobutyl ether (EGME) 2-Butoxyethanol |  | Poly(<i>N</i> -vinyl azacyclooctanone) VACO/VIMA copolymer (1:1) PVCap/1,3-bis(caprolactamyl)butane | C1-C2-C3-C4-i-C4-N ₂ -CO ₂ C1-C2-C3-C4-i-C4-N ₂ -CO ₂ THF | II II II | Chua and Kelland [50] Reyes and Kelland [120] Perrin et al. [121] |

| | | | | | |
|--|---|---|--|-------|---------------------------------|
| Ethylene glycol ether-monoethyl (EGME)/diethyl (EGDE)/ethyl (EGEE)/phenyl (EGPE)/Propylene glycol ether-propyl (PGPE)/methyl (PGME)/phenyl (PGPhE) |  | PVCap | C1-C2-C3-N ₂ -CO ₂ | II | Yang and Tohidi [122] |
| Diethylene glycol monoethyl ether (DEGBE) |  | PVP | C1-C2-C3 | II | Tang <i>et al.</i> [123] |
| Butyl glycol ether (BGE) |  | PVCap | C1; C1-C3 | I; II | Gulbrandsen and Svartaa [124] |
| Butyl glycol ether (BGE) |  | N-vinylformamide; N-isobutyl-N-vinylformamide copolymer NIPAAm/tBAAm; NIPAAm/DMAAm | C1-C2-C3-C4-i-C4-N ₂ -CO ₂ | II | Zhang <i>et al.</i> [125] |
| Mono ethylene glycol (MEG) |  | PVCap | C1 | I | Kim <i>et al.</i> [126] |
| Mono ethylene glycol (MEG) |  | PVP-BP | Gas condensate | I; II | Tohidi <i>et al.</i> [127] |
| Triethylene glycol (TEG) |  | Inhibex 301 | C1-C2-C3-C4-i-C4-C5-i-C5-N ₂ -CO ₂ | II | Qin <i>et al.</i> [128] |
| Polyethylene glycol (PEG) |  | Luvicap-EG | C1-C2-C3 | II | Chen <i>et al.</i> [129] |
| Polyethylene oxide (PEO) |  | Luvicap-EG | C1 | I | Daraboina <i>et al.</i> [130] |
| Polyethylene oxide (PEO) |  | Luvicap-EG | C1-C2-C3-C4-i-C4-C5-i-C5-C6-N ₂ -O ₂ | II | Daraboina <i>et al.</i> [131] |
| Polyethylene oxide (PEO) |  | Chitosan | C1; C1-C2 | I | Xu <i>et al.</i> [102] |
| Polyethylene oxide (PEO) |  | Cationic starches | C1; C1-C2; C1-C3 | I; II | Lee <i>et al.</i> [67] |
| Polyethylene oxide (PEO) |  | GHI 101 | C1-C2 | I | Lee and Englezos [132] |
| Polyethylene oxide (PEO) |  | Luvitec VPC/GHI 101/Inhibex 501/Luvicap EG/Luvitec K90/VC-713/PVP/NEI-411-31 | C1; C1-C2 | I | Lee and Englezos [133] |
| Polyethylene oxide (PEO)/Polypropylene oxide (PPO) |  | PVP/L-tyrosine/modified starch | C1; CO ₂ ; C3; i-C4; C1-C3; C1-i-C4 | I; II | Talaghat [103;134;135] |
| Soy lecithin |  | PVP | C1 | I | Garcia Chui <i>et al.</i> [136] |
| Sodium Chloride | NaCl | PVP | C1-C2-N ₂ -CO ₂ | II | Zhao <i>et al.</i> [137] |

experiments, preferably in the presence of *in-situ* monitoring device and in-site rheological measurements.

4.2. Glycol ether compounds

Several glycol ether compounds have been investigated for their roles as synergists to KHIs. Chua and Kelland [50] found ethylene glycol monobutyl ether (EGME) as a synergist to Poly(*N*-vinyl azacyclooctanone) (PVACO) when applied to sII gas hydrates. Reyes and Kelland [120] also tested EGME as a synergist to VACO/VIMA copolymer (1:1) on sII hydrate formation and found that EGME was both a solvent and a synergist for the examined KHI. More recently, Perrin *et al.* [121] studied the synergistic effect of 2-butoxyethanol with two KHIs, PVCap and a dimeric model compound, 1,3-bis(caprolactamyl)butane upon THF hydrate formation using small-angle neutron scattering (SANS). Technically speaking, 2-butoxyethanol is equivalent to EGME in molecular structure as studied by Kelland's group. Their results indicate that the atomic interactions in the solution caused by dosing of polymer molecules should not be attributed to, as one may have expected, the PVCap-2-butoxyethanol interactions, but rather PVCap-water interactions *via* hydrogen bonding instead. On the one hand, this confirms that polymeric KHI molecules such as PVCap could effectively perturb and disturb the water phase and prevent hydrate formation, as the KHI perturbation mechanism has proposed. On the other hand, it suggests that the synergetic mechanism between KHI and synergist molecules may have nothing to do with KHI-synergist interactions at the molecular level. The interactions between synergist and water molecules, and emerging hydrate nuclei may be of more interest and more significance when it comes to the mechanism of how synergists work to boost the KHI performance. The Yang and Tohidi [122] tested seven glycol ether compounds of ethylene and propylene series. They were ethylene glycol monobutyl ether (EGME), ethylene glycol diethyl ether (EGDE), ethylene glycol ethyl ether (EGEE), ethylene glycol phenyl ether (EGPE), propylene glycol propyl ether (PGPE), propylene glycol methyl ether (PGME), and propylene glycol phenyl ether (PGPhE). They found that all glycol ether compounds, except PGME, had synergistic effect to PVCap when applied to s-II hydrates. Such synergistic effects were observed irrelevant of the ethylene or propylene series but are rather associated with the molecular size of the tested glycol ether compound. In addition, Tang *et al.* [123] found that diethylene glycol monobutyl ether (DEGME) was a synergist to PVP when applied together to sII hydrates.

Butyl glycol, or butyl glycol ether (BGE) is a well-known synergist for polymeric inhibitors in the KHI industry. For instance, the Inhibex-series products from Ashland are grafted VP-VCap copolymers dissolved in BGE. Gulbrandsen and Svartaas [124] compared the effect of a formula of 1:1 PVCap/butyl glycol on s-I and s-II hydrate dissociation. They found that the presence of butyl glycol as a synergist caused a lower hydrate dissociation temperature. Thus, it is possible to add an effective synergist that can both help inhibit hydrate formation and reduce the stabilizing effect of the KHI on formed hydrates. More recently, Zhang *et al.* [125] evaluated BGE as a solvent synergist for a series of their newly synthesized KHIs. They found that the best performing product they screened, the *N*-vinylformamide:*N*-isobutyl-*N*-vinylformamide copolymer (NVF-*i*BuNVF) or what they call RK1-135, has an *i*-butyl group and shows good synergy with straight-chain *n*-BGE. On the contrary, a similar copolymer containing a straight *n*Pr group shows very good synergism with iso-BGE and less ideal with *n*-BGE. Therefore, they postulated a theory that a product with a branched alkyl group would have better synergy with another product containing a straight alkyl group. The theory holds true within their scope of study, and it definitely deserves further and systematic studies on the chain-chain interactions in KHI-synergist screening and evaluations.

Tohidi *et al.* [127] found that mono ethylene glycol (MEG), a most common thermodynamic hydrate inhibitor, served as a good synergist to PVCap, when applied to s-I and s-II hydrates of gas condensates. Their work revealed that a combined use of KHIs and MEG is a good

alternative for field applications and KHIs may regain their market share in the near future. With specific consideration on methane production from submarine hydrate sediments, Kim *et al.* [126] synthesized a series of NIPAAm-based tBAAm or DMAAm copolymers and tested their inhibition performance in the presence of 10% MEG. Their results demonstrated that the synergistic inhibition of MEG with these KHIs could be a good strategy to facilitate methane gas production from offshore hydrate deposits. However, they still need to solve the fouling problem due to precipitation of the tested KHIs before such combined recipes could be properly applied for commercial use.

Another less common but promising alcohol that may be applied as KHI synergist is triethylene glycol (TEG). Experimental studies by Qin *et al.* [128] showed that as compared to other alcohols including methanol, ethanol and mono ethylene glycol, TEG showed better synergistic effect to enhance the kinetic inhibition performance of PVP-BP for natural gas hydrates. Their research also indicates a general rule that a KHI or KHI synergist has a higher tendency to perform well if it could effectively reduce the surface tension of the aqueous phase. However, this must be considered case by case. It is not a rule of thumb and probably applies to their tested PVP-based polymers and selected alcohols only. A well-known example that conflicts with their observation on surface tension is sodium dodecyl sulfate (SDS). Dosing of SDS at as low as several hundred ppm would be sufficient to reduce the interfacial tension and promote hydrate formation at the same time. Apart from this, the work provides a useful insight upon KHI mechanism that a KHI molecule with stronger hydrophobic groups may have higher kinetic inhibition power if an effective synergist is present helping to reduce the interfacial tension and enhance the adsorption of the KHI molecules onto the surface of hydrate particles.

4.3. Polyethylene and polypropylene oxide

Polyethylene glycol (PEG) and polyethylene oxide (PEO) are synonymous for a same polymer with same chemical formula (*cf.* Table 4). PEG usually refers to polymers with a molecular weight below 20000 g·mol⁻¹, whereas PEO has been used for polymers with larger molecular weights. They have been extensively investigated for their synergistic effects to KHIs.

Chen *et al.* [129] found that 5%–20% PEG (with an average molecular weight of 400) was sufficient to increase the subcooling level Inhibex 301 could suppress upon s-II hydrates. They also observed that PEG, as a kind of thermodynamic hydrate inhibitor, was not able to inhibit crystal growth after hydrate formation commenced. Daraboina *et al.* [130,131] found that PEO as a synergist could enhance the nucleation inhibition capability of Luvicap EG for the formation of both s-I and s-II hydrates. Xu *et al.* [102] studied chitosan as a KHI to sI hydrate, with a small amount of PEO added. They found that the synergistic effect of PEO to chitosan was negligible. Lee *et al.* [67] however, when they studied the inhibition effect of cationic starches on both s-I and s-II hydrates, found that PEO was an effective synergist to cationic starches. Lee and Englezos [132,133] tested PEO as a synergist to a variety of KHIs, including GHI 101, Inhibex 501, Luvicap EG, Luvitec K90, Luvitec VPC 55 K65 W, Gaffix VC-713, PVP, and NEL-411-31, when applied to s-I hydrate. They confirmed the synergistic effect of PEO to all the tested KHIs during the nucleation stage, but no effect was found during the growth stage. Moreover, the addition of PEO has reduced the memory effect of hydrate formation in the presence of KHIs. The memory effect refers to easier and faster hydrate formation from water containing a previous hydrate or ice formation history.

Talaghat [103,134,135] found that both PEO and Polypropylene oxide (PPO) enhanced the inhibiting performance of PVP, L-tyrosine and modified starch on s-I or s-II hydrates. In this case, PPO worked as a better synergist than PEO. The additional methyl group anchored on the polymeric carbon chain in the PPO structure may have increased its efficiency in disturbing the water phase.

4.4. Other synergists reported

In addition to the aforementioned, most studied synergists including the quaternary ammonium and phosphonium salts, glycol ether compounds, and polyethylene or polypropylene oxide (PEO), several less common types of chemicals were also reported to have synergistic effects when used in conjunction with KHIs. Garcia Chui *et al.* [136] studied soy lecithin as a mix of phosphor-lipids and found that it could serve as a synergist to PVP when applied to s-I hydrate. The optimal synergistic effect was observed at a lecithin–PVP ratio of 3:1. Zhao *et al.* [137] found sodium chloride as a synergist to PVP when used in combination to inhibit s-II hydrate formation in water-based drilling fluid. NaCl showed a strong synergistic effect on the performance of PVP during both hydrate nucleation and growth stages. The results are to a large extent expected as sodium chloride itself is an effective thermodynamic hydrate inhibitor that is able to shift hydrate equilibrium towards higher pressures and lower temperatures.

5. Conclusions

Kinetic hydrate inhibitors as an increasingly important family of petroleum chemicals have been under extensive study and development worldwide, as an integral part of hydrate prevention and management strategies for flow assurance. This review has briefly looked back on the fundamental properties of natural gas hydrates, the prevailing polymeric kinetic hydrate inhibitors and the commonly studied KHI synergists for the boosting of KHI performance. The proposed hypotheses for hydrate nucleation and KHI inhibition were also reviewed and discussed. The majority of the polymeric KHIs studied nowadays for the industry includes poly-*N*-vinylacetamide polymers, hyper-branched polyesteramides, and isopropylmethacrylamide (IPMA) polymers. The most influential KHI inhibition hypotheses proposed are adsorption–inhibition, perturbation–inhibition, and crystal growth inhibition mechanisms. Further experimental and computational studies are required to understand the various KHI working modes under different conditions. The three major categories of KHI synergists are quaternary ammonium ionic liquids, glycol ether compounds, and polyethylene oxide (PEO). Their effectiveness may depend on factor such as KHI-synergist interactions and optimized mixing ratio. In the near future, new KHI formulations as well as innovative recipes combining KHIs and effective synergists may booster their use in the oil and gas industry and help alleviate the flow assurance problem caused by hydrate plugging.

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