Minireview Article

Structure-property relationship of flavonoids as potential green inhibitors for oilfield scales: a mini-review

Abstract

Scale deposits are a significant flow assurance issue in oil and gas operation, with huge financial consequences. Not only does scaling drastically impair well performance,but it also has the potential to permanently destroy formation and equipment. Scale inhibitors are commonly used to prevent the accumulation of scales. A good scale inhibitor should be stable at the minimum effective inhibitor concentration under imposed operating conditions without interfering with or being affected by other chemical additives. However, most conventional scale inhibitors that possess these attributes, do not meet environmental restrictions which make them unfavorable for continuous application, prompting the industry to focus more on developing eco-friendly substitutes. This paper reviews the various types of scale inhibitors, general scale inhibition mechanism, summarizes scale concepts and most importantly, assesses the potential of flavonoids from natural plants as potential green scale inhibitors.

Keywords: scale inhibition; scale inhibitors; flavonoids; quercetin; chelating agents; natural products; scale inhibitors; eco-friendly

Glossary: HEDP - HydroxyethylideneDiphosphonic Acid; AMPS- 2-Acrylamido-2-methylpropane sulfonic acid; ATMP - Amino Trimethylene Phosphonic Acid; EDTA - Ethylenediamine tetraacetic acid; PASP-polyaspartic acid; SI(s)- Scale Inhibitor(s)

Introduction

Scale refers to water-borne mineral deposits and suspended solids that form as a result of temperature changes, pressure decreases, mixing of different waters, and agitation in

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oilfield waters. Once scale deposit downhole, they can reduce oil output or even block the flow into a producing well. In surface facilities, scale deposition can restrict normal flow or limit the efficiency with which produced fluids are separated and processed to meet quality criteria. Calcium (Ca^{2+}), barium (Ba^{2+}), and strontium (Sr^{2+}) are common scaling cations found in the oil and gasaqueous systems(Garba and Sulaiman 2014; Crabtree, et al. 1999; Sorbie and Mackay 2000).

Scale formation is a complex crystallization process that necessitates the simultaneous fulfillment of three conditions: supersaturation, nucleation, and crystal growth (Al-Roomi,Hussain, and Riazi 2012; Crabtree, et al. 1999; Kelland, 2014). Calcium carbonate and/or calcium sulfate are formed by Ca^{2+} ions, whereas barium sulfate and strontium sulfate are formed by Ba^{2+} and Sr^{2+} ions, respectively. The mixing of incompatible waters, such as seawater with a high sulfate ion concentration and formation water with high Ca^{2+}, Ba^{2+}, and/or Sr^{2+} ion concentrations, is usually connected to sulfate scaling (Garcia, Thomsen andStenby 2005; Sorbie and Mackay 2000). Carbonate scale is usually caused by the loss of carbon dioxide gas (CO_2) from the water to the hydrocarbon phase(s) as pressure drops (Graham, Dyer and Shone, 2002). Sulfides and iron hydroxides, which form as a result of corrosion, are less common scales (Crabtree, et al. 1999).

Scale prevention is critical to ensuring sustained production from existing brine deposits reserves (Kan and Tomson 2012). The oil and gas sector has developed three types of scale prevention techniques over the years: Sulfate ion sequestration from sea injection waters; scale removal/dissolution by chemical or mechanical means; use of scale inhibitors (SIs). The first two approaches can be used for short-term treatment and are beneficial for minor scaling problems (Frenier2008), but continuous injection or

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chemical scale squeeze treatment with inhibitors has been demonstrated to be the most efficient and cost-effective (Laing, Graham and Dyer 2003).

2: SCALE INHIBITOR TYPES

2.1: Organic and Inorganic Inhibitors

Scale inhibitors are broadly divided into two categories: organic and inorganic scale inhibitors. The two types of organic scale inhibitors now in use are phosphonates and polymers (Viloria et al. 2010). Inorganic inhibitors include condensed phosphates, such as poly(metaphosphate)s or phosphate salts (Ducciniet al. 1997).

Phosphonates contain phosphorus, in comparison to polymeric scale inhibitors, they are tiny compounds with molecular weights ranging from 200 to 600. Nitrilotris (methylene phosphonic acid) and 1-hydroxyethane 1, 1-diphosphonic acid (HEDP) are two examples (ATMP). Phosphonates work well against crystalline, sparingly soluble salts such as calcium carbonate as well as barium, calcium, and strontium sulfate salts. Sulfonated polymers are more effective at low temperatures, whereas phosphonates are most effective at high temperatures (Talbot and Jones 2009).

Polymeric scale inhibitors on the other hand are frequently employed in the oil and gas industry because of their improved thermal stability and environmental compatibility. In conventional squeeze treatment, however, the squeeze efficiency of such threshold inhibitors, including polymeric scale inhibitors and phosphonates, is often poor (Viloria et. al. 2010; Garba and Sulaiman 2014). Examples of polymeric SI are Polyacrylic acid, polymaleic acid, and a variety of copolymers and terpolymers made from acrylic acid, maleic acid, AMPS, and other monomer. This category includes all scale inhibitors with carboxylate (-COOH) functional groups. The molecular weights of polymeric scale inhibitors range from roughly 1000 to 4500.

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These inhibitors have the disadvantage of not being compatible with quaternary amine coagulants.

2.2: Biodegradable Polymers

As environmental restrictions become more stringent, research and development in the scale inhibitors market is increasingly focused on biodegradable and ecologically friendly polymers (Popov et al. 2016). The dehydration of maleic acid yields the synthetic polymer based on maleic anhydride, which is frequently employed in scale inhibition. These polymers' copolymers were made utilizing unsaturated monomers and free radical polymerization. In the presence of an organic peroxide, such as benzoyl peroxide, di-tertbutyl peroxide, tertbutyl peroxy benzoate, tertbutylhydroperoxide, dicumyl peroxide, or azobis, the polymerization reaction occurs (isobutyronitrile). Some researchers successfully synthesized a poly (maleic anhydride), copolymer, or synthetic terpolymer of maleic anhydride as a polymeric product using this common synthetic technique (Davies, Dawkins andHourston 2005; Nasirtabriziet al. 2013, Fukumoto and Moriyama, 1987).

2.3: Green Scale Inhibitors

Green scale inhibitors provide several advantages, including voluntary biodegradability, high efficiency, and nontoxicity (Jing and Tang 2011). Examples are, Amino acids, alkaloids, polyphenols, plant extracts, widely disseminated and have low economic value, such as byproducts of agro industrial operations and agricultural wastes. Also, polyaspartic acid (PASP) is regarded as a promising green scaling inhibitor because of its performance and ecologically friendly qualities. It's a biodegradable polymer with no phosphorus atoms that performs well on both calcium sulfate and carbonate scales. (Migahedet al. 2016; Gao et al. 2015)

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Plant-derived extracts are extremely cost-effective. Chaussemier et al. (2015) used chronoamperometry to investigate the scale inhibition of fig leaves for the deposition of $CaCO_3$ on a steel electrode at 40°C. It had a high inhibitory efficacy of around 85%. Chaussemier et al. (2015)also did another investigation using olive leaf extract instead of fig leaf extract. Other research groups (Bonoliet al. 2004; Lee et al. 2009) have proven the scale inhibition performance of the polysaccharides and soybean extracts derived from seaweeds. These extracts were thought to be more effective at inhibiting the production of $CaCO_3$ than polyaspartic acid. The inhibition efficiency of seaweed extracts (polysaccharides and soybean) was found to be 16.7%, whereas poly-aspartic acid inhibitory efficiency was determined to be 6.6 percent.

Abdel-Gaber et al (2012) conducted a study on the scale mitigation of $CaCO_3$ scale using Punica granutum hull and leaf extract. The hull extract inhibited scale growth better than the leaf extract, according to their findings. In another research, the inhibition efficiency of Nypafruitcans was 75.11 percent, while the inhibition efficiency of 1,5-diphenylcarbazone was only 70.18 percent (Abd-El-Khaleket al. 2019). Several other studies on creating green scale inhibitors have also been published inliterature(Binmerdhah2010; Zhang et al. 2020; Olajire 2015; Yuan et al. 2020).

3: Scale inhibition Mechanism

3.1: Threshold Inhibition

The slowing of crystal formation by scale inhibitors at very low concentrations is known as threshold inhibition. This delay is referred to as an induction period by physical chemists. This mechanism is characterized by the addition of a substoichiometricamount of inhibitors that intermingle with developing crystals and cause crystal growth to be delayed (Abdel-Aal and Sawada 2003; Issabayevet al. 2019).

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A scale inhibitor is thought to intervene in the development of nucleation, according to several studies on the threshold mechanism undertaken by several researchers (Garba and Sulaiman 2014; Crabtree et al. 1999; Kelland 2014). They adsorb onto the crystals' dynamic sites, causing the morphology to be altered. Under the threshold mechanism, polymeric organic and phosphinopolycarboxylic acid scale inhibitors primarily act as nucleation inhibitors. (S. Kumar,Naiya,and T. Kumar2018; Sorbie and Mackay 2000; AT 2015)

3.2 Crystal Modification

Scale inhibitors bind to crystal structures as they expand, distorting their shape. Crystals on membrane surfaces grow slower as a result of this modification. Basically, inhibitor molecules are incorporated into the crystal structure by associating the crystal cations with the inhibitor's negative functional groups. (AT 2015; Garba and Sulaiman 2014)

3.3: Dispersion

Scale inhibitor compounds have negative functional groups that can augment the negative electrostatic charge already existing on colloids and particles. The negative electrostatic charge of the colloids, along with the steric hindrance caused by the adsorption inhibitor, enhances repulsion between colloids and particulates, delaying crystal development on membrane surfaces once more. The inhibitor must bind to the surface for dispersancy to occur, just as it must for growth stopping. However, in order to be an effective dispersion, the solution must contain a charged group that repels other charged particles (David and Kelly 2011;kelland 2014; Garba and Sulaiman 2014; AT 2015).

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4.0: Flavonoids in metal complexes

Use of chelating agents for scale inhibition is advantageous due to their low corrosivity compared to the conventional methods of scale management using mineral and organic acids. Traditional chelating agents for scale inhibition in the petroleum industry are mainly aminocarboxylic acids, notably ethylenediamine tetraacetic acid (EDTA) (Kamal et al. 2018). However, the high cost of these chelating agents and their eco-toxicity are major drawbacks (Kamal et al. 2018). Flavonoids ubiquitous in nature have the potential to fill this gap. Flavonoids are natural polyphenolics which are found mainly in the tissue of higher vascular plants. They structurally consist of two benzene rings (A and B) joined by an oxygen-bearing heterocyclic ring (C) (Figure 1).

Thousands of distinct flavonoids exist in nature, some of the most common being quercetin, rutin, catechin, kaempferol, myricetin and fisetin (Kyei et al. 2021). Flavonoids are derivatives of 2-phenyl-1-benzopyran-4-one. Depending on their structure, they can be classified as flavones, flavonols, flavan-3-ols, flavanones, isoflavones and anthocyanidins (Kyei et al. 2021). Their basic structure is the aglycone, but they also occur as the glycosides and methylated derivatives. Flavonoids are weak polybasic acids and are generally non-toxic (Riha et al. 2014; Symonowicz and Kolanek 2012). Due to the multiple hydroxyl groups and the carbonyl group, flavonoids have many sites for metal complexation. Flavonoids have been extensively investigated *in vivo* and *in vitro* as antioxidants and metal chelators in biological systems and have shown remarkable performance. However, their application for same purpose in industrial systems has received relatively low attention despite their enormous advantages such as low-cost, biodegradability, renewability, and non-toxicity.

Flavonoids based on the flavone skeleton form metal complexes with moderate to high stability constants (Figure 2) (Markovic et al. 2011). The flavone-based

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flavonoids possessing a: (i) 3-hydroxy group, (ii) 5-hydroxy group and/or (iii) 3',4'-dihydroxy group (catechol moiety) are of great interest as metal chelators due to their high metal binding capacity (Grazuland Budzisz2009). Major flavonoids with these structural features include quercetin, rutin, myricetin, fisetin and kaempferol; with quercetin and rutin being prime candidates for industrial application as metal chelants due to the presence of all the three structural features and their abundance in agro-waste biomass such as red onion skin and citrus (orange) mesocarp respectively (Jiang, Liu and Zhai 2018). ***[Figure 1 and 2 near here]***

4.1: Stoichiometry and Stability of Flavonoid-Metal Complexes

The stoichiometry of flavonoid- Metalcomplexes depends on the structure of the flavonoid, the identity of the metal cation and its oxidation state, pH of the media and mole ratio of metal to flavonoid (Jiang, Liu and Zhai 2018; Fernandez et al. 2002). The affinity of a particular flavonoid complexation site for a metal cation depends on the structure of the flavonoid (especially the relative strengths of the intramolecular hydrogen bonds), the metal ion and the medium (Kasprzak,ErxlebenandOchocki 2012; Markovic et al. 2011; Leopoldini et al. 2006). The optimal pH for complexation of metals by flavonoids is around 6 but varies with the metal ion. Apart from the common 1:1, 1:2 and 2:1 complex, other higher ligand-metal stoichiometries exist including 1:3, 2:2, 2:3 and 3:1. However, due to steric restrictions, complexes with more than two flavonoid molecules are unstable and rare (Manman et al. 2019). Majority of 1:1 flavonoid-metal complexes have moderate to high stabilities (Kasprzak,ErxlebenandOchocki 2012). The stability of metal-flavonoid complexes is influenced by the chemistry of the medium. It is generally higher in neutral or alkaline medium due to the increasing mole ratio of the flavonoid in the complex driven by

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increasing pH. Typically, flavonoid-metal complexes show good stability between pH 3 -10. Fisetin – Al^{3+} complexes were reported to be stable at pH 2, while quercetin complexes with Al and Fe were partially stable up to pH 12 and 14 respectively (Erdogan, Karadag and Dolen2005).

4.1.1: Quercetin

Quercetin (3,5,7, 3', 4'- pentahydroxyflavone) is one of the most abundant flavonoids in plants. Due to its structure-activity relationship, quercetin is considered one of the most powerful flavonoid metal chelators, effectively complexing main group metals and transition metal ions from alkali metals such as Na^{+}, alkaline earth metals (Ca^{2+}, Mg^{2+}) to heavy metals such as Ba^{2+}, Fe^{3+} and Pb^{2+} as well as metals of the lanthanide series (Lutoshkin et al. 2018; Kalinowska et al. 2016; Markovic et al. 2011). In a study by De Castilho et al. (2018), the complexation ability of quercetin for some common scaling cations was found to be in the order $Mg^{2+} < Ca^{2+} < Al^{3+} < Ni^{2+}$, increasing with the metal charge to size ratio. The 3-hydroxy-4-keto group, 5-hydroxy-4-keto group and 3',4'-dihydoxy groups (catechol group) are the three sites for potential metal chelation (Figure3). Due to the higher acidity of the C3-OH proton, the 3-hydroxy and 4-keto group is the first site of complexation followed by additional complexation at the 3',4'-site. The 5-hydroxy group is the least favorable site for complex formation due to its low acidity and the steric hindrance arising from the first complexation at the 3-hydroxy position (De Souza and Giovanni 2004). Alkaline conditions favor the participation of the catechol moiety in complex formation because under this condition, the C3'-OH and C4'-OH groups are both deprotonated. As a result, the stoichiometry of the complexes is pH dependent. Usually, quercetin: metal complexes of 2:1 and 1:1 stoichiometry is formed in acidic (pH < 6) and neutral/ alkaline media respectively (Markovic et al.

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2011).***[Figure 3 near here]***

4.1.2:Rutin

Rutin (quercetin-3-O-rutinoside) shown in Figure4,forms stable complexes with many metal ions including those prevalent in inorganic scales such as calcium, magnesium, aluminum, iron, manganese, vanadium, copper, cobalt, zinc and lead (Jiang,Liu, and Zhai2018). Rutin-rich orange mesocarp extract and its carboxylated derivative was successfully used for the sequestration of Mg^{2+}, Cd^{2+}, Zn^{2+}, Cu^{2+} Co^{2+}, Ni^{2+} and Pb^{2+} from aqueous solution (Ezeani, Okoye, and Akaranta2012; Ogali,Akaranta,and Aririguzo 2008). Stable 2:1 rutin-Pb^{2+} complex was also reported in acidic media (pH 4.5) with the complex stability increasing with increasing pH (Radovic and Malesev, 1985). The dissacharide component of rutin also undergoes some interaction with the metal ion (Escandar and Sala 1991)***[Figure 4 near here]***

4.1.3: Myricetin, Fisetin and Kaempferol

Myricetin (3,5,7, 3', 4', 5'- hexahydroxyflavone) obtainable from leaves of sweet potato is an excellent iron chelant. Similar to quercetin and rutin, it forms particularly strong complexes with iron in acidic media, probably due to the ability to reduce Fe^{3+} to Fe^{2+} (Fernandez et al, 2002). This metal reductant ability is most pronounced in myricetin due to the higher number of hydroxyl groups in the molecule. Myricetin has high affinity for Al^{3+} than Fe^{3+} and relatively lower affinity for Zn^{2+} (Sungur and Uzar, 2008)

Fisetin (3,7, 3',4'-tetrahydroxyflavone) possesses two sites for potential metal chelation, that is the 3-hydroxy-4-keto group and 3',4'-hydroxy groups of the catechol moiety. In acidic media, fisetin forms 1:1 complex with Al^{3+} and 2:1 complexes with Fe^{2+}, highlighting the influence of the metal cation on stoichiometry of flavonoid-metal complexes (Markovic et al. 2011; 2009). Fisetin serves as an effective

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chelant for aluminum and iron over a wide pH range with the stoichiometry of the fisetin: Al^{3+} complex changing from 1:1 to 1:2 at higher pH and metal concentration, whereas the stoichiometry of fisetin: Fe^{3+} complex changes from 2:1 to 1:1 with pH increase above 6 (Markovic et al. 2011; 2009). The 1:2 stoichiometry arises when two Al^{3+} cations are ligated by one molecule of fisetin via four oxygen atoms of the 3-hydroxy-4-keto group and the now deprotonated hydroxyl groups at the 3',4'-site (Markovic et al. 2009).

Due to the lack of the catechol moiety, metal complexation by kaempferol (3,4',5,7, -tetrahydroxyflavone) can only occur at the 3-hydroxy-4-keto group or the 5-hydroxy-4-keto with the former being more favorable, explaining the consistency of the 1:1 stoichiometry of kaempferol: Fe^{3+} complex in acidic (pH 4.5) and alkaline solutions (pH 8) (Markovic et al. 2014)

4.2: Aqueous Solubility of Flavonoids and their Metal Complexes

Solubility in water is a critical factor in the effectiveness of a given flavonoid as a metal chelating agent. Generally, aglycone flavonoids have poor solubility in water whereas the glycosidated form is readily soluble because the dissacharide component of the flavonoid, which can be rhamnose, galactose, glucorhamnose or arabinose, increases the aqueous solubility. (Grazuland Budzisz 2009; Escandar and Sala, 1991). It is also important that after complexation, the flavonoid: metal complex remains in solution. Quercetin and rutin complexes with calcium and magnesium were reported to be soluble in neutral conditions and up to pH 8 (Jiang, Liu and Zhai 2018; Fernandez et al. 2002).

The aqueous solubility of flavonoids and their complexes can be enhanced via simple chemical modifications by glycosidation, carboxylation or sulfonation (Lutoshkin et al. 2018). Depending on the reaction conditions, flavonoids can be

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sulfonated at the 5' and/or the 8 position (Fig 4). Sulfonated quercetin was noted to be readily soluble in water, non-selective and efficiently complexed a wide range of metals leading to the formation of stable complexes (Woznicka et al. 2014).

Conclusions

Sequestration of metal cations is a reliable technique for the inhibition of oilfield scales. Conventional chelating agents, which are usually amino carboxylic acids, are effective scale inhibitors, but due to the stoichiometric amounts of the additive required for performance, their high cost and environmental persistence is a subject of concern for their continued application in this field. Natural products, especially flavonoids are potential green scale inhibitors due to their proven high metal binding capacity, non-toxicity, and biodegradability. Specifically, flavone-based flavonoids such as quercetin, rutin and myricetin form moderate to highly stable complexes with all metal cations responsible for oilfield scale formation due to their unique structural features. For a given flavonoid, the exact stoichiometry and stability of the flavonoid-metal complexes are influenced by the identity of the metal ion and chemistry of the medium, especially pH.

In addition to their excellent metal chelation ability, the appeal of flavonoids as metal chelators for potential scale inhibition lies in their renewability as bio-resources and their ubiquity and accessibility in agricultural waste biomass such red onion skin and orange mesocarp. The availability of these flavonoids in commercial quantity in agro-waste materials and the feasibility of directly applying the crude natural extracts in industrial systems makes them highly cost-effective. However, the effectiveness of flavonoids in their pristine state, as metal chelators may be limited by their moderate solubility in water both in the free and complexed state. This challenge can be overcome

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by simple, facile derivatization of flavonoids by carboxylation and sulphonation which also increases the metal binding capacity. A systematic investigation of additional potential routes for the chemical modification of flavonoids is necessary to develop more effective flavonoid-based metal chelating agents for application as oilfield scale inhibitors.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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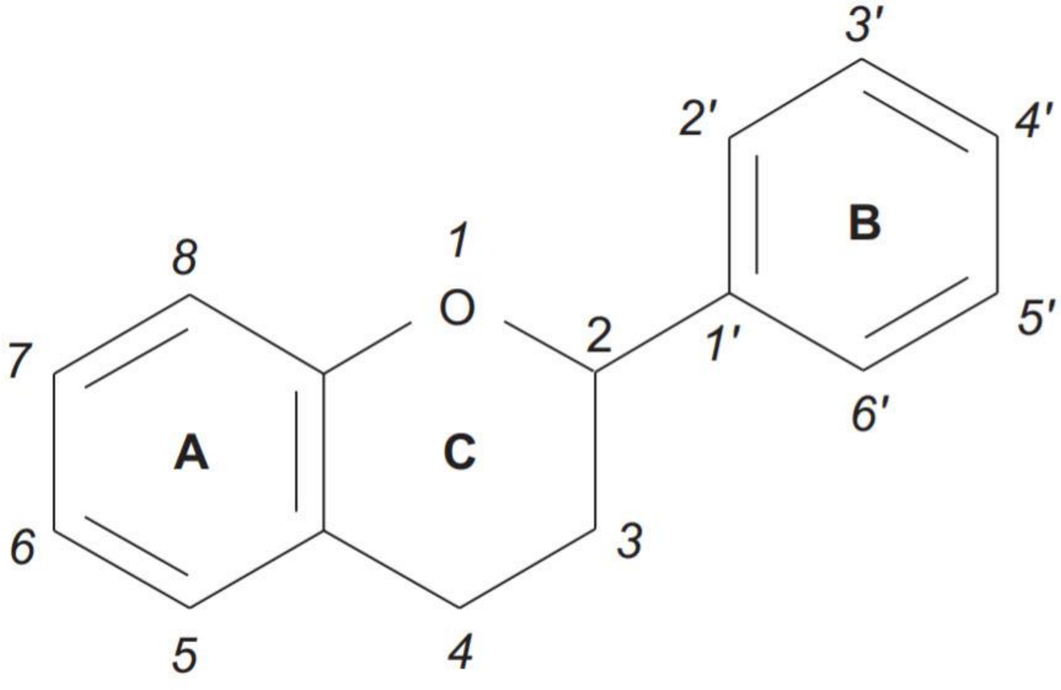

Figure 1. Basic skeleton of flavonoids(Cooper,Chopra, andThurnham2004)

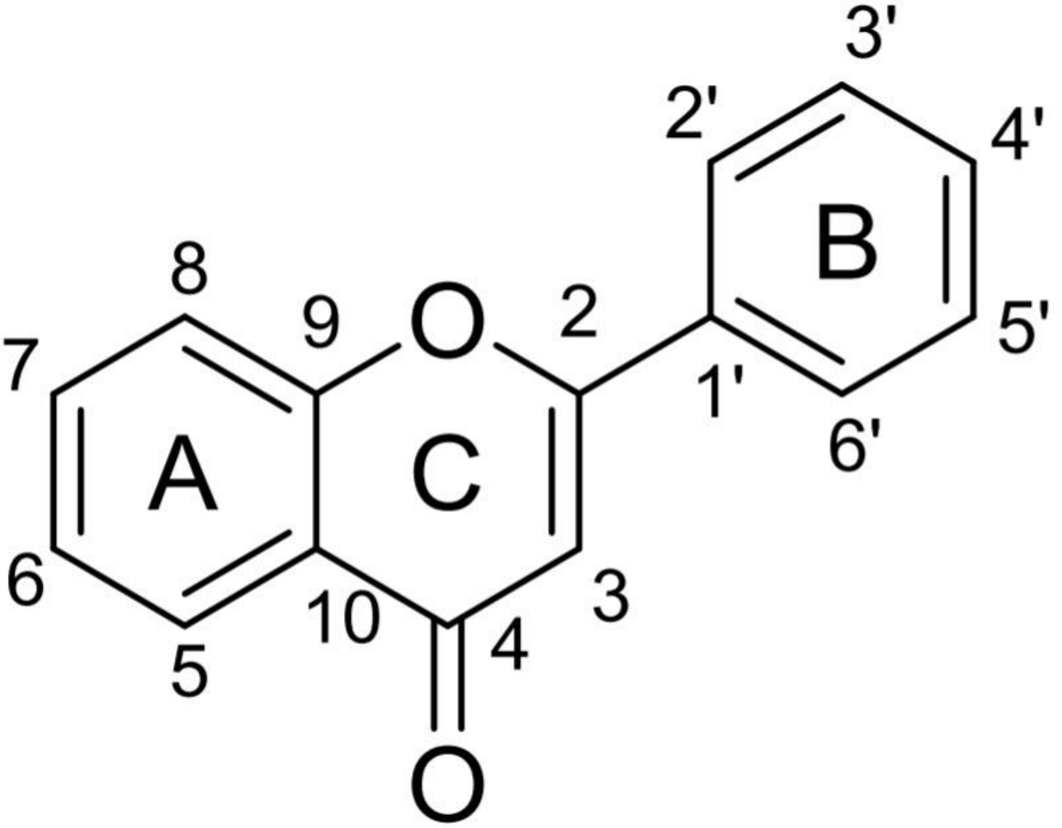

Figure 2. General structure of flavones (Catarino et al., 2014)

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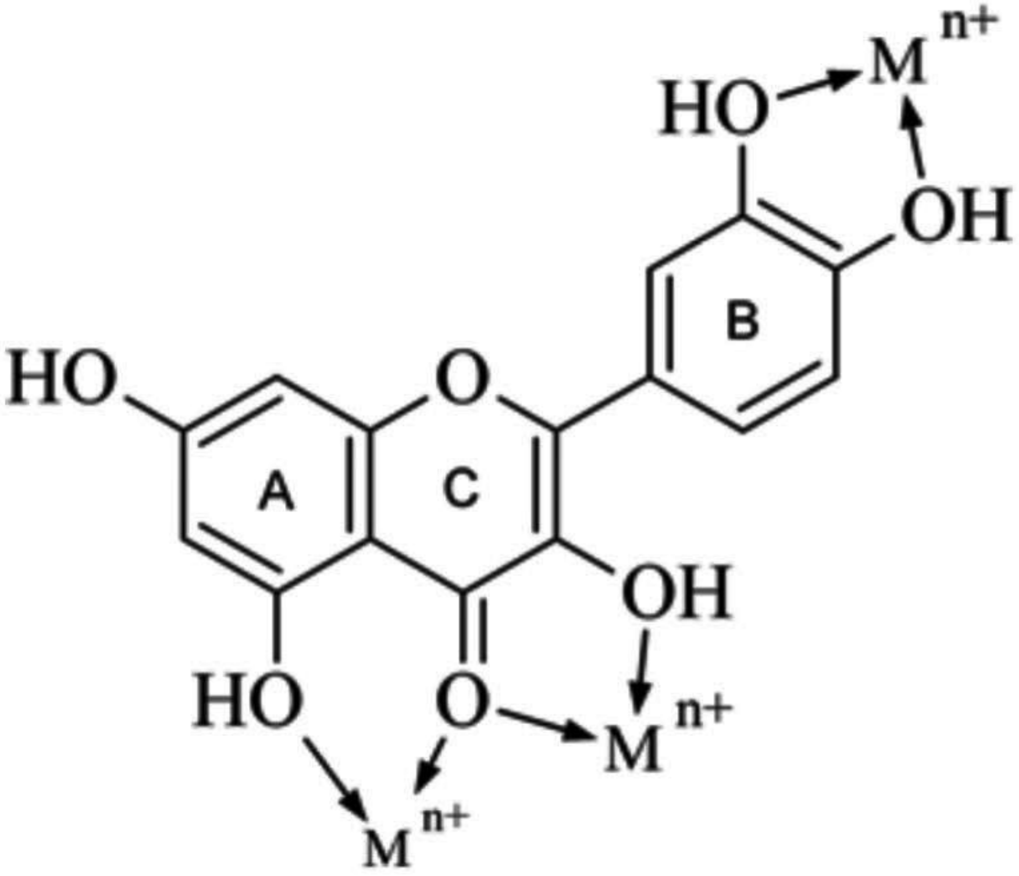

Figure 3. Chemical structure of quercetin showing possible sites for metal chelation(Kasprzak,Erxleben, Ochocki2012)

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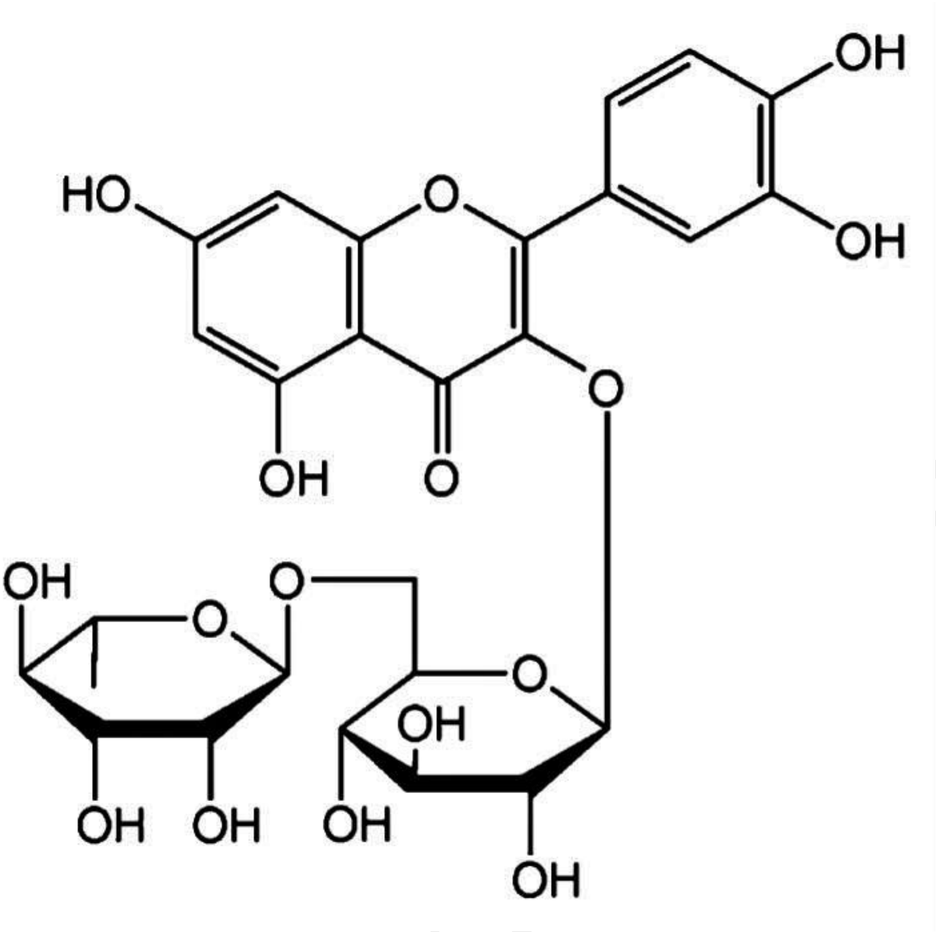

Figure 4. Molecular structure of rutin (Mauludin and Muller, 2013)

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