SYNTHESIS OF A NOVEL COBALT-CONTAINING METALLOGEL USING 5´ADENOSINE MONOPHOSPHATE AS A SMALL MOLECULE HYDROGELATOR

M.Sc. Thesis

By

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DISCIPLINE OF CHEMISTRY

INDIAN INSTITUTE OF TECHNOLOGY INDORE

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A THESIS

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CANDIDATE'S DECLARATION

I hereby certify that the work which is being presented in the thesis entitled **SYNTHESIS OF A NOVEL COBALT CONTAINING METALLOGEL USING 5′-ADENOSINE MONOPHOSPHATE AS A SMALL MOECULE HYDROGELATOR** in the partial fulfillment of the requirements for the award of the degree of **MASTER OF SCIENCE** and submitted in the **DISCIPLINE OF CHEMISTRY, Indian Institute of Technology Indore**, is an authentic record of my work carried out during the period from July 2019 to June 2020 under the supervision of Dr. Tridib K. Sarma, Assistant Professor, IIT Indore.

The matter presented in this thesis has not been submitted by me for the award of any other degree of this or any other institute.

Nitin Kumar

Nitin Kumar

This is to certify that the above statement made by the candidate is correct to the best of my/our knowledge.

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Nitin Kumar

M.Sc. 2nd year

DEDICATION

Dedicated to My Family and Friends

Abstract

Hydrogels are attractive biomaterials, due to their soft nature resembling the biological tissues and ability to absorb a large amount of water inside its matrix. Subsequently hydrogels have found interesting applications in biomedical areas, tissue engineering, targeted drug delivery, and several others. Most of the molecular architectural designs for the hydrogelators are based on polymers which form entangled fibril networks through a combination of noncovalent interactions such as π- π interactions, hydrogen bonding and vander Waals interactions that can entrap large volume of water. On the other hand, native biomolecules, such as carbohydrates, peptides and nucleic acids form an exclusive class of small molecule hydrogelators. Equipped with various noncovalent binding sites, nucleotides represent a naturally occurring gelator, that can bind metal ions through coordination bonds. The biocompatibility and stimuli-responsiveness of the resultant coordination polymer hydrogels can be harneseed towards fascinating functional materials taking advantage of the inherent characteristics of both the metal and organic counterparts. Herein, we report the synthesis of a novel coordination polymer hydrogel by coordinating cobalt ions (Co^{2+}) with 5′-AMP. A blue color gel was produced as a consequence of heating the aqueous solutions of both metals as well as gelator mixed in the molar ratio of 1:1 (v/v). This coordination polymer hydrogel is expected to exhibit diverse magnetic, electric, and bio-mimetic properties that might influence a wide range of applications such as enzyme mimetics, magnetic soft materials and energy applications.

There are many processes in which we need enzymes to work as catalysts but their limited availability often limits their use. Esterase enzyme is one such hydrolase enzyme that is used to catalyze the conversion of ester into acid and alcohol. Although we performed the enzymatic assay for esterase activity with the synthesized hydrogel, we could not obtain the desired outcome. As Co^{2+} metals are known to catalyze a diverse class of organic transformations, we expect these hydrogels to be utilized as heterogeneous catalysts in a biocompatible environment.

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NOMENCLATURE

mM	Millimolar
Nm	Nanometer
ºC	Degree Centigrade
Da	Daltons
Mm	Millimeter
Rad	Radian
S	Second
K	Kelvin
kV	Kilo Volt

ACRONYMS

AMP	Adenosine Monophosphate
ATP	Adenosine Triphosphate
IMP	Inosine Monophosphate
GMP	Guanosine Monophosphate
TEM	Transmission Electron Microscope
SEM	Scanning Electron Microscope
Co	Cobalt
Ni	Nickel
LMWG	Low-Molecular Weight Gelator
AFM	Atomic Force Microscopy
XRD	X-ray Diffraction

Chapter 1

Introduction

1.1. General Introduction

In the late eighteenth century, Alfred Werner, a Swiss chemist, reported the structure of octahedral transition metal complexes and provided a new definition of valency. According to him, in a coordination compound, there are two types of valency, the primary valency that corresponds to the oxidation state and the secondary valency that represents the coordination number of the metal ion. Back then, these compounds were known as double salts. By understanding Werner's work, various synthetic methodologies of installing desired ligands are now possible. Over a century, his work led us to advances in our understanding of the chemistry of coordination and also diversified the scope of inorganic chemistry as well. It not only helped us to understand the structure but to synthesize, the reactivity of novel catalysts and simple metal-ligand to complex organometallic materials. From past decades, two major branches of coordination chemistry have emerged, metal-organic frameworks (MOFs) and supramolecular self-assemblies (SSAs). MOFs are the caged systems (infinite networks) comprising of metal-ligand coordination bonds. MOFs have acquired a lot of attention due to their porous structure and stability in organic solvents [1-6]. These can be used for storing gases or capturing small molecules for that reason several separations could be made possible [7-8]. SSAs on the other hand, are the autonomous organization of constituent molecules resulting in an ordered pattern or structure at any scale. However, at the nanoscale level, it reveals the characteristic properties of individual molecules such as shape, polarizability, charge, etc which determines the type of interaction present between them. One of the major focus areas has been to develop artificial enzymes, which can mimic specific catalytic activity like natural enzymes. Although natural enzymes are highly active and specific towards particular organic reactions, they become denatured under harsh reaction conditions, such as a change in pH, temperature, or change of solvents. As several enzymes contain metal ions in their active sites, therefore the supramolecular self-assemblies governed by the coordination bonds are expected to play a major role in studying biomolecular interactions, biomimetic chemistry, enzyme-mimetics and in several other areas. If the organic component contains the natural biomolecules, the resultant coordination polymer assemblies can influence the generation of a new set of functional materials with biocompatible properties that can address important characteristics such as mechanical robustness, responsiveness (smart materials), specificity, and other critical properties [9]. An outline classification of gels is given below (**Figure 1.1**).

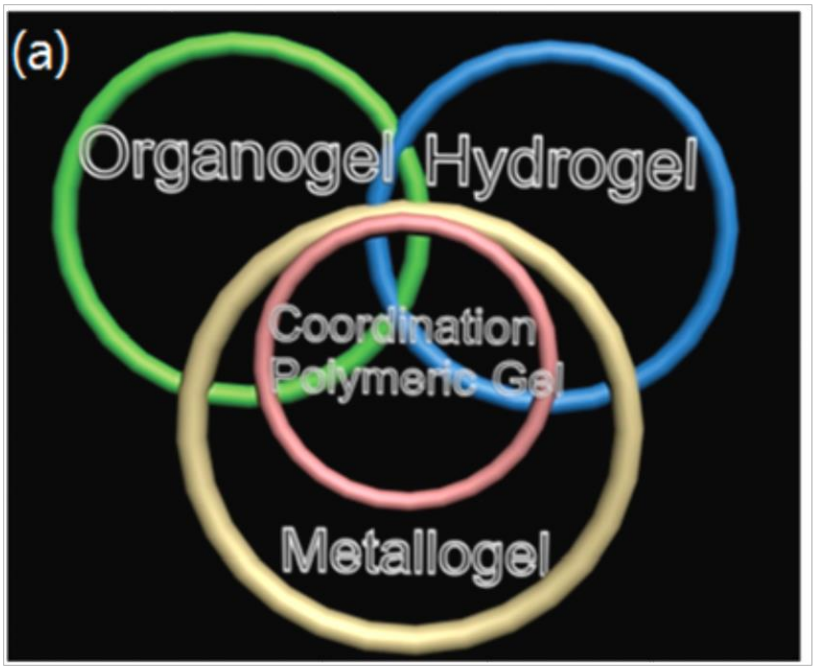

Figure 1.1. Outline classification of gels.

1.2. Hydrogels

A hydrogel is defined as a microscopic structure with macroscopic dimensions and solid-like rheology in spite of having a large amount of water in its matrix. A gel restricts the flow of liquid by establishing a fibrous network around the liquid (**Figure 1.2.**) and the solvent constitutes up to 99% of the weight of material [10-12]. When the solvent used to form a gel network is water, it is termed as a hydrogel. A large number of gels can be obtained even in the organic medium and these materials are classified as organogels. The gels can be formed both chemically and physically. A chemical gel is formed by irreversible covalent linking which also includes the breaking of covalent bonds whereas a physical gel is formed by reversible non-covalent interactions such as hydrogen bonding, π-π stacking, van der Waals forces and coulombic interactions [13-27]. Due to the resemblance of the hydrogels to soft tissue environments, these classes of materials have attracted tremendous attention for applications in biomedical areas such as drug and gene delivery, tissue engineering, and soft electronic devices for diagnosis of diseases. However, for the majority of the applications, several parameters such as mechanical stiffness, stimuli-responsiveness, self-healing properties, stability under reaction conditions, etc. play an important role. Most of the naturally occurring bio gels are formed from long-chain polymers, where the non-covalent interactions between polymeric chains play a major role in directing the self-assembly into fibril structures.

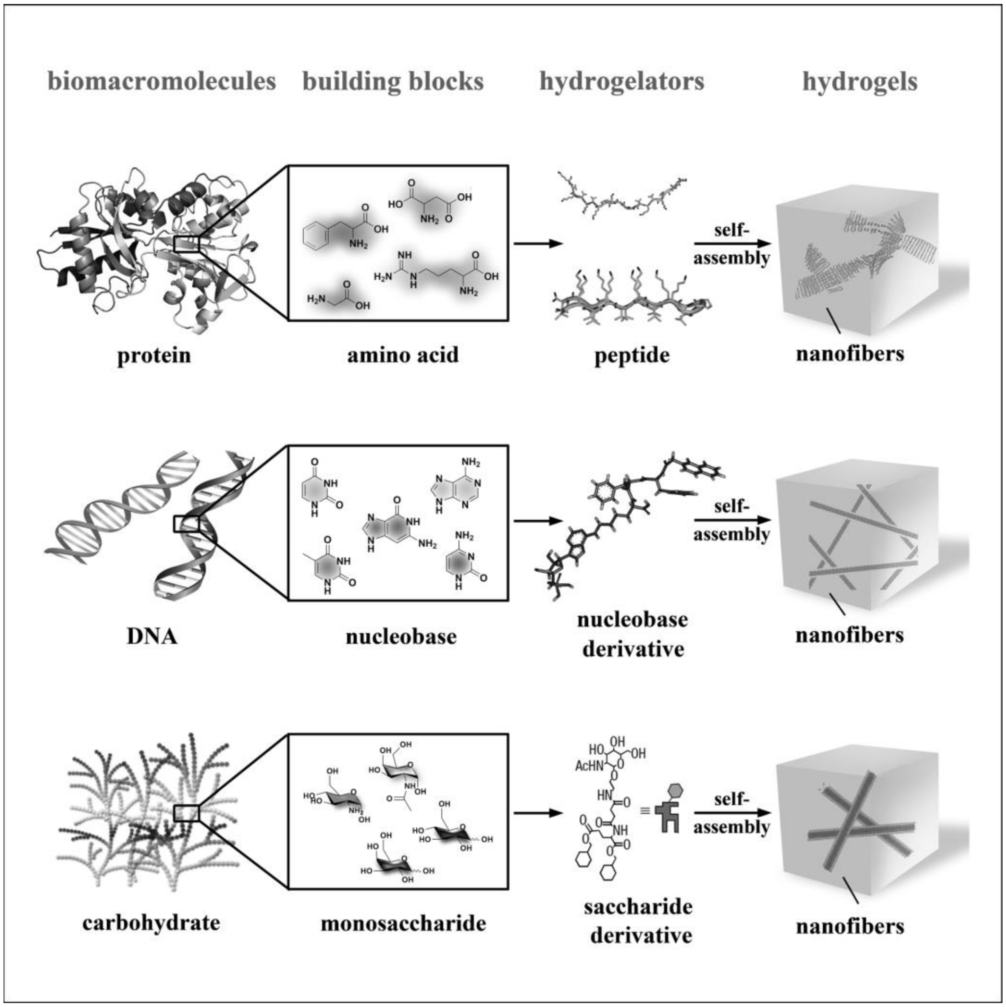

Figure 1.2. Various hydrogels made from basic biomolecules.

Gelation can sometimes occur just by adding "low molecular weight" gelators (LMWG), compounds that have a molecular weight less than 3000 Da, at room temperature, or by heating it to dissolve the gelator. After cooling, the supersaturated solution forms the gel. The resultant gel also often responds to external stimuli because it includes reversible, multistep assembly thereby attractive for many applications. The first molecular gel was synthesized by Lipowitz in 1841 when he reported the gelation of water with lithium urate, which is itself a nucleobase analog. Since then many LMWGs were discovered, designed, and developed. Various supramolecular gels were made from complexes of quaternary ammonium salts, Gemini surfactants, poly-ureas and amides, dendrimers, alkanes, polyaromatics, and metal coordination complexes to name only a few groups of gelators. There are also many examples of combining two or more gelators to form molecular gels [28-42].

1.3. Metal-organic hydrogels

The gel that contains both metal ions and LMWGs is called metal-organic hydrogel or simply metallogel. With the development of supramolecular chemistry, several researchers started designing organic gelators that can bind with the metal ions to form coordination complexes. Although the formation of organic supramolecular hydrogels was attractive for several applications, the possibility of incorporating several properties that a metal ion component can bring forth, the interest towards the metal-organic supramolecular hydrogels has increased manifold. The diversity of metal-ligand coordination can control the self-assembly process and as a result, alters the gel properties. Further, the inherent physicochemical properties of the metal ions impart additive applications to the supramolecular systems [43-45].

1.3.1. Nucleobases as Low-molecular-weight hydrogelators

The supramolecular assembly of commonly available biomolecules into nanoscale materials often leads to functional systems with novel and advanced properties. Nucleobases, nucleotides, and nucleotides are building blocks of nucleic acids and are important components in the natural system. These classes of materials are considered versatile bioentity for the generation of functional nanomaterials, owing to their fundamental diversity, availability of multiple binding sites, self-assembly properties, biocompatibility, and chirality.

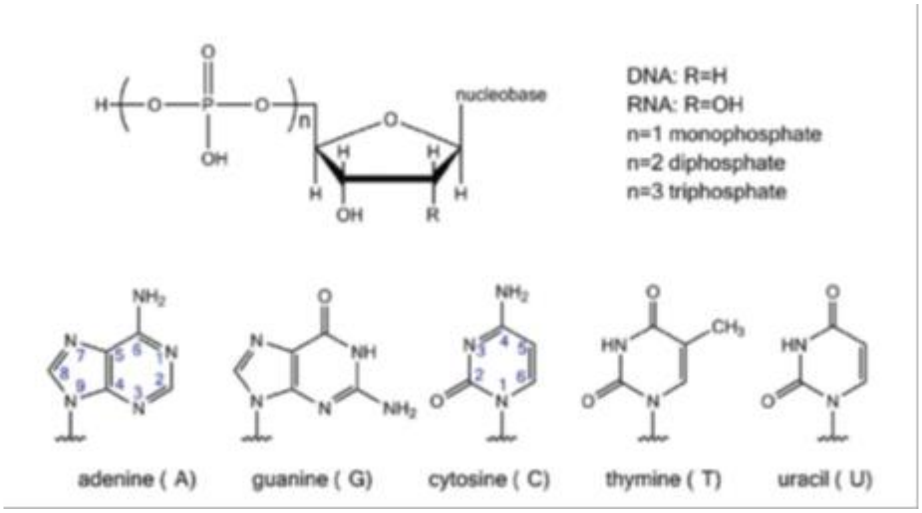

Figure 1.3. Chemical structure of nucleobases, nucleosides, and nucleotides.

The supramolecular self-assembly of the nucleic acids into the double helical structure through A-T and G-C base pairs forms the fundamentals of molecular self-assembly in nature. Further, the self-assembly of guanine monophosphate into a quadruplex structure in presence of alkali metal ions (G-quadruplex) or i-motif formation of cytosine in the acidic environment is prevalent in natural systems. Along with these hydrogen-bonding interactions, nucleobases have several metal-binding sites. For example, N6 from the amino, N1, and N3 on the pyrimidine ring, and N7 and N9 on the imidazole ring are preferential interacting positions in adenine. Similarly, N1, N7, and O6 of guanine are the probable sites for metal coordination. In the pyrimidine bases, cytosine, thymine, and uracil, metal ions preferentially bind to N3. Along with this, in the nucleotides, the phosphate groups can have extensive interaction with metal ions through interaction with Lewis acid/base. Indeed the different binding interactions with the nucleotides will depend on the characteristics of metal ion [46-50].

There are several reports of amorphous coordination polymer particles formed through the interaction of metal ions with nucleotides. However, the production of coordination polymer hydrogels formed by the interaction of metal ions with nucleotides is rather limited. Dash *et. al*. proposed that the interaction of Ag^+ with GMP led to the formation of a supramolecular hydrogel at neutral pH, and fibril networks were formed through Ag-GMP dimer formation. Liu *et. al*. reported the formation of a supramolecular hydrogel through the interaction of Zn^{2+} with AMP. The hydrogelation was highly selective for AMP as the interaction of Zn^{2+} with ADP or ATP led to the formation of only white precipitates. The results suggested that the binding of the metal ion with both the nucleobase and the phosphate moiety is essential for the hydrogel formation. The interaction of Ag^+ with inosine monophosphate led to the formation of a mechanically robust, self-healable, stimuli-responsive hydrogel that showed effective antibacterial properties. Further, the interaction of Fe^{3+} with GMP leads to the formation of a robust metallogel at room temperature, that can be used for the zero-order release of an anticancer drug [51-53].

The use of simple biomolecules as a hydrogelators is often advantageous for the construction of low-cost, biocompatible hydrogels under physiological conditions, that can be harnessed for several applications such as drug delivery, catalysis, conducting surface, sensing and other important applications. To synthesize coordination polymer hydrogel, first, we need rational LMWGs with a minimum of two metal ion binding sites. This metal ion binding influences the self-assembly to form 1D/2D/3D coordination polymers which further gather to produce the nanofibrous architecture **[Figure 1.4.]**.

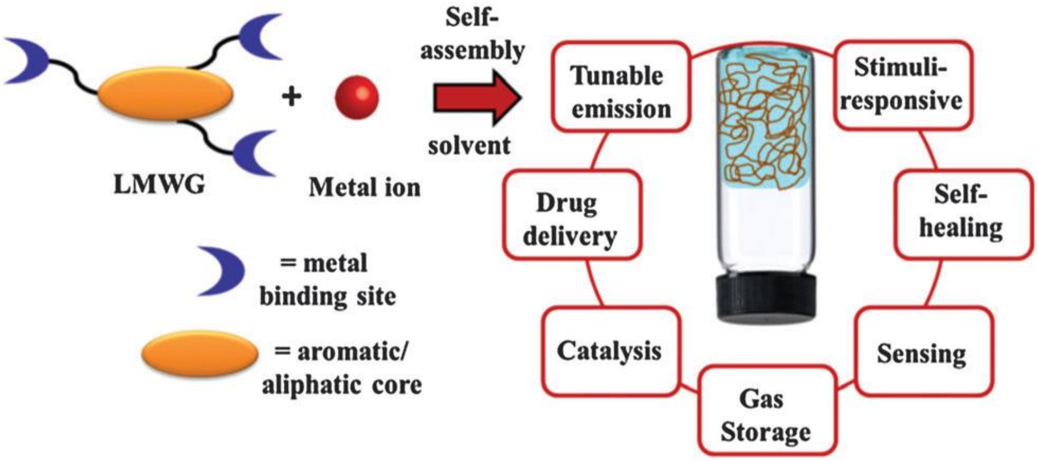

Figure 1.4. Schematic representation of synthesizing coordination polymer gels and their diverse applications.

Chapter 2

Review of the past work

2.1. Previous Reports

Cobalt is a transition metal that lies between nickel and iron in the 3d series of the periodic table. There are two oxidation states of cobalt (Co^{2+} and Co^{3+}) which occur naturally, but it can also show oxidation between -1 to +5. This is one of the rarest essential trace elements found in nature. It plays a crucial role in nutrition and is a key metal in vitamin B_{12} corrin macrocycle. In addition to corrin enzyme, non-corrin cobalt enzymes are becoming more active in both bioinorganic chemistry and biotechnology today, and its ease of access and exceptional flexibility make cobalt an amazing catalyst in the chemical industry (e.g. hydroformylation in oxo process). A novel protein with a cobalt transporter function has recently been found [55-58].

2.2. The objective of the Thesis

In this project, we report a novel Co^{2+}-containing coordination polymer hydrogel through the interaction of the metal salt with 5´-AMP as an organic component. Synthesis includes mixing of the aqueous solution of both the metal salt as well as 5´-AMP salt in the same molar ratio and heating the later solution at around 65 ºC. The methodology provides a simple pathway for the development of a mechanically robust supramolecular hydrogel for potential applications in catalysis and bioluminescence.

Chapter 3

Instrumentation and Experimental Section

3.1. Instrumentation

UV-visible investigations were carried out using a spectrophotometer from Varian Cary 100 Bio. Transmission electron microscopy (TEM) pictures were captured at an acceleration voltage of 200 kV on a Philips Cm 200 electron microscope. Field emission scanning electron microscopy (FESEM) pictures were captured on a Carl Zeiss Supra 55 instrument after successive mounting the glass slide with carbon. Atomic force microscopy (AFM) pictures were captured in tapping mode on smart SPM 10000, AIST-NT. Rheological investigations were carried out using an Anton Paar Physica MCR 301 rheometer by using 50 mm parallel plate geometry. Powder X-ray diffraction (XRD) studies of the xerogel were performed on a Rigaku Smartlab, Automated Multipurpose X-ray diffractometer with Cu Kα source (0.154 nm wavelength).

3.2. Instrumentation Techniques

3.2.1. Microscopic Studies

The gel samples were prepared in water for AFM, SEM, and TEM. A small quantity of gel was added in a centrifuge tube, and soon the water was also added, the gel was squeezed with a micro pestle. The dispersed samples were then dropped cast on a carbon-mounted copper grid (for TEM). For SEM, the samples were made by using the diluted gel, dropped cast on a glass slide, and dried in vacuum. For AFM, the samples of diluted gel were spin-mounted on a new freshly carved mica surface.

3.2.2. Rheological Studies

Rheological studies were performed using a 50 mm diameter parallel plate geometry. The hydrogel was placed on the plate of the rheometer using a spatula. The temperature was held at 298 K by using Julabo's integrated temperature regulator. Dynamic strain sweep investigations were carried out using a persistent frequency of 10 rad s^{-1}. The hydrogel's dynamic frequency sweep was calculated as a frequency function within the 0.05--100 rad s^{-1} range. To check the reliability, each investigation was performed thrice, and a mean value was used for discourse.

3.3. Experimental Section

3.3.1. Chemicals and Reagents

Adenosine 5’ monophosphate (AMP) disodium salt hydrate and Cobalt (II) Chloride hexahydrate were purchased from Sigma-Aldrich. During the experiments, Milli-Q water was used.

3.3.2. Synthesis of the Co: AMP Hydrogel

(0.1 M) stock solutions of AMP and Co^{2+} salts were prepared by dissolving them in milli-Q in separate vials. In another vial, 1mL of each of these solutions was added such that the ratio became 1:1 (v/v). The resultant solution was then pink in color. After heating it on a temperature of ~65 ºC for a minute, the solution was converted to a blue color gel which is evidenced through a physical test called inverse vial test, where the movement of liquid under the influence of gravity was observed in an inverted vial (**Figure 3.1.**).

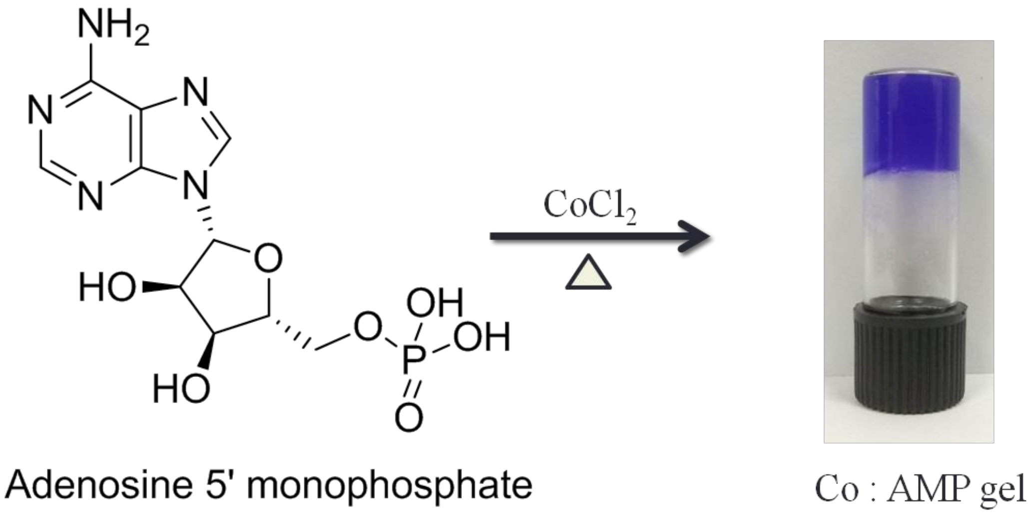

Figure 3.1. Steps to synthesize Co: AMP hydrogel.

Chapter 4

Results and Discussion

4.1. Optimization and Characterization of Hydrogel

The synthesis of coordination polymer hydrogel was carried out using Co: AMP salt aqueous solutions mixed in the molar ratio of 1:1 at a temperature of 65 ºC (approx). We have also used other transition metal salts such as Ni^{2+} and Cu^{2+} with AMP, IMP, GMP, separately under all physiological conditions but it did not result in any hydrogelation. As we know purines have electron-rich oxygen and nitrogen sites present in them, Cobalt must have been binding to one of those and to confirm that several other experiments were carried out. In our first experiment, we took adenine as gelator, and by using the same molar ratio, we mixed both aqueous salt solution but nothing happened. Then, in the second experiment, we took adenosine (keeping the same molar ratio) but no gelation was observed in that too. Until now, it confirmed that neither oxygen nor nitrogen was taking part in bonding with cobalt. Finally, we took ATP (again keeping the molar ratio the same) but that did not result in the hydrogel formation either. From all those, experiments we can conclude that it might be due to the one phosphate group (present in 5′-AMP) which is binding to the metal through electrostatic interactions. $CoCl_2$ (100 mM) aqueous solution was added to an aqueous solution of AMP (100 mM) in a 1:1 molar ratio (v/v) and upon heating results in the hydrogel generation. The production of hydrogel was evident by the inverted vial test. The lowest concentration for the gel to be formed was observed to be 50 mM.

4.1.1. Morphology and structural characterization

The morphological studies of the Co:AMP gel was done by practicing many microscopic techniques. Scanning electron microscopy (SEM) pictures of the vacuum-dried gel displayed the generation of highly twisted nanofibers (**Figure 4.1.**). Transmission electron microscopy (TEM) pictures of the hydrogel unveiled the 3-D thread-like network (**Figure 4.2.**), that has acquired a length of some hundred nm. Atomic force microscopy (AFM) studies were performed by scanning of dropped cast hydrogel solution which disclosed that the gel consists of an interlinked fibrous network with an average height of 2 nm (**Figure 4.3.**).

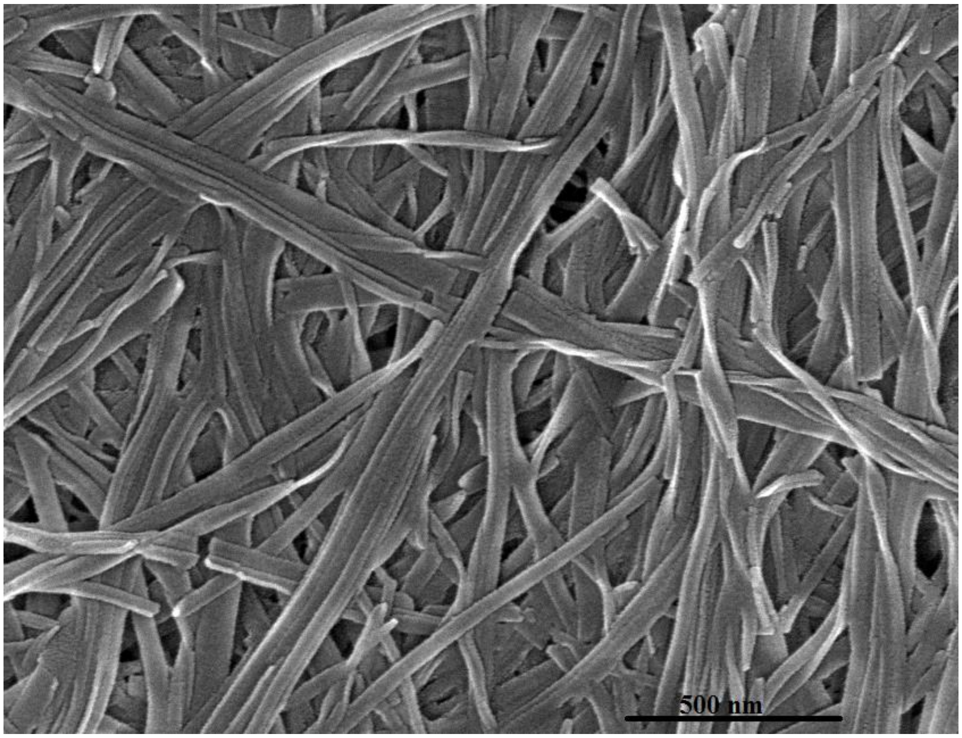

Figure 4.1. SEM images of the synthesized coordination polymer hydrogel.

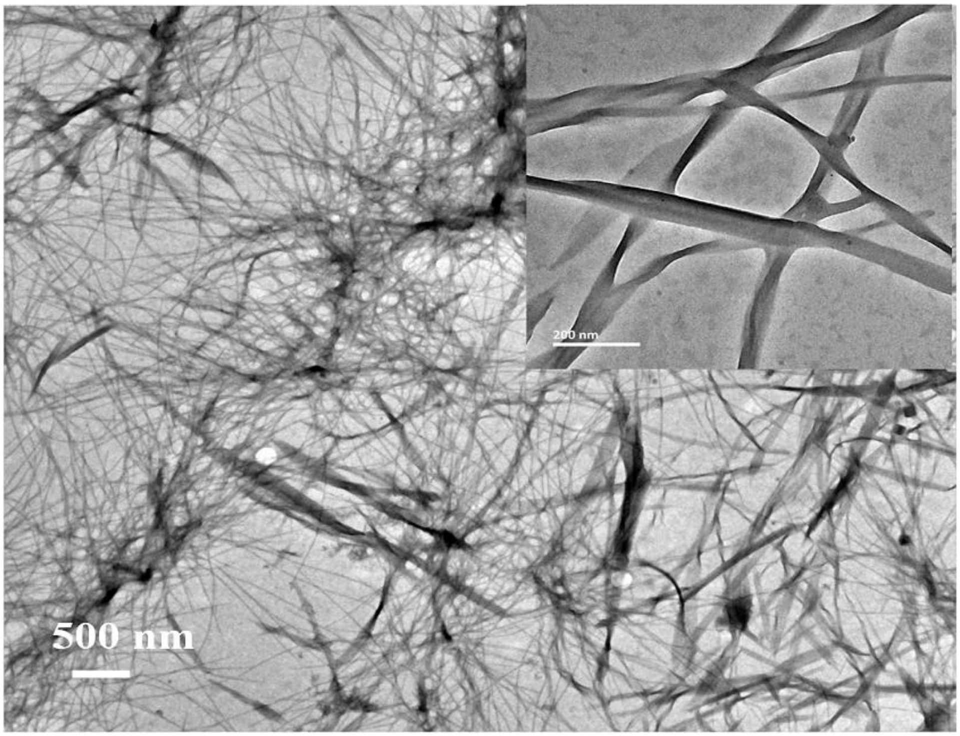

Figure 4.2. TEM images of the synthesized coordination polymer hydrogel.

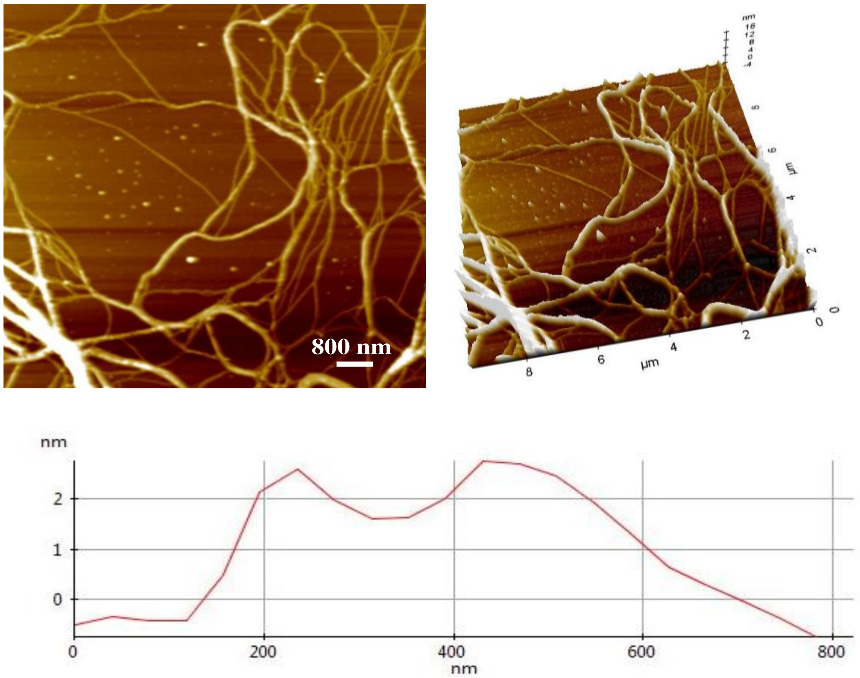

Figure 4.3. AFM images of the synthesized coordination polymer hydrogel.

The Co: AMP gel was found to be stable at room temperature for several months. This hydrogel can also be synthesized on a large scale by following a similar procedure. At high temperatures, this gel also performed well, as it didn't disintegrate easily and endure up to 90 ℃ without any visual change on its appearance, which most of the gels cannot.

4.1.2. Spectroscopic Characterization

UV-visible investigations were performed to acknowledge the bonding of Co^{2+} ions with 5′-AMP. A definite bathochromic shift or redshift at max absorption wavelength (510 nm) can be observed after coordination with AMP (**Figure 4.4.**). From the UV-visible data interpretation, it could be presumed that the changes in absorptions intensities might be due to the formation of a hydrogel. Also, change in color occurs due to metal to ligand charge transfer A graph was plotted using Job's method, a method of continuously varying the concentration to determine the stoichiometry, from UV at 510 nm of wavelength at various Co^{2+} to AMP ratios suggested a stoichiometry of 1:1 (v/v) molar ratio (**Figure 4.5.**). From the powder X-ray diffraction pattern of the xerogel (freeze-dried), a sharp peak can be observed at 2θ = 31.22° (d = 0.283 nm), which suggests an ordered arrangement in the gel (**Figure 4.6.**)

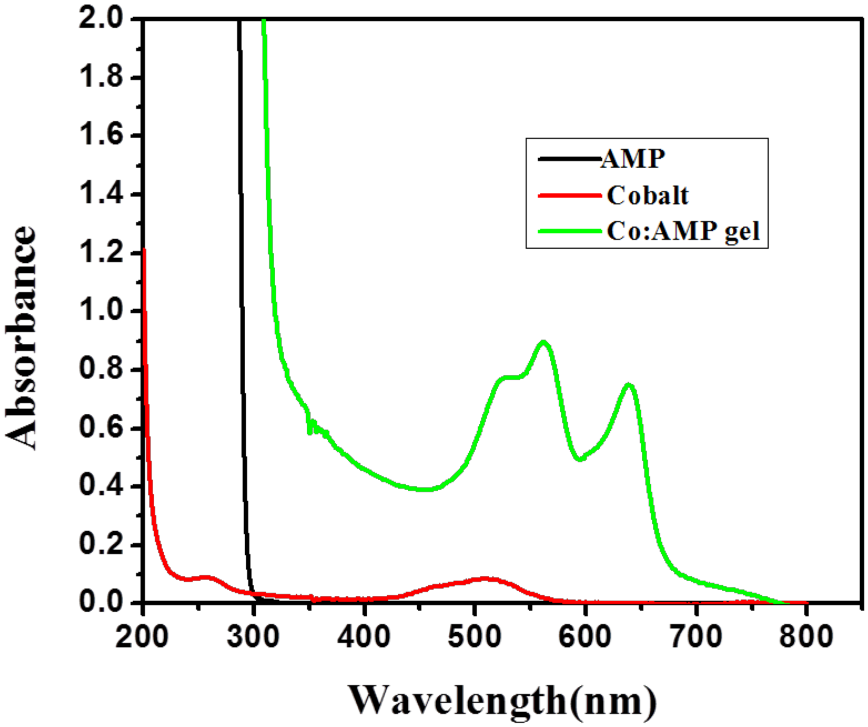

Figure 4.4. UV-visible spectra of the synthesized hydrogel.

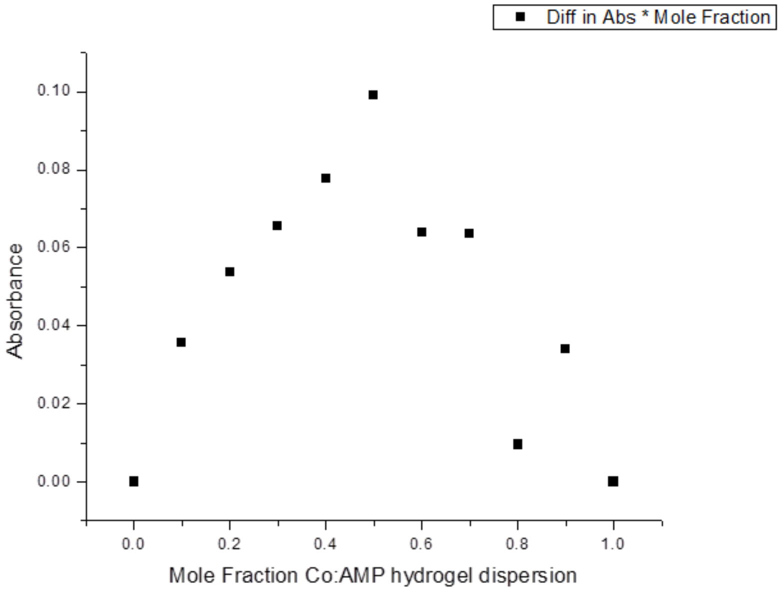

Figure 4.5. Job's plot of the hydrogel dispersion.

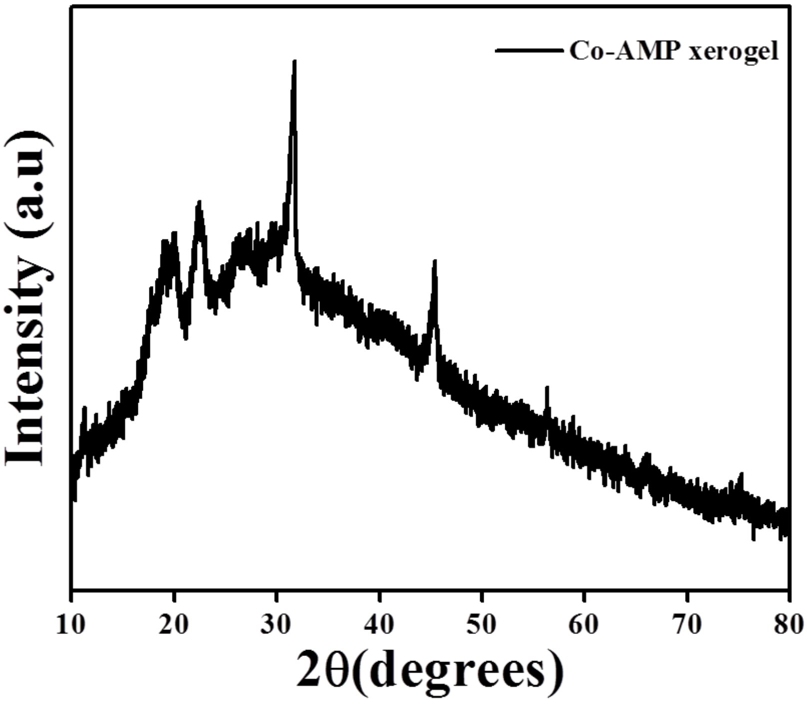

Figure 4.6. Powder XRD pattern of freeze-dried Co: AMP.

4.1.3. Rheological Analysis

To understand the visco-elastic property and mechanical robustness of the gel, these experiments were performed. In the first experiment or strain sweep experiment (**Figure 4.7.**), it can be observed that the magnitude of storage modulus, G´ was greater than the loss modulus, G´´ by various orders indicating that the elastic behavior is more pronounced in the gel as compared to the viscous behavior of the gel. In the second experiment or frequency sweep experiment (**Figure 4.8.**), which additionally proved that the elastic behavior dominates the viscous behavior of gel.

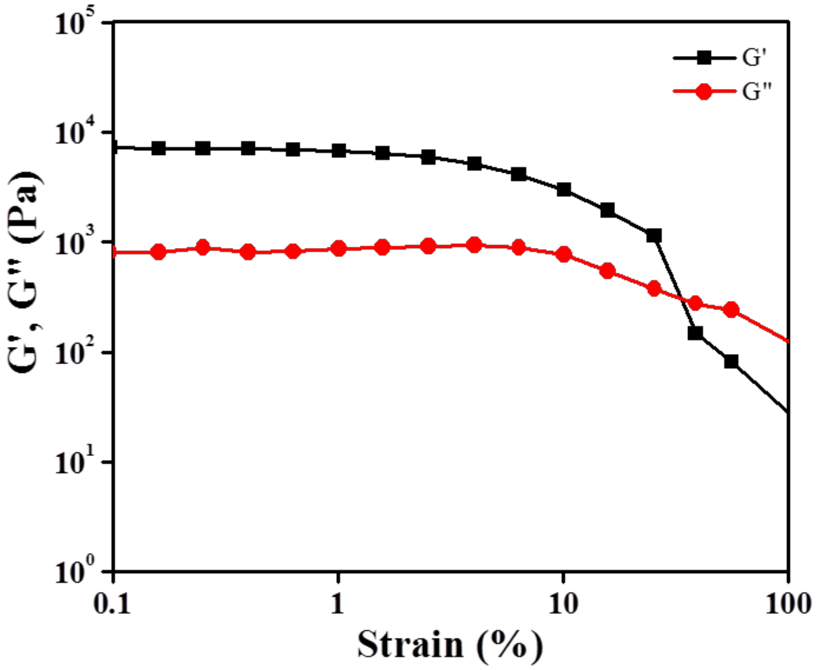

Figure 4.7. Dynamic strain sweep of Co: AMP hydrogel.

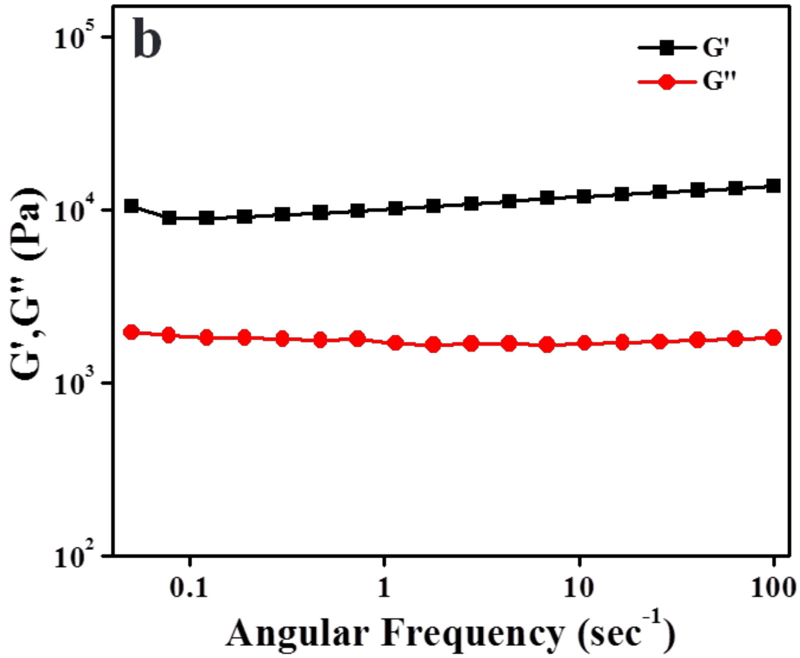

Figure 4.8. Dynamic frequency sweep of Co: AMP.

4.2. Application of synthesized Co: AMP hydrogel

4.2.1. Esterase activity:

An assay can be performed to confirm the esterase activity using a simple chromogenic substrate p-nitrophenyl acetate (p-NPA), confirmation of activity is being done by detecting the appearance of a yellow color hydrolyzed product i.e., p-nitrophenolate (p-NP) in a standardized solution using tris-HCl buffer (25 mM, pH = 7). Further confirmation can be done by observing the increase in absorption at 400nm.

A similar assay was performed with the synthesized gel and a decrease in absorption was observed which certainly means the failure of the application part (**Figure 4.9.**). However, soon we will be looking towards some other applications.

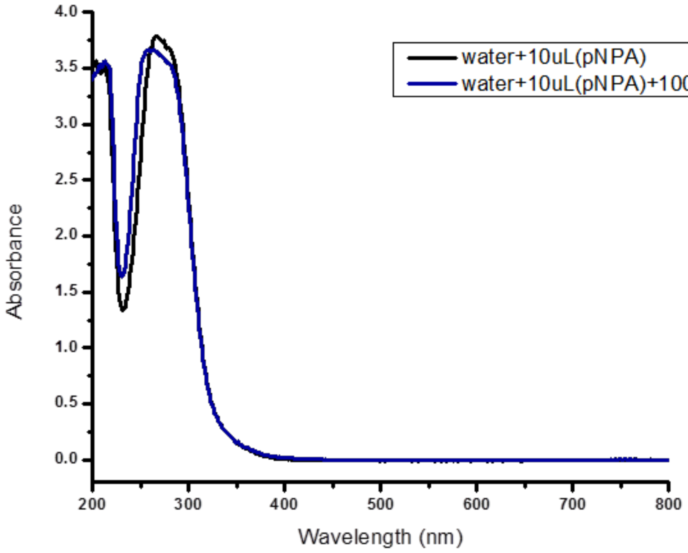

Figure 4.9. Absorption spectra of esterase activity.

CONCLUSION

In summary, adenosine 5′ monophosphate worked as a hydrogelator to produce a metallogel by coordinating with Co^{2+} ions. The metallogel was synthesized simply by mixing the two components and heating the latter solution, which suggests the effectiveness of naturally occurring small biomolecule to incorporate into the complex supramolecular structure through the indulgence of noncovalent interactions that are present between the heterocycles of nucleotide and Co^{2+} metal ions. Forces of interactions, such as electrostatic interaction, hydrogen bonding, π-π stacking as well as the van der Waals interactions constructively combine to form the self-assembled fibrillar nano-hybrid Co:AMP hydrogel, attributed by the spectroscopic studies. The microscopic studies confirmed the existence of highly entangled fibrillar morphology of Co:AMP hydrogel network, showing the capability of a fibrous network to hold the bulk solvent molecules within the gel matrix. The Co:AMP metallogel showed good mechanical stability. However, the application part was a failure but due to the hybrid nature of the gel and various functional properties, it can be used in many other applications. The robustness and potential enzyme-mimicking features of Co metal ions might enhance the applicability of this soft hybrid hydrogel, in combination with the low cost and biocompatible small biogelator 5'-AMP. The development of such a metal-organic nano-hybrid hydrogel system with enhanced versatility may present promising applications in the biological fields.

REFERENCES

[1] Chen X., Wang Y., Liu Q., Zhang Z., Fan C. and He L. (2006) Construction of molecular logic gates with a DNA-cleaving deoxyribozyme, *Angew. Chem. Int. Ed*, **45**, 1759-1762.

[2] Li T., Wang E. and Dong S. (2009) Potassium-lead-switched G-quadruplexes: A new class of DNA logic gates, *J. Am. Chem. Soc*, **131**, 15082-15083.

[3] Li J. R., Sculley J. and Zhou H. C. (2012) Metal-organic framework for separation, *Chem. Rev*, **112**, 869-932.

[4] Liu B. (2012) Metal-organic framework based devices: separation and sensor, *J. Mater. Chem*, **22**, 10094-10101.

[5] Ma L. and Lin W. (2010) Designing metal-organic frameworks for catalytic applications, *Top. Current. Chem*, **293**, 175-205.

[6] Corma A., Garcia H. and Llabres I Xamena. (2010) Engineering metal-organic frameworks for heterogeneous catalysis, *Chem. Rev*, **110**, 4606-4655.

[7] Yoon M., Srirambalagi R. and Kim K. (2012) Homochiral metal-organic frameworks for asymmetric heterogeneous catalysis, *Chem. Rev*, **112**, 1196-1231.

[8] Long D. L., Tsunashima R. and Cronin L. (2010) Polyoxometalates: Building blocks for functional nanoscale system, *Angew. Chem. Int. Ed*, **49**, 1736-1758.

[9] Langer R. and Tyrrell, D. A. (2004) Designing materials for biology and medicine, *Nature*, **428**, 487–492.

[10] Zweep N. and Van Esch J. H. (2014) Functional molecular gels, Royal Society of Chemistry. pp. 1-29.

[11] Weiss R. G. and Terech P. (2006), Molecular gels, materials with self-assembled fibrillar networks, ed, Springer Dordrecht, The Netherlands.

[12] Nishinari K. and Tokita M. (2009) In gels: structures, properties and functions, *Springer*, **136**, 87-94.

[13] Hirst A. R., Escuder B., Miravet J. F. and Smith D. K. (2008), High-tech applications of self-assembling supramolecular nanostructured gel-phase materials: from regenerative medicine to electronic devices, *Angew. Chem. Int. Ed*, **47**, 8002-8018.

[14] Skilling K. J., Citossi F., Bradshaw T. D., Ashford M., Kellam B. and Marlow M. (2014) Insights into low molecular mass organic gelators: a focus on drug delivery and tissue engineering applications, *Soft matter*, **10**, 237-256.

[15] Liu X. Y. and Li J. L. (2013) Soft fibrillar materials: fabrication and application, ed. Wiley-VCH, Weinheim.

[16] Peters G. M. and Davis J. T. (2016) Supramolecular gels made from nucleobase, nucleoside and nucleotide analogs, *Chem. Soc. Rev*, **45**, 3188-3206.

[17] Sangeetha N. M. and Maitra U. (2005) Supramolecular gels: functions and uses, *Chem. Soc. Rev*, **34**, 821-836.

[18] Loose M. de., Feringa B. L. and Van Esch J. H. (2005) Design and application of self-assembled low molecular weight hydrogels, *Eur. J. Org. Chem*, 3615-3631.

[19] Van Esch J. H. (2009). We can design molecular gelators, But do we understand them?, *Langmuir*, **25**, 8392-8394.

[20] Yu G., Yan X., Han C. and Huang F. (2013) Characterization of supramolecular gels, *Chem. Soc. Rev*, **42**, 6697-6722.

[21] Buerkle L. E.and Rowan S. J. (2012) Supramolecular gels formed from multi-component low molecular weight species, *Chem. Soc. Rev*, **41**, 6089-6102.

[22] Estroff L. A. and Hamilton A. D. (2004) Water gelation by small organic molecules, *Chem. Rev*, **104**, 1201-1218.

[23] Raeburn J. and Adams D. J. (2015) Multicomponent low molecular weight gelators, *Chem. Commun*, **51**, 5170-5180.

[24] Steed J. W. (2011) Supramolecular gel chemistry: developments over the last decade, *Chem . Commun*, **47**, 1379-1383.

[25] Weiss R. G. (2014) The past, present, and future of the molecular gels. What is the status of the field, and where is it going?, *J. Am. Chem. Soc,* **136**, 7519-7530.

[26] Abdallah D. J. and Weiss R. G. (2000) Organogels and low molecular mass organic gelators, *Adv. Mater*, **12**, 1237-1347.

[27] Escuder B. and Miravet J. F. (2014) Functional molecular gels, ed. Royal Society of Chemistry, Cambridge.

[28] Lu L. and Weiss R. G. (1996) New lyotropic phases (thermally-reversible organogels) of simple tertiary aminesand related tertiary and quaternary ammonium halide salts, *Chem. Commun*, **17**, 2029-2030.

[29] Menger F. M., Seredyuk V. A., Apkarian R. P. and Wright E. R. (2002) Colloidal assembly of branched geminis studied by cryo-etch-HESEM. High-resolution scanning electron microscopy, *J. Am. Chem. Soc*, **124**, 12408-12409.

[30] Menger F. M., Zhang H., Caran K. L., Seredyuk V. A. and Apkarian R. P. (2002) Gemini-induced columnar jointing in vitreous ice. Cryo-HRSEM as a tool for discovering new colloidal morphologies, *J. Am. Chem. Soc,* **124**, 1140-1141.

[31] Berthier D., Buffeteau T., Leger J. M., Oda R. and Hue I. (2002) The design of molecular gelators, *J. Am. Chem. Soc*, **124**, 13486-13494.

[32] Shankar B. V. and Patnaik A. (2007) A new pH and thermo-responsive chiral hydrogel for stimulated release, *J. Phys. Chem, B*, **111**, 9294-9300.

[33] Fages F., Vogtle F. and Zinic M. (2005) Systematic design of amide and urea type gelators with tailored properties, *Top. Curr. Chem*, **256**, 77-131.

[34] Biginn U., Sheiko S. and Moller M. (2000) Molecular gels: nanostructured soft materials, *Macromol. Chem. Phys*, **201**, 1008-1015.

[35] Schoonbeek F. S., Van Esch J. H., Hulst R., Kellogg R. M. and Feringa R. L. (2000) Geminal bis-ureas as gelators for organic solvents: gelation properties and structural studies in solution and in the gel state, *Chemistry*, **6**, 2633-2643.

[36] Loos M. de., Lightenbarg G. J., Van Esch J. H., Kooijman S., Spek A. L., Hage R., Kellogg R. M. and Feringa B. L. (2000) Tripodal tris-urea derivatives as gelators for organic solvents, *Eur. J. Org. Chem*, **22**, 3675-3678.

[37] Hirst A. R. and Smith D. K. (2005) Dendritic gelators, *Top. Curr. Chem*, **256**, 237-273.

[38] Soler M. and Newkome G. R. (2012) In supramolecular chemistry: from molecules to nanomaterials, ed. Gale P. A. and Steed J. W. John Wiley and Sons, pp. 3283-3319.

[39] Abdallah D. J. and Weiss R. g. (2000) n-alkanes gel (many other organic liquids), *Langmuir*, **16**, 352-355.

[40] Babu S. S., Praveen V. K. and Ajayaghosh A. (2014) Functional π-gelators and their gelators, *Chem. Rev*, **114**, 1973-2129.

[41] Yagai S. (2011) In supramolecular soft materials, ed. Nakanishi T., John Wiley and Sons, Hoboken, New Jersey, pp. 77-95.

[42] Piepenbrock M. M., Lloyd G. O., Clarke N. and Steed J. W. (2010) Metal and anion binding supramolecular gels, *Chem. Rev*, **110**, 1960-2004.

[43] Halder R., Matsuda R., Kiagawa S.,George S. J. and Maji T. K. (2014) Amine-responsive adaptable nanospaces: fluorescent porous coordination polymer for molecular recognition, *Angew. Chem. Int. Ed,* **126**, 11966-11971.

[44] Sikdar N., Jayaramulu K., Kiran V., Rao K. V., Sampath S., George S. J. and Maji T. K. (2015) Redox-active metal-organic frameworks: highly stable charge-separated states through strut/guest-to-strut electron transfer, *Chem. Eur. J*, **21**, 11701-11706.

[45] Hazra A., Gurunatha K. L. and Maji T. K. (2013) Charge-assisted soft supramolecular porous frameworks: effect of external stimuli on structural transformation and adsorption properties, *Cryst. Growth Des*, **13**, 4824-4836.

[46] Araki K. and Yoshikawa I. (2005) Nucleobase-containing gelators, *Top. Curr. Chem*, **256**, 133-165.

[47] Saenger W. (1984) Principles of Nucleic acid structure. Springer-Verlag, New York.

[48] Blackburn G. M., Gait M. J., Loakes D. and Williams D. M. (2006) Nucleic acids in chemistry and biology, ed. Royal Society of Chemistry, Cambridge.

[49] Davis J. T. (2004) G-quartets 40 years later: from 5′-GMP to molecular biology and supramolecfular chemistry, *Angew. Chem. Int. Ed*, **43**, 668-698.

[50] Balasubramanian S. and Neidle S. (2006) Quadruplex nucleic acids, Royale Society of Chemistry, Cambridge.

[51] Thakur N., et al. (2018) Multifunctional ionosine monophosphate coordinated metal-organic hydrogel: multistimuli responsiveness, silf-healing properties and separation of water from organic solvents, *ACS Sustainable Chem. Eng*, **6**, 8659-8671.

[52] Liang H., Zhang Z., Yuan Q. and Liu J. (2015) Self-healing metal-coordinated hydrogels using nucleotide ligands, *Chem. Commun*, **51**, 15196-15199.

[53] Das R. N., Kumar Y. P., Pagoti S. and Dash J. (2012) Diffusion and birefringence of bioactive dyes in a supramolecular guanosine hydrogel, *Chem. Eur. J*, **18**, 6008-6014.

[54] Kumar A. and Gupta S. K. (2013) Synthesis of 5′-GMP-mediated porous hydrogelcontaining β-FeOOH nanostructures: optimization of its morphology, optical and magnetic properties, *J. Chem. Mater. B*, **1**, 5818-5830.

[55] Kobayashi M. and Shimizu S. (1999) Cobalt-proteins, *Eur. J. Biochem*, **261**, 1-9.

[56] Battersby A. R. (1993) Biosynthesis of vitamin B_{12}, *Acc. Chem. Res*. **26**, 15-21.

[57] Pino P., Piacenti F. and Bianchi M. (1977) Reactions of carbon monoxide and hydrogen with olefinic substrates: the hydroformylation (OXO) reaction, In *organic synthesis via Metal Carbonyls*, **2**, 43-135.

[58] Komeda H., Kobayashi M. and Shimizu S. (1997) A novel transporter involved in cobalt uptake, *Proc. Natl Acad. Sci*, **94,** 36-41.