



Metallopharmaceuticals Compound -Past Lessons And Future Directions - A Review

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Article History	Abstract:
Received: 3 Oct 2023 Revised: 8 Nov 2023 Accepted: 5 Dec 2023	This article is an overview that discusses the history, chemistry, synthesis, prospects, and applications of Schiff bases and related metal compounds. This provides an update on recent facts regarding Schiff's performance, which consisted of a variety of challenging elements. The field of therapeutic inorganic chemistry lies at the crossroads of medicine and inorganic chemistry. It consists of metal-based drugs, professionals who can sequester and mobilise metal, and demonstrative aids that contain metal. Drugs that are formed of organometallic compounds have been used for the treatment of a wide variety of ailments for many years. At the level of individual atoms, the following metal elements play significant roles in the architecture of living organisms: When antimicrobial drugs interact with particular metal particles, the drugs might become more effective against microbes. It is possible to enhance the activity of bioactive molecules by utilising coordination compounds that contain metal. In this article, several different applications of metals in biological systems will be discussed in depth.
CC License CC-BY-NC-SA 4.0	Keywords: Inorganic- Metal complexes, Metallopharmaceuticals, Biological activity, Bio-ligands, etc.

1. Introduction

This review comprehensively analyzes the history, chemistry, synthesis, prospect, and applications of Schiff bases and their metal compounds. The analysis is based on current research in the field. This review also provides an update on new knowledge in the performance of Schiff had a few complexes. [1] Ligand photo dissociation also provides an approach to selective drug delivery. [2]. Therapeutic inorganic chemistry is at the interface between medication and inorganic chemistry and incorporates metal-based drugs, metal sequestering and mobilizing specialists and metal-containing demonstrative helps [3]. Within the early precise consideration of metals in medication (amid the early to center portion of the twentieth century), acknowledgment of the

essentiality of a few metal particles (e.g. press, zinc, and copper) for the evasion of lack of illness was a major step forward. Not as it were several, metal particles fundamental supplements, but numerous are to getting to be progressively predominant components of demonstrative or restorative operators to ponder or treat a wide assortment of infections and metabolic disarranges [4,5]. The list of metal ions is advisable for every basic circumstance requisite to be completed. It does not consist of elements such as zinc, copper, and manganese as conventional but Also, many elements a certain act once treated as harmful, such as selenium and molybdenum [6, 7]. Unprecedented competition such as arsenic, nickel, silicon, and vanadium are on the "to be important" list. [8,9]. Organometallic compounds have been used as medicines to treat various ailments for centuries. Metal complexes are essential to the pharmaceutical and agricultural industries. At the atomic level, the following metal elements are significant in biological structures. [10] The moving metal particles account for how proteins typically operate. In order to attain various modes of action, biometals form complexes with distinctive bioligands shown in Fig.1. The thermodynamic and motor characteristics of the complex determine its organic activity. Due to the medication's capacity to access the site of action, the chelate structure enhances the lipophilicity of the drug and, generally, boosts pharmacological activity. [11,12] Compared to free ligands, the interaction of antimicrobial drugs with different metal particles might increase the efficiency of such substances. This has prompted fresh study into antibacterial agents, including the investigation of contemporary ones, the development of current ones utilizing contemporary tools and techniques, or the modification and redefinition of historical ones. [13]

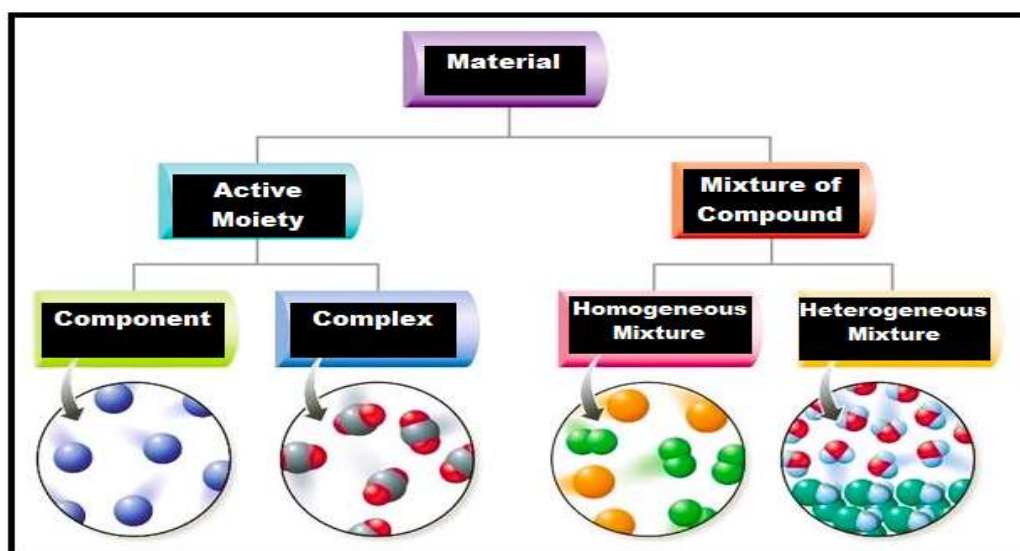


Fig.1 Diagrammatic presentation of various sources of metal compound

A metal complex is a complex with any metal compound. Metal complexes have a central metal atom (or) ion attached to an anion called a ligand. A connection with links is called a link. Metals are positively charged Lewis acids and form hydrating compounds when dissolved in water. [14] Metal ions form bonds with ligands in some processes in biological systems, oxidation, and reduction. Iron is an essential element in living organisms, which plays an important role in all cells. [15]. Iron is mainly used to transport oxygen in the blood and tissues. An adult consumes 250 ml of fresh air per minute. This oxygen is transported by siderophores called heme. The heme group is a metal complex with iron as the central metal atom, which can bind and release molecular oxygen.

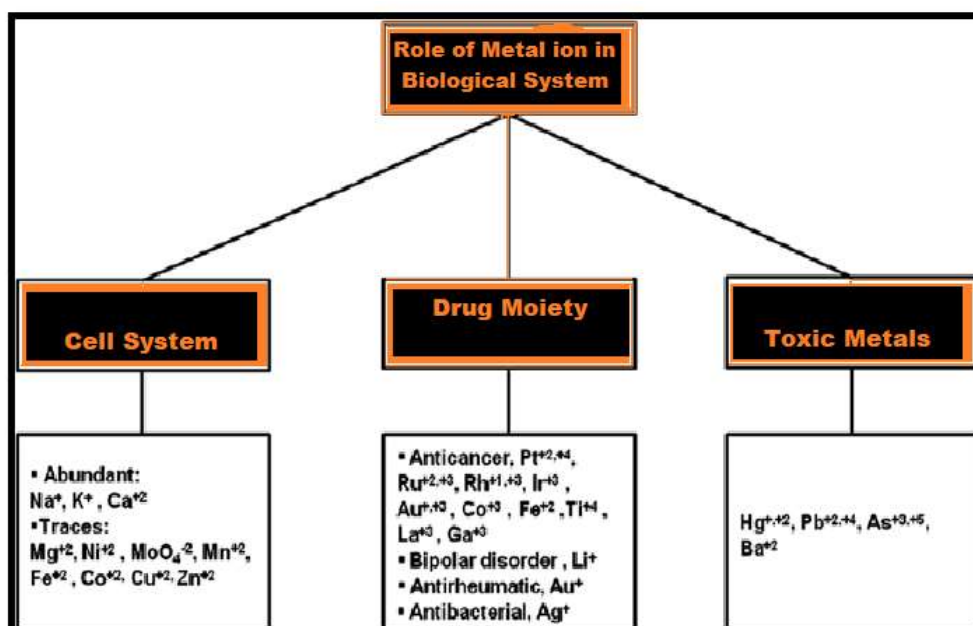


Fig.2 flow diagram represents the metal ion in a biological system

2. Metal Complexes in the Treatment of Cancer:

Treatment using metal complexes in medicinal chemistry, cancer, and leukemia has been reported since the 16th century. an inorganic substance. The CISPLATIN complex was discovered in 1960; It is still one of the world's best-selling anti-inflammatory drugs today. Complexes with other metals such as Cu, Au, Ga, Ge, Sn, Ru, Rh, and Ir have been shown to be beneficial for animals shown in Fig.2. Many recent developments provide new targets for anti-cancer drugs by forming DNA inserts with cancer cells and inhibiting DNA replication. However, it also affects the normal body such as hair follicles and intestinal mucosa. Various methods have been used to improve these outcomes by reducing side effects, avoiding drug use, and increasing efficiency. [16]. Drugs are coupled with porphyrin rings to enhance their anti-tumor activity. Titanium complexes and gold complexes also have important functions in the immune system. Ruthenium compounds containing arylsopyridine ligands exhibit cytotoxic activity in the treatment of ovarian cancer shown in Fig.3. Metal complexes in the form of nanoshells are currently used to treat many types of cancer [17].

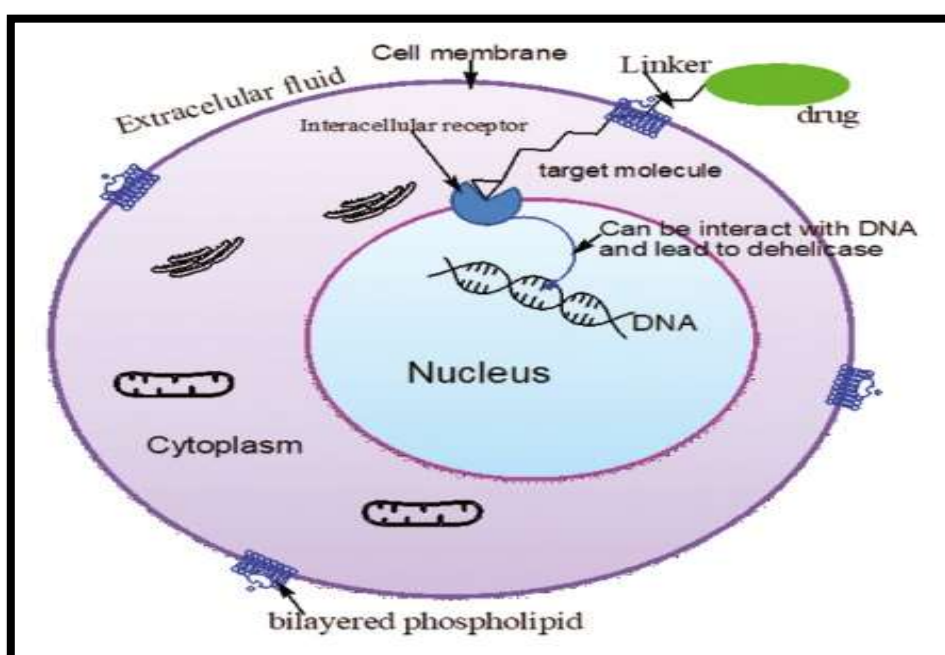


Fig.3 Diagram represents the Metal Complexes in Target-Specific Anticancer Therapy[18]

3. Metal Complexes in Treatment of Neurological Disorder

Iron complexes also play an important role in the treatment of various diseases of the nervous system. Complexes of lithium molecules and drugs can treat many neurological diseases such as Huntington's disease, Parkinson's disease, organic brain disorders, epilepsy, and stroke. Other transition metals, such as copper and zinc, are involved in signaling pathways in neurons [19].

4. Metal Complexes for Diabetes Treatment

Diabetes is a chronic disease caused by hyperglycemia, that is, hyperglycemia. Hyperglycemia is caused by a lack of insulin shown in Fig.4. Consumption of chromium metal complexes in diabetics may reduce blood sugar levels [20]. A new insulin-mimetic zinc(II) complex with different structures and hypoglycemic effects has been discovered for the treatment of type 2 diabetes in animals [21].

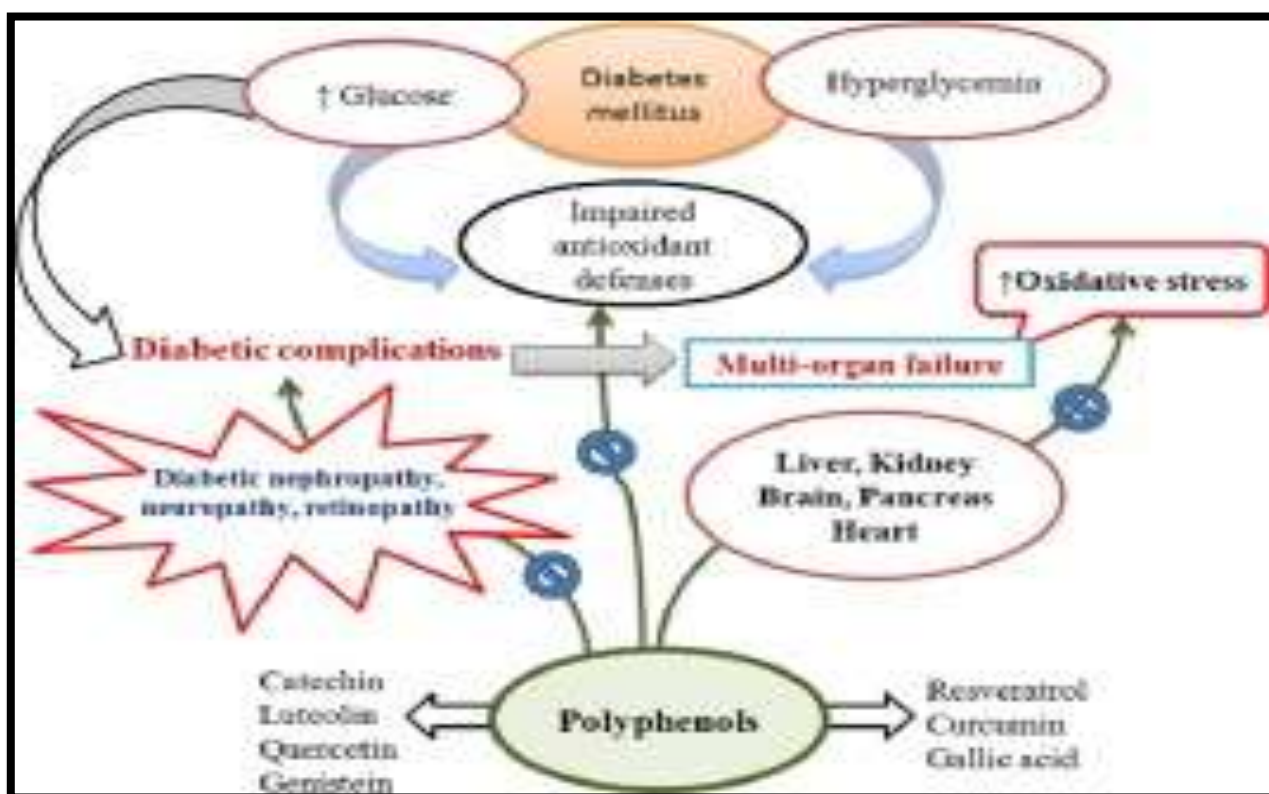


Fig.4 Complementary and alternative medicine for the treatment of diabetes and associated complications[22]

5. Schiff Bases Metal Complexes

Studies have shown that metal complexes reduce antibacterial activity compared to Schiff bases, which produce metals such as thallium, molybdenum, manganese, zinc, cadmium, copper, and silicon. Schiff bases such as pyridone, pyrrolidone, o-phenylenediamine and their metal complexes have good antibacterial properties [23]. Schiff bases containing metals such as arsenic, antimony, and bismuth showed antimicrobial activity against *A. niger* and *A. alternate*. Schiff bases and their metal complexes consisting of furan or furanglyoxal and amines have been shown to have antibacterial activity against various diseases [24]. Schiff bases and silver complexes have been found to have many antibacterial properties. Oxidized silver complexes have an inhibitory effect on cucumber mosaic disease [25]. Schiff bases and metal complexes have anti-inflammatory, anti-allergic, antioxidant and analgesic effects. Metal complexes of furan semicarbazone exhibit significant anthelmintic and analgesic activities [26]. Schiff base metal complexes have antifertility and enzymatic activity [27,28] Chromium imine complexes and Schiff base cobalt complexes are also used in leather, food packaging and wool dyeing [29,30].

6. Transition metals in Cosmetics

In hair, hair fibers are mostly used as cosmetics. Hair fiber is made up of about 85% of the complex protein keratin and about 7% of water. Other essential content: 3% lipids and 2% dyes. [31,32] This final amount is melanin, which is formed as a result of the biosynthesis of the amino acid tyrosine. In addition, many metals such as aluminum (Al) and calcium (Ca) and many transition metals (Zn) such as iron (Fe), manganese (Mn), magnesium (Mg), copper (Cu), chromium (Cr), zinc, For 100 g of hair, the latter is a very high level – 22 mg [33].

Conclusion

Metal complexes have reduced antibacterial activity compared to Schiff bases, which produce metals such as thallium, molybdenum, manganese, zinc, cadmium, copper, and silicon. Schiff bases and silver complexes have antibacterial properties, anti-inflammatory, anti-allergic, antioxidant and analgesic effects, and antifertility and enzymatic activity. Metal complexes administer a platform for the advancement of chemical compounds. Metal complexes have been used for medicinal chemistry, cancer, and leukemia since the 16th century, with cisplatin being one of the world's best-selling anti-inflammatory drugs. Recent developments provide new targets for anti-cancer drugs, but also affect the normal body. Key points and advancement of various approaches for metal complex synthesis are being designed. Although it has more side effects, it is still used in cancer treatment. Despite the modern achievement of the metal complex, it accepts a few adverse circumstances. Therefore, there must be a new way to affect these adverse circumstances.

Legend of Figure

S. No.	Figure	Caption
01	Figure 01	Diagrammatic presentation of various sources of metal compound
02	Figure 02	flow diagram represents the metal ion in a biological system
03	Figure 03	Diagram represents the metal complex in target specific anticancer-therapy
04	Figure 04	Complementary and alternative medicine for the treatment of diabetes and associated complications

CONFLICT OF INTEREST: The authors declare no conflict of interest

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References

- Boulechfar C, Ferkous H, Delimi A, Djedouani A, Kahlouche A, Boubliia A, Darwish A.S, Lemaoui T, Verma R and Y. Benguerba: Schiff bases and their metal Complexes: A review on the history, synthesis, and applications, *Inorganic Chemistry Communications* 2023; 150:110451.
- Sanjanwala D and Patravale V: Aptamers and nanobodies as alternatives to antibodies for ligand-targeted drug delivery in cancer, *Drug Discovery Today* 2023; 28:103550.
- Wang Y and Guo N: A new photoluminescent Zn(II) complex and its therapeutic effect on lung cancer, *Inorganic and Nano-Metal Chemistry* 2022; 1–6.
- L. H. Khoi, L. T. H. Thom and P. T. Tien, Components of the Space of Weighted Composition Operators Between Different Fock Spaces in Several Variables, *Mediterranean Journal of Mathematics*; 20 ;(2023).
- S. Bi, J. Qi, W. Zhang and X. Jiang, Liquid Metal Dressing for Anti-inflammation and Anti-infections to Treat Diabetic Wound, *Chemical Communications* (2023).
- M. Alwash and N. Jaber, Trace elements (selenium, copper and zinc) in de novo acute leukemia: serum levels and their relation with some clinical and laboratory parameters, *Iraqi Journal of Hematology* ;12; (2023); 105.

7. R. Katturajan and S. Evan Prince, L-carnitine and Zinc supplementation impedes intestinal damage in methotrexate-treated adjuvant-induced arthritis rats: Reinstating enterocyte proliferation and trace elements, *Journal of Trace Elements in Medicine and Biology* 78 (2023) 127188.
8. D. Valencia, Chemical bonding and aromaticity analyses of petroporphyrins with vanadium or nickel, *Fuel* ;**333**; (2023); 126344.
9. M. K. Wojnar, J. W. Ziller and A. F. Heyduk, Two-Electron Mixed Valency in a Heterotrimetallic Nickel–Vanadium–Nickel Complex, *Inorganic Chemistry* ;**62** ;(2023) 1405–1413.
10. M. M. Samra and M. A. R. Basra, Synthesis, spectroscopic, in vitro, in vivo biological evaluation, and in silico docking analysis of new meloxicam metal complexes, *Applied Organometallic Chemistry* ;**37** ;(2023).
11. X. Huang, Q.-K. Shen, H.-Y. Guo, Z.-S. Quan and X.-T. Li, Research, Development and Pharmacological Activity of Fusidic acid and its derivatives, *Journal of Molecular Structure* (2023) 135942.
12. M. A. Mahmood, Pharmacological Action of Taxifolin: A Review, *Open Access Journal of Pharmaceutical Research* ;**7**; (2023), 1-5
13. S. Mor and M. Khatri, Convenient synthesis of benzothiazoinoindol-11-ones and benzoindeno-thiazin-11-ones, and antimicrobial testing thereof, *Molecular Diversity*; **27** (2022); 1223–1241.
14. Complex parts from nature, *Metal Powder Report* ;**78**; (2023), 1-4.
15. SUZUKI, T. K. (2021). Biological Physics in Phenotypic Systems of Living Organisms. *Seibutsu Butsuri*, 61(1), 031–035. <https://doi.org/10.2142/biophys.61.031>
16. Mark Peplow, special to C&EN. (2021, May 16). Catalytic patch activates cancer drug while avoiding side effects. *Chemical & Engineering News*, 7–7.
17. Pak, V. (2022). Alpha-Fetoprotein Binds Toxins and Can Be Used to Treat Cancer. *Medical Research Archives*, 10(10).
18. Shumi, G., Desalegn, T., Demissie, T. B., Ramachandran, V. P., & Eswaramoorthy, R. (2022, May 17). Metal Complexes in Target-Specific Anticancer Therapy: Recent Trends and Challenges. *Journal of Chemistry*, 2022, 1–19. .
19. Hindawi, Shumi G, Desalegn T, et al. Metal Complexes in Target-Specific Anticancer Therapy: Recent Trends and Challenges [Internet]. *Metal Complexes in Target-Specific Anticancer Therapy: Recent Trends and Challenges*, 2022.
20. Kurdi, F., Abidin, Z., Priyanti, R. P., & Kholis, A. H. (2021, October 27). Management Of Diabetes Mellitus Type 2 For Elderly: Taichi Exercise To Reduce Blood Sugar Levels. *Nursing and Health Sciences Journal (NHSJ)*, 1(2), 112–117.
21. Once-Weekly Insulin for Type 2 Diabetes without Previous Insulin Treatment. (2021, February 25). *New England Journal of Medicine*, 384(8), e26.
22. Sharma, P., Hajam, Y. A., Kumar, R., & Rai, S. (2022, February). Complementary and alternative medicine for the treatment of diabetes and associated complications: A review on therapeutic role of polyphenols. *Phytomedicine Plus*, 2(1), 100188.
23. Preeti S., Younis Ahmad H., Rajesh K., Seema R; Complementary and alternative medicine for the treatment of diabetes and associated complications: A review on therapeutic role of polyphenols; *Phytomedicine Plus*, 2, 1, 2022, 100188.
24. Marshes Research Center, I., Kadhema, B., Alshawi, J., Kadhema, B., & Abdalla, M. (2021, December 12). Novel Schiff Bases Ligands and Their Complexes: Thermal Analysis, Antibacterial Activity, and Molecular Docking. *Egyptian Journal of Chemistry*, 0(0), 0–0.
25. Van de Walle T., Briand M., Mitrović A., Sosić I., Gobec S., Kos J., Persoons L., Daelemans D., De Jonghe S., Ubiparip Z., et al. Synthesis of Novel Nitroxoline Analogs with Potent Cathepsin B Exopeptidase Inhibitory Activity. *Chem. Med. Chem.* 15: ,(2020), 2477–2490
26. Schmiermund, T., Acid-Base Theories. In: *The Chemistry Knowledge for Firefighters*. Springer, Berlin, Heidelberg, (2023).
27. Irena Kostova, The Role of Complexes of Biogenic Metals in Living Organisms; *Inorganics*, 11(2), 56; (2023).
28. Çetin Z, Dede B. A novel Schiff base ligand and its metal complexes: Synthesis, characterization, theoretical calculations, catalase-like and catecholase-like enzymatic activities. *Journal of Molecular Liquids Elsevier BV*; 2023; 380, 121636.
29. Yin L, Zhang S, Zhou T, Zhen'guang H, Zhang S. Synthesis, characterization, and anticancer activity of mononuclear Schiff-base metal complexes. *Journal of Molecular Structure Elsevier BV*; 2023; 1275 : 134683
30. Malav R, Ray S. Carbon-carbon cross coupling reactions assisted by Schiff base complexes of Palladium, cobalt and copper: A brief overview. *Inorganica Chimica Acta Elsevier BV*; 2023; 551 :121478.

31. Bhandarkar SE, Pathare PP, Khobragade BP. New Nickel (II), Copper (II) and Cobalt (II) Complexes Based Salicylaldehyde Schiff Base: Synthesis, Characterisation, and Antiviral Activity. *Materials Today: Proceedings Elsevier BV*; 2023;1-5.
32. D. venkatachalam, A review on herbal cosmetics used in skin and hair care. *International Research Journal of Modernization in Engineering Technology and Science*; 2023;120-125.
33. Wei S, Hou X, Liu L, Tian Y, Li W, Xu H. Improving the Adsorption Properties of Keratin-Based Goat Hair Toward Reactive Dyes in Dyeing Wastewater by Steam Explosion. *Journal of Natural Fibers Informa UK Limited*; 2022; 20.
34. Manaka T, Otoshima A. Improving hydrogen embrittlement resistance of an Al-Zn-Mg-Cu alloy by retrogression and re-aging treatment. *Journal of Japan Institute of Light Metals Japan Institute of Light Metals*; 2023; 73 : 205–11.