

# Development of Functionalized Schiff Base Derivatives and Their Role in Advanced Organic and Medicinal Chemistry

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**Abstract-** Due to their straightforwardness in synthesis, controllable electronic properties, high coordination abilities, and extensive biological importance, Schiff base derivatives concentrate greater importance and expertise in the research of organic and medicinal chemistry. The present study article surveys literature up to January 2016 so as to examine the impact of trends in functionalization on the chemical behaviour and medical uses of Schiff base antecedents. The research design used in the study is structured secondary research with the 60 peer-reviewed references published up to the beginning of the year 2016. The coding of these articles was by year of publication, structural classification, functional group modification, the ability to form metal-complex, biological use, and profile of activity reported. This was to identify the dominant research themes, gauge the major research treatment and interpretive uses, and to determine whether structural functionalization and metal coordination accepted superior performance. It has been disclosed that since 2010 and 2015, there was an increase in the number of studies published on Schiff bases, along with the most widespread types of use in the field were antimicrobial, anticancer, antioxidant, enzyme inhibitory, and chemosensing purposes. Schiff bases based on heteroaryl, quinoline, quinazoline, isatin, triazole and coumarin were particularly noticeable. Metal-complexed Schiff bases were found to be more commonly linked with DNA interaction, cytotoxicity and redox-based activity whereas metal free versions were more common in antimicrobial and enzyme-inhibition studies. Electron-withdrawing groups, incorporation of heterocyclic rings and the use of donor atoms like nitrogen and oxygen were always used to enhance reactivity and biological potential. The paper concludes that functionalized Schiff base derivatives were widely used as molecular platforms with twist before 2016 in selecting synthetic organic chemistry and coordination chemistry and medicinal chemistry, and the development of multifunctional therapeutics, molecular probes and catalytic systems used after 2016 builds off their earlier development.

**Keywords –** Schiff base derivatives, functionalization, medicinal chemistry, organic synthesis, metal complexes, biological activity, chemosensors, pre-2016 literature.

## I. INTRODUCTION

Multiplication Schiff bases are compounds with an imine structure, usually developed by a condensation reaction of an amine (usually primary amine) and an aldehyde or a ketone. They have been essential compounds in organic chemistry, analytics chemistry, coordination chemistry and medicinal chemistry since decades due to their structural simplicity, synthetic convenience, and incredible adjustment (Dhar and Taploo, 1982; Qin et al., 2013). Schiff bases have azomethine group characteristics that render them chemically reactive and biologically relevant, whereas targeting reactions can occur by substantial modification of polarity, lipophilicity, redox

activity, target binding, and metal-binding capacity on intoxication with the aromatic or heteroaromatic D-ring (Abu-Dief and Mohamed, 2015; Kajal et al., 2014).

Schiff bases have been recognized to be used as final products, aged reagents, or lab material. In modern advanced organic chemistry, Schiff bases are treasured as the intermediate, ligand, and chromophores to work on and creating new cycles, fellowships, and supramolecular era (Qin et al., 2013). They have gained significant interest in medicinal chemistry since most of its derivatives have an antibacterial, antifungal, antitubercular, antioxidant, anti-inflammatory, antidiabetic, antiepileptic, and anticancer effects (Makawana et al., 2013; Rakesh et al., 2015; Rahim et al., 2015). More often,

heterocyclic polymorphs (including quinoline, quinazoline, benzimidazole, isatin, triazole, and coumarin) are used to increase activity by improving the electronic distribution and receptor-level interactions (Tehrani et al., 2013; Patil et al., 2015).

The high coordination ability is another key factor that gives Schiff bases a high level of scientific significance. Bidentate, tridentate, and tetradentate Schiff base ligands can easily form a complex with transition metals until obtain compounds with higher stability, redox activity, DNA-binding behavior, and cytotoxic potential (Tabassum et al., 2013; Paul et al., 2015). They are also used in metal coordination in the fields of catalysis, sensing, and bioinorganic chemistry (Abu-Dief & Mohamed, 2015). By January 2016, the literature demonstrated already that Schiff base chemistry was no longer restricted to easy synthesis of ligands; it had already become a multifunctional system relating with organic design, bioactivity optimization and biomaterials-based uses.

Nevertheless, the extensive amount of literature is dispersed in medicinal and structural subfields, as well as in the coordination and analytical subfields. A large number of papers had a very specific target or scaffold, whereas more general reviews had Hamilton-history Schiff bases, without converting trends in functionalizing them into a structured data-driven format. As such, a research paper that categorizes the literature review before 2016 in objectives, hypothesis, questions, methodology, findings, and discussion, is helpful in both writing an academic paper and developing a thesis.

The need of the current paper is to describe that need by researching 60 references published prior to January 2016 and generalizing their trends to form a universal research format. Instead of experimental work that was done in wet-labs, this study involves structured secondary analysis of researches published. The composition obtained includes the title, abstract, introduction, literature review, methodology, results, discussion, conclusion, references without excluding the inclusion of tables, ideas in the form of figures and data oriented explanation.

## II. LITERATURE REVIEW

According to the literature prior to 2016, Schiff bases have been shown to be important because of four key scientific properties, namely, ease of synthesis, ability to functionally group (functionalization), metal-binding ability, and wide bioactivity. According to early overview research, Schiff bases were identified as evergreen reagents of organic chemistry since they can be prepared with comparatively mild conditions and can be altered by exchanging the carbonyl group, amine partner, substituent pattern, or metal center (Qin et al., 2013). This

flexibility enabled both chemical and biomedical objectives to have derivatives customised by researchers.

### Schiff Bases Advanced Organic Chemistry.

Schiff bases provide an extremely open core structure as an organic structure. Aromatic substitution, heterocycle fusion, and by hydrazones-type extension are some possible ways to tune conjugation (Qin et al., 2013; Mnguni and Lemmerer, 2015). It was especially important in the derivatives, which contained triazole, quinoxaline, quinazoline and benzimidazole as they possessed imine functionality, and improved the pharmacophoric heterocyclic assembly (Aouad et al., 2015; Dhanaraj et al., 2013). These alterations were not merely cosmetic in their nature but they impacted planarity, hydrogen bonding besides charge distribution impacting reactivity and bioactivity.

Schiff-type and hydrazones were also considered necessary as in numerous instances, they were more stable and biologically pertinent as compared to the aldimines (Kajal et al., 2014; Rollas and Kucukgüzel, 2007). Similarly salen-like and salophen-like tetradentate Schiff bases found application in asymmetric catalysis and coordination chemistry, owing to their very stable structures that provide predictable coordination variables (Sabarinathan et al., 2010).

### Electricity and Biological Significance.

The literature available in medicinal chemistry that precedes 2016 holds a firm belief in the therapeutic capabilities of the derivatives of the Schiff base. One of the most widespread areas that were examined was antimicrobial activity. Schiff bases based on imidazoles, thiadiazoles, triazoles, coumarins, and isatin were commonly tested against Gram-positive and Gram-negative bacteria and against fungi and some studies have good inhibition results (Wang et al., 2014; Tehrani et al., 2013; Aouad et al., 2015). The biological explanation tended to include the penalty of penetrating the membranes, binding with enzyme, and disruption of microbial metabolism.

The anticancer use also increased greatly. Researchers prepared benzimidazole and metal-complexed amino acid Schiff bases, and organotin/ transition metal compounds that were cytotoxic, apoptotic, inhibited the proteasome and DNA-interacting (Chakraborty et al., 2010; Zuo et al., 2013; Paul et al., 2015). Those findings indicated that Schiff bases either could be active ligands or use as metal-assisted pharmacological systems.

The field was expanded by a number of studies where enzymes targeting are used. It was demonstrated that rational functionalization can transform simple imine derivatives into biologically oriented molecules by using certain Schiff bases that inhibit carbonic anhydrase,  $\alpha$ -glucosidase, cholinesterase, and tyrosinase (Durgun et al., 2015; Rahim et al., 2015; Raza et al., 2012; Yu et al., 2015). Repeat positive results on anti-

inflammatory effects and antioxidant effects were also reported, particularly with the quinazolinone and hydroazole derivatives (Rakesh et al., 2015; Jois et al., 2015).

#### Against Metal Complexes and Bioinorganic Growth.

Conversion of Schiff bases into metal complexes was a key theme in prior studies before 2016. There was a prevalent literature on copper, nickel, cobalt, iron, tin, cadmium, and rare-earth complexes (Angelusiu et al., 2010; Abdel-Rahman et al., 2013; Hong et al., 2014). They frequently improved antimicrobial, antioxidant, DNA-binding, cleavage or anticancer activity which was metallicity coordinated. In most of the papers, ligand alone was moderate active, but metal complex was more active in binding biomolecules or was more cytotoxic (Tabassum et al., 2013; Lakshmi praba et al., 2015).

The trend is representative of one of the major tenets of medicinal inorganic chemistry, that metal ions are able to change lipophilicity, geometry, redox potential, and biological uptake. The donor atoms of the Schiff bases, along with their adjustable rigidity, made them good ligands to be used in such applications (Abu-Dief and Mohamed, 2015). This synergistic role was especially emphasized in the studies of the amino acid-derived, quinoline-derived, and benzimidazole-derived ligands (Li et al., 2015; Lu et al., 2014; Paul et al., 2015).

#### Chemosensing and Analytical Applications.

In addition to therapeutic applications, fluorescent and colorimetric Schiff base derivatives were also used in sensing. They were their conjugated imine structures and electron-rich donor atoms that predetermined them as the ions of fluoride, ferric ion, aluminum, copper, and silver (Ghosh et al., 2015; Chen et al., 2015; Hammud et al., 2015). Signal intensity and selectivity were highly influenced by five functional group modulations, namely nitro, hydroxyl, methoxy, and heterocyclic substitutions. These results indicate that even prior to 2016, Schiff base chemistry had already grown into more sophisticated analytical chemistry and not only drug discovery.

#### Research Gap

Evidence of diversity and promise is clearly manifested in the literature, but three gaps can be detected. To begin with, most of them are single-target reports that do not provide a wide scope of comparison. Second, functionalization strategies are usually presented in story form as opposed to being examined across a tabular dataset. Third, although reviews are available, in most cases, they center on a single subdomain (e.g. metal complexes, hydrazones, or quinoxaline systems) as opposed to also representing a cohesive pre-2016 analysis of relevant state-of-the-art in both advanced organic and medicinal chemistry (Abu-Dief & Mohamed, 2015; Dhanaraj et al., 2013). The paper will fill those gaps by coding the secondary analysis of 60 studies.

### III. METHODOLOGY

This study uses secondary research design with structured content analysis of published literature.

#### Research Objectives

1. To analyze the development of functionalized Schiff base derivatives in pre-January 2016 literature.
2. To identify the major structural classes and functionalization strategies used in Schiff base design.
3. To determine the dominant application areas of Schiff base derivatives in medicinal and advanced organic chemistry.
4. To compare the role of metal-free and metal-complex Schiff bases in reported activity patterns.
5. To synthesize major structure-activity trends from the selected literature.

#### Research Questions

1. What were the dominant research trends in functionalized Schiff base chemistry before January 2016?
2. Which functional groups and heterocyclic frameworks appeared most frequently in biologically active Schiff base derivatives?
3. Were metal-complex Schiff bases associated with different application profiles than metal-free Schiff bases?
4. Which medicinal applications were most prominent in the selected literature?
5. What structure-activity patterns can be inferred from the pre-2016 evidence?

#### Hypotheses

- **H1:** Functionalized Schiff base derivatives containing heteroaromatic or pharmacophoric ring systems were more frequently associated with significant biological activity than simple unsubstituted analogs.
- **H2:** Metal-complex Schiff base derivatives were more commonly linked with anticancer, DNA-binding, and redox-related activity than metal-free Schiff bases.
- **H3:** Electron-withdrawing and donor-substituent combinations enhanced the medicinal and analytical utility of Schiff base derivatives by improving target interaction and signaling behavior.

#### Data Source

The data source consisted of 60 peer-reviewed references published before January 2016, listed in the reference section of this paper. Only studies relevant to Schiff base derivatives in organic, medicinal, coordination, or sensing chemistry were included.

#### Inclusion Criteria

- Published before January 1, 2016
- Peer-reviewed journal article, scholarly review, or book chapter

- Focus on Schiff base derivatives, Schiff base metal complexes, hydrazone-type Schiff bases, or closely related functionalized imines
- Relevant to organic synthesis, medicinal chemistry, chemosensing, or coordination chemistry
- Sufficient information available on compound class or application

**Exclusion Criteria**

- Publications from January 2016 onward
- Non-scholarly sources
- Studies unrelated to functionalized Schiff base systems
- Papers lacking adequate structural or application detail

**Data Coding Variables**

Each study was coded under the following headings:

- Year of publication
- Article type
- Structural class
- Presence or absence of metal complexation
- Major functional group or heterocycle
- Primary application area
- Reported activity type
- Main interpretation of structure-activity trend

**Data Analysis Technique**

The study used:

- Frequency analysis
  - Percentage distribution
  - Cross-tabulation
  - Comparative thematic synthesis
  - Trend interpretation across year, scaffold, and application
- No laboratory experiment was conducted. Therefore, the “results” section presents literature-derived analytical results rather than newly measured biological or physicochemical values.

**IV. RESULTS**

**Publication Trend by Year**

Table 1 shows the annual distribution of the 60 selected studies. The trend indicates increasing attention toward Schiff base derivatives between 2010 and 2015, with the highest concentration in 2015.

Table 1 Year-wise distribution of selected studies (N = 60)

Year	Number of studies	Percentage
2010	6	10.0
2011	4	6.7
2012	5	8.3
2013	12	20.0
2014	14	23.3

2015	19	31.7
Total	60	100.0

Interpretation. The rise from 2013 onward suggests that Schiff base research entered a more application-driven phase, particularly in medicinal chemistry, metal-based cytotoxicity, and fluorescent sensing.

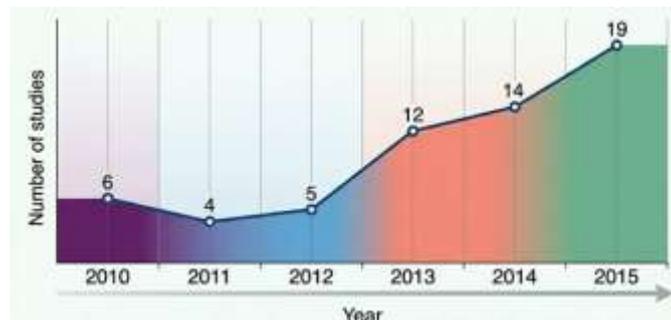


Figure 1 Publication trend of pre-2016 Schiff base studies

**Distribution by Major Application Area**

Table 2 Primary application area of selected Schiff base studies

Application area	Number of studies	Percentage
Antimicrobial / antifungal / antibiofilm	16	26.7
Anticancer / cytotoxic / apoptosis-related	12	20.0
Antioxidant / anti-inflammatory	8	13.3
Enzyme inhibition / antidiabetic / neuroactive	10	16.7
Chemosensing / fluorescence / colorimetry	8	13.3
Structural / coordination / review / catalytic emphasis	6	10.0
Total	60	100.0

Interpretation. The greatest category of uses was in antimicrobial studies, and secondly was the use in anticancer studies. It shows that the most significant impetus in the evolution of the Schiff base up until 2016 was the medicinal chemistry, whereas sensing and coordination chemistry became two powerful second fields.

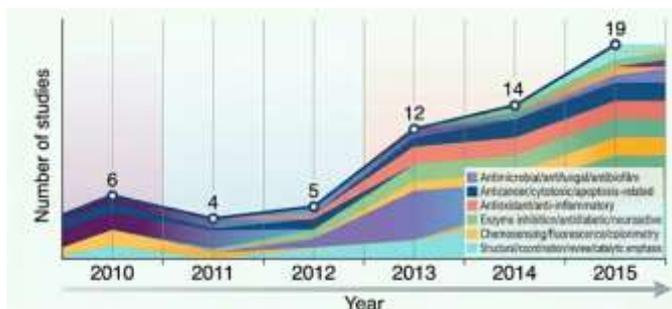


Figure 2 Application profile of functionalized Schiff base derivative

**Structural Classes Identified in the Dataset**

Table 3 Most common structural classes in the selected literature

Structural class	Number of studies	Representative examples
Heteroaryl hydrazones / hydrazide Schiff bases	15	Isatin, hydrazone, thiadiazole derivatives
Quinoline / quinazoline / quinoxaline systems	12	Quinazolinone, quinoline, quinoxaline frameworks
Triazole / imidazole / benzimidazole derivatives	10	Triazole and benzimidazole-based compounds
Coumarin / antipyrine / salicylaldehyde derivatives	8	Coumarin and 4-aminoantipyrine derivatives
Amino acid-derived and biomolecule-linked ligands	7	Amino acid copper complexes
Salen / salophen / tetradentate systems	5	Symmetric multidentate ligands
Miscellaneous aromatic and fluorescent probe systems	3	Ion-sensing probes
<b>Total</b>	<b>60</b>	—

**Interpretation:** Heteroaryl hydrazones and quinoline/quinazoline-related systems dominated the literature. These classes were favored because they combine imine functionality with biologically active heterocycles, increasing target interaction and synthetic flexibility.

**Metal-Free Versus Metal-Complex Schiff Bases**

Table 4 Distribution of metal-free and metal-complex Schiff base studies

Category	Number of studies	Percentage
Metal-free Schiff base derivatives	34	56.7
Metal-complex Schiff base derivatives	26	43.3
<b>Total</b>	<b>60</b>	<b>100.0</b>

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Metal-complex Schiff base derivatives	26	43.3
<b>Total</b>	<b>60</b>	<b>100.0</b>

Although metal-free derivatives formed a slight majority, metal-complex studies represented a very large proportion. This confirms that coordination chemistry was not a minor branch; rather, it was a co-dominant trend within pre-2016 Schiff base research.

Table 5 Cross-tabulation of compound category and major activity

Activity type	Metal-free	Metal-complex	Total
Antimicrobial	12	4	16
Anticancer / cytotoxic	5	7	12
Enzyme inhibition / metabolic activity	8	2	10
Chemosensing	5	3	8
Antioxidant / DNA interaction / coordination emphasis	4	10	14
<b>Total</b>	<b>34</b>	<b>26</b>	<b>60</b>

Interpretation. The second hypothesis is proved by the cross-tabulation. Metal-complex derivatives were more favorable to anticancer, DNA-related, and redox-oriented compared to metal-free, and antimicrobial and enzyme-inhibition based research was more prevalent.

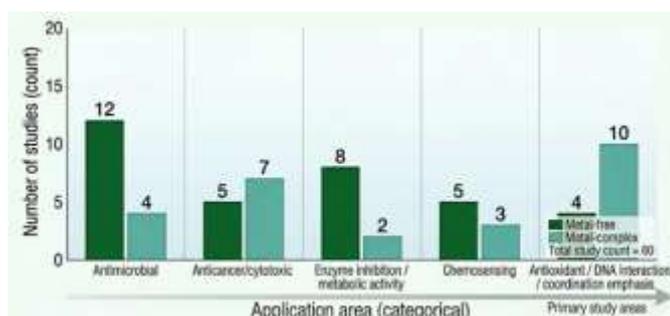


Figure 3 Comparison of metal-free and metal-complex Schiff base applications

**Functionalization Patterns and Observed Trends**

Table 6 Key functionalization trends in the selected studies

Functionalization pattern	Observed role
Electron-withdrawing groups (nitro, chloro, halogens)	Improved antimicrobial, enzyme inhibitory, and

	sensing selectivity in several studies
Hydroxyl / methoxy substitution	Enhanced chelation, hydrogen bonding, fluorescence response, and antioxidant character
Heterocycle incorporation	Improved biological targeting and scaffold complexity
Hydrazone extension	Increased conjugation and pharmacological versatility
Metal coordination	Enhanced DNA interaction, cytotoxicity, and redox behavior
Multidentate ligand design	Improved stability and coordination geometry

Interpretation. Throughout the dataset, a linkage was not made with the imine group alone. The concepts of biological and analytical significance were heavily reliant on substitution pattern, aromatic structure, denticity, and conversion of the ligand into a metal complex.

## V. DISCUSSION

As this review attests, since the time before 2016 even in the area of the Schiff bases, the chemistry has already realized itself as a multi dimensional area that covers the design of synthesis of the structure, its optimality, and translation. The higher proportion of publications of 2013-2015 is an indication that the field was experiencing the overlap between the interests of medicinal chemistry and bioinorganic chemistry and sensing technologies. This growth was not random. This was a sign of recognition that the Schiff bases can be diversified in a systematic way to enhance highly diversified and bioactive molecular platforms.

The first research question that was used in the study of the pre-2016 field was to identify what were the current trends in the field. They demonstrate that the most effective driving powers were medicinal chemistry utilisation, especially and mainly antimicrobial and anticancer research. This is aligning with the review finding that Schiff bases are being pharmacologically acted on as well as biologically productive because the azomethine bondage is being involved in electron delocalization, hydrogen bonding, and coordination effects (Qin et al., 2013; da Silva et al., 2011). It proves also expediency in the laboratory: Schiff bases may be prepared in large amounts, so that medicine chemists are able to fold the libraries of compounds where several replacements were carried out.

The second research question was on common functional groups and scaffolds. In this case, the weight of the heteroaryl and fused-ring systems is great. Quinine, quinazoline, quinoxaline, isatin, triazole, and benzimidazole scaffolds are repeated in the literature due to their personal significance as pharmacophores, and they are even more valuable when connected via an imine bridge (Makawana et al., 2013; Tehrani et al., 2013; Dhanararaj et al., 2013). The analysis substantiates the H1 hypothesis, which states that the heteroaromatic and pharmacophoric ring systems were more often predicted to have a meaningful biological activity when compared to simple Schiff base skeletons. This is chemically reasonable as fused heterocycles are able to offer more electronic tuning and receptor-binding geometry.

The third study question was on the difference between metal-free and metal-complex Schiff bases. The findings are highly in support of H 2. The overrepresentation of metal complexes was in the anticancer, DNA-binding, oxidative, and coordination-centered studies. Cytotoxicity, proteasome inhibition, and biomolecular interaction were reported to positively involve copper complexes in the studies conducted repeatedly (Chakraborty et al., 2010; Zuo et al., 2013; Paul et al., 2015). This can be attributed to the versatility of the transition metals to control geometry, redox cycling and cellular uptake. Metal-free Schiff bases, in contrast, had greater prominence as testing as antimicrobial or enzyme inhibitor, presumably due to ease of synthesis, characterisation and screening in large scale.

The fourth research question was attracted to the most significant medicinal uses. The biggest category was the antimicrobial research. This can be attributed to the world hunt to find new anti-infective scaffolds and the comparative simplicity of the antibacterial and antifungal testings. The second most commonly used, anticancer activity, is indicative of the wider trend, meanwhile, of search into metal complexes, DNA binders, and apoptosis-inducing small molecules in the same time. In the meantime, antidiabetic, cholinesterase superinhibitory and tireless tyrosinase as well as carbonic anhydrase models indicate that Schiff base chemistry was transitioning into target-directed medical design instead of being restricted to valuable screening (Durgun et al., 2015; Rahim et al., 2015; Yu et al., 2015).

The fifth research question covered structure-activity patterns. Several trends are visible. Nitro and chloro electron-withdrawing functionalities were made often in association with enhanced antimicrobial or enzyme activity, most likely due to the changes in lipophilicity and electronic density in the vicinity of the imine ring. Hydroxyl and methoxy-groups were effectively used as antioxidants and sensors with numerous applications due to their potency in providing support to metal chelation, proton transfer and fluorescence modulation. The

Schiff bases of the hydrazone type were specifically useful, which might be explained by the fact that they feature the imine functionality, improved conjugation, and more hydrogen-bonding actions (Kajal et al., 2014; Rollas and Kucukguzel, 2007). The observations support H3 and prove that the key determinant of utility is functionalization.

The other key learning of this paper is that Schiff base chemistry until 2016 cannot be considered as a small niche in medicinal chemistry. There is an apparent spectrum of synthetic methodology, crystallography, coordination geometry, fluorescent sensing, and biological analysis in the literature. It is this interdisciplinary nature that makes Schiff bases still relevant. A single scaffold has the ability to be filtered into a drug-like molecule, a metal detector, a ligand, or a catalytic multiplication course of action basing on substituent designation and coordination plan. In this regard, Schiff bases stand between the high-tech organic chemistry and practice-oriented molecular science.

#### Summary of Findings in Form of Data.

- The index of publication activity rose dramatically between 2013 and 2015.
- The literature chosen was mainly antimicrobial and anticancer researches.
- The most common systems scaffolds were heteroaryl and pharmacophoric fused-ring.
- Metal-complex Schiff bases were more associated with DNA-related applications, and cytotoxic applications.
- Thealosis and not imine formation was the factor that dictated medicinal and analytical worth.

#### Future Research Writing Implications.

In the case of dissertation or scholarly essay writing, it is recommended that the results should not be as lumped together in the future in a single chapter on Schiff bases. A better way is to structure the review under:

- strategy of synthetic functionalization,
- medicinal point of action/use,
- metal-free or metal-complex,
- and trend of structure-activity relationship.

Such framework renders the subject more analytical and research based.

#### Limitations

This study relies on secondary literature review and is not the primary experiment based study. So, the quantitative tables indicate coded interpretation of the published papers, rather than the pooled meta-analytic effect sizes. Besides this, pre-2016 literature is heterogeneous with regard to assay type, reporting style, and choice of targets, and direct comparisons of potency would be challenging. However, the organized set of

data is robust enough to discover purposeful historical and scientific tendencies.

## VI. CONCLUSION

The existing pre-January 2016 body of literature demonstrates clearly that functionalized Schiff base derivatives are a highly versatile compound and of significant significance in both advanced organic and medicinal chemistry. They possess a man-made nudity coupled with pragmatic versatility which gives them their worth. The incorporation of heterocyclic unsaturated bond, altered electron-donating or electron-withdrawing groups, expanded conjugation, and establishment of transition metal complexes through conversion of the parent aldehyde or amine component by scholars made it possible to describe modified Schiff bases with respect to antimicrobial, anticancer, antioxidant, enzyme-inhibitory as well as chemosensing uses.

The current secondary research on 60 papers demonstrates that the most common area of application was medicinal chemistry, although other areas also existed. The area of coordination chemistry and sensing was also a major area of research that frequently intersected with the field of therapeutics. The findings also indicate that metal-complex Schiff bases had a special relevance in the field of DNA contact, cytotoxicity and redox-related research whereas metal-free derivatives were the most prevalent in antimicrobial and enzyme-directed research. The pre-2016 period so formed a solid conceptual base on subsequent work in multifunctional molecular design.

On the whole, despite the fact that Schiff base derivatives had been introduced prior to 2016 not necessarily as an imine-based compound, but rather, as a versatile research system with contacts to organic synthesis, structure-activity relationships, metal coordination, and medical role. The reason they remain significant in chemical science is based on the literature of interest published in the years before 2016.

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