2. Review of literature

1) British Pharmacopoeia 2016, appendix III D. Liquid Chromatography (Ph. Eur. method 2.2.29):
It mentions the details of liquid chromatography instrumentation. The Apparatus, Pumping Systems, Injectors, Stationary Phases, Mobile phases, Detectors, Method are mentioned sequentially which gives the information of requirements of HPLC as a complete system. This pharmacopoeia is informative and regulatory requirement to follow.

2) United States Pharmacopoeia 2016 (USP 39-NF 34) (621) Chromatography:
It describes all details of chromatography including liquid chromatography. It also mentions the chromatographic columns and definition and interpretation of chromatograms. The terms like Dwell volume, Hold up time, Hold up volume, Number of theoretical plates, peak, peak to valley ratio, relative retardation, relative retention, relative retention time (RRT) and so many other terms are well defined. These all terminologies will help to understand the basic requirements for HPLC method creation and subsequent requirements for method validation.

United States Pharmacopoeia 2016 (USP 39-NF 34) (1225) Validation of Compendial Procedures describes under section validation typical analytical characteristics used in method validation. These analytical characteristics used are Accuracy, Precision, Specificity, Detection limit, Quantitation Limit, Linearity, Range and Robustness. Each chapter is described in detail and requirements of this chapter is mentioned in detail. Detection limit and quantitation limit, system suitability as well as data elements required for validation is well informed. This all details will be useful to perform the future work on analytical method development and validation.

The peak purity parameter ensured noninterference by product of degradation. This method can be applied to determination of stability of Fluindione. The suitability of this HPTLC method for quantitative determination of Fluindione was proved by validation in accordance with requirements of ICH guidelines. This reference will be useful for the determination of HPLC related studies.

Schiff bases are important class of organic ligand, which played an integral role in the expansion of coordination chemistry and various aspects of biocoordination chemistry. The synthesized transition metal complexes were characterized by molar conductance, elemental analyses and spectral studies such as UV-Vis., FTIR and EPR. Non-electrolytic nature of the complexes was confirmed by molar conductance.


A pentadentate Schiff base ligand (H3L) was synthesised from 1,3-diaminopropan-2-ol and 2'-hydroxy-5'-methylacetophenone and a series of copper(II) complexes were synthesised using H3L and copper(II) precursor complexes of substituted benzoic acids. Enterococcus faecalis, and Escherichia coli and antifungal activities against Aspergillus niger, Aspergillus flavus and Candida albicans by well diffusion method. In addition, the antioxidant activities were also done for all the complexes. Biological activity determination is referred in this research paper.


The present review article deals with the method developed for itraconazole by HPLC method. A wide variety of columns, mobile phase combinations, degassers used for the study. Different flow rates were adjusted for mobile phase combinations. In some methods forced degradation studies was also carried out and the methods developed were validated according to the ICH guidelines. After studying different research articles it came to light that HPLC method development of itraconazole has been done in different dosage forms of itraconazole and still there is huge potential for new methods to be developed with different mobile phase and column combinations. These new method data are required by regulatory agencies.


The present investigation states that the study of antibacterial activity and spectrophotometric analysis with both expired and non-expired medication. The microorganisms were used for the antibacterial activity which was done by agar well diffusion method. Escherichia coli, Pseudomonas fluorescence bacteria were given the high cytotoxic effect in both expired and non-expired drugs of amoxicillin trihydrate were Streptococci aureus given the less inhibition zone once compare with gram -positive bacterium.

A series of binary complexes of Co(II), Ni(II), Cu(II) and Ru(II) with (R)-N-(phenyl)ethyl-2-hydroxy-1-salicylaldimine (L or NPEHS) have been synthesised. The ligand (NPEHS) is co-ordinated to the metal ion with the N, O donor atoms in 1:2 (metal : ligand) ratio and it is determined by spectrophotometric studies. Reference will be useful for further determination of the HPLC analysis.

9) Mustapha C. Mandewale, and etal, (2015), "Journal of Chemical and Pharmaceutical Research":

The synthesis of a novel series of Schiff bases of 2-hydroxy-6-chloro-3-formylquinoline (4a–e) and its Zn (II) and Cu (II) complexes are described in the present paper. The chemical structures of compounds have been elucidated by IR, 1H NMR and Mass spectral data. Fluorescence properties of all the synthesized compounds have been tested. Molecular modeling tools were also used for a further analysis in order to estimate the druggability of the reported quinoline Schiff base derivatives.

10) Mustapha C. Mandewale, and etal,(2015), "Der Pharma Chemica":

Five new quinoline Schiff bases were synthesized starting from 6-fluoro-2-hydroxyquinoline-3-carbaldehyde. In the reaction sequence, Fluorine substituted anilines were condensed to 6-fluoro-2-hydroxyquinoline-3-carbaldehyde. Further Zn (II) and Cu (II) complexes of Schiff bases were synthesized.


New Schiff base derivatives CSB01-CSB05 have been synthesized by reaction between 6-Aminocoumarin and various salicylaldehyde derivatives in ethanol under reflux in good yields (84–90%) and their biological properties have been evaluated against Mycobacterium tuberculosis (H37 RV strain). Most of the newly synthesized compounds displayed 100% inhibitory activity at a concentration of 12.5 g/ml against Mycobacterium tuberculosis. Compound CSB01-CSB04 showed most effective inhibition.


Benzofuran and its derivatives are widely used for industrial purposes and also exhibit a broad range of biological activities. This review compiles examples of the most promising antimalarial, antibacterial, antifungal, and antiviral benzofuran compounds. An overview of synthetic methodologies used for the preparation of benzofurans is also described.

The 7-methoxy-2-(3,4,5-trimethoxyphenyl)-1-benzofuran-5-carbaldehyde was synthesized by known literature method (Wittig reaction approach) from vanillin. To deduce the anticancer and antibacterial activity of the 7-methoxy-2-(3,4,5-trimethoxyphenyl)-1-benzofuran-5-carbaldehyde, it is docked with different biomarkers of cancer cell and bacteria.


A series of Co(II), Ni(II), Cu(II), Zn(II) and La(III) complexes of N’-[(E)-(2-hydroxyquinolin-3-yl)methylidene]-1-benzofuran-2-carbohydrazide has been prepared. It is synthesized by the condensation of 2-hydroxy-3-formylquinoline with benzofuran-1-carbohydrazide in absolute ethanol. All the synthesized compounds have been screened for the antibacterial study against microorganisms such as Escherichia coli, Salmonella typhi, Corynebacterium diptheriae and Staphylococcus aureus.

15) Mustapha C. Mandewale (2015) Bioinorganic Chemistry and Applications:

A new series of quinoline hydrazone derivatives and their metal complexes have been synthesized and their biological properties have been evaluated against Mycobacterium tuberculosis (H37 RV strain). Most of the newly synthesized compounds displayed 100% inhibitory activity at a concentration of 6.25–25 g/mL, against Mycobacterium tuberculosis. Fluorescence properties of all the synthesized compounds have been studied.

16) Liu Yan, and etal (2014), Journal of Chemical and Pharmaceutical Research:

All tested samples contained the 12 common peaks, 7 of which were verified, and the similarity of chromatographic fingerprints was from 0.912 to 0.991. The above new method is to be a new quality evaluation pattern for Traditional Chinese medicine.

17) Shadia A. Galal and etal (2014), European Journal of Medicinal Chemistry:

A molecular docking study was also performed to gain comprehensive understanding into plausible binding modes and to conclude the structure activity relationships of the synthesized compounds. Moreover, anti-inflammatory activity was studied. Compounds 12, 15, 18 and 22 were found to be potent and selective against COX-2.
18) **Indian Pharmacopoeia 2014 Volume I (2.4.14) Liquid Chromatography** referred to understand the adjustments of chromatographic conditions, HPLC capacity factor, column efficiency, symmetry factor, signal to noise ratio and some other useful terminologies of liquid chromatography.


A simple and regioselective synthesis of 2-chloro-3-formylquinoline by the cyclisation of Narylacetamide has been reported by the Vilsmeier Haack reaction/cyclisation which is further undergoes hydroxylation to 3-formyl-2-hydroxyquinoline by using acetic acid. In 3-formyl-2-hydroxyquinoline, the formyl group shows condensation with p-iodoaniline and forming Schiff base as 3-[(E)-[4-iodophenyl]imino]methyl]quinolin-2-ol. It acts as 1,5-bidentate ligand and forming complex of the type [ML2] where M is Zn, Cu, Ni and La which are further subjected to fluorescence study. The Schiff base shows weak emission at 461 nm (weak) for the absorption wavelength 387 nm whereas its complexes shows strong emission at 462 nm (moderate) [ZnL2, at 387 nm], 478 nm (strong) [CuL2, at 387 nm], 465 nm (moderate) [NiL2, at 387 nm] and 461nm (moderate) [LaL2, at 387 nm]. The complexes having very high quantum efficiency than the schiff base.

20) **Ramesh S Yamgar, and et al (2014), Bioinorganic Chemistry and Applications**

The synthesis and antimicrobial activity of novel Zn(II) metal complexes derived from three novel heterocyclic Schiff base ligands 8-[(Z) -[3-(N-methylamino)propyl]iminomethyl]-7-hydroxy-4-methyl-2H-chromen-2-one, 2-[(E)-[4-(1H-1,2,4-triazol-1-ylmethyl)phenyl]iminomethyl]phenol, and (4S)-4-[(E)-(2-hydroxybenzylidene)amino]benzyl]-1,3-oxazolidin-2-one have been described. These Schiff base ligands and metal complexes are characterised by spectroscopic techniques. According to thesedata, we propose an octahedral geometry to all the metal complexes. Antimicrobial activity of the Schiff base ligand and its metal complexes was studied against Gramnegative bacteria: E. coli and Pseudomonas fluorescens, Grampositive bacteria: Staphylococcus aureus, andalsoagainst fungi.


Novel transition metal Zn(II) complexes of bidentate Schiff base ligands were obtained from 4-Methyl 7-hydroxy 8-formyl coumarin, and Dimethylamino propylene diamine and N-methylamino propylene diamine. Zn(II) complexes
were also prepared by condensing with schiffs base of Ethyl 2-(3-formyl-4-
hydroxyphenyl)-4-ethyl-1,3-thiazole-5- carboxylate with Dimethylamino
propylene diamine .The scope for HPLC method development is for these
compounds.

22) Adediji Johnson F, and etal, (2012), “Journal of Chemical and
Pharmaceutical Research”

The elemental analysis, magnetic measurements, conductivity measurements
and spectral studies of the complex were carried out. 2,5-diamino-1,3,4-
thiadiazole acts as neutral tridentate ligand and coordinates through the sulphur
atom and nitrogen of the amines. It was tentatively inferred that complex
exhibited octahedral geometry.HPLC analysis is not performed for this metal
complexes.

23) Adediji Johnson F, and etal (2012). “Journal of Chemical and
Pharmaceutical Research”

The new mixed 2,5-diamino-1,3,4-thiadiazole and Benzoic acid[L1] was then
synthesized by Mannich reactions(Condensation). The chemical structures were
confirmed by means of Elemental analysis, IR, UV/Visible, 1H- and 13C-NMR..
UV absorbance and studies again proves that schiff bases have potential to be
analysed on hplc techniques.

24) Dipali Tajane, and etal ( 2012) , Journal of Chemical and
Pharmaceutical Research :

RP-HPLC-PDA method has been developed and validated for quantitative
determination of ROSUVASTATIN and AMLODIPINE from tablet formulations.
All the parameters for the two titled drugs met the criteria of ICH guidelines for
method validation.

25. B. R. Thorat, and etal, (2012), "Journal of Chemical, Biological and
Physical Sciences" :

Vaniline is nitrated by using known literature method to 4-hydroxy-3-methoxy-5-
nitrobenzaldehyde. The haloanilines used for the synthesis of Schiff bases was
synthesized by known literature methods and by referring Vogel's Practical
Organic Chemistry, 5th Edition. The nitrovaniline is reactive towards amine and
forming 4-{(E)-[(4-aryl)imine]methyl}-2-methoxy-6-nitrophenol. The final
compounds 4-{(E)-[(4-aryl)imine]methyl}-2-methoxy-6-nitrophenol and are
further subjected to fluorescence study.
26. B. R. Thorat, and etal, (2012), "Journal of Chemical, Biological and Physical Sciences" :

The pharmaceutical important 4-(4-hydrazinylbenzyl)-1,3-oxazolidin-2-one hydrochloride is condensed with salicylaldehyde (2) in methanol in presence of sodium methoxide forming schiff base 4-{4-[(2Z)-2-(2-hydroxybenzylidene)hydrazinyl]benzyl}-1,3-oxazolidin-2-one. It is characterized by TLC, FT-IR, and NMR spectroscopy. The IR peak at 1781, 3318 and 3230 cm$^{-1}$ is due to O-CO-NH, -CO-NH- and =N-NH- stretching vibrations. The new peak at 1616 cm$^{-1}$ is due to -C=N- (imino) group. The compound 3 mentioned in research paper is further subjected to fluorescence study. The Schiff base(3) shows excitation at 276 nm ($\varepsilon$ 9.203) and 400 nm ($\varepsilon$ 3.129) and emission at 413 nm ($\varepsilon$ 580) for excitation at 276 nm & 403 nm ($\varepsilon$ 234.58) and 403 nm ($\varepsilon$ 432.70) for the excitation at 400 nm.

27) B. R. Thorat, and etal (2012), “Journal of Chemical and Pharmaceutical Research” :

Vanilin is nitrated by using known literature method to 4-hydroxy-3-methoxy-5-nitrobenzaldehyde. The haloanilines used for the synthesis of Schiff bases was synthesized by known literature methods and by referring Vogel’s Practical Organic Chemistry, 5th Edition. The nitrovaniline is reactive towards amine and forming 4-{(E)-[(4-aryl)imine]methyl}-2-methoxy-6-nitrophenol. The final compounds 4-{(E)-[(4-aryl)imine]methyl}-2-methoxy-6-nitrophenol along with starting impurities are subjected to HPLC analysis.

28) Sangeeta V. Chavan and etal (2011), Asian Journal of research and Chemistry

Some novel transition metal [Mn(II), Co(II), Ni(II), Cu(II), Pd(II)] complexes of multidentate Schiff base ligand obtained from semicarbazide and substituted benzopyronone have been prepared and characterized by physical, spectral and analytical data. The synthesized Schiff base act as tridentate ligand for the complexation reaction with Mn(II), Co(II), Ni(II), Cu(II) and Pd(II) ions. The new compounds, possessing the general formula [M(L)2.H2O] where [M= Mn(II), Co(II), Ni(II), Cu(II) and Pd(II)] show an octahedral geometry. In order to evaluate the effect of metal ions upon chelation, the Schiff base and their metal complexes have been screened for antimicrobial activity. The transition metal complexes have shown enhanced antimicrobial activities as compared to Schiff base. Scope for HPLC method development and validation is seen for this compounds.

29) S. Karmarkar and etal (2011) Journal of Chromatographic Science :
In this paper, an application of Quality by Design (QbD) concept to the development of a stability indicating HPLC method for a complex pain management drug product containing drug substance, two preservatives, and their degradants is described. The QbD approach consisted of (i) developing a full understanding of the intended purpose, (ii) developing predictive solutions, (iii) designing a meaningful system suitability solution that helps to identify failure modes, and (iv) following design of experiments (DOE) approach.


Series of La(III), Pr(III), Nd(III), Sm(III), Eu(III), Gd(III), Tb(III), Dy(III) and Yb(III) complexes have been synthesized with the Schiff base (PHC) derived from the condensation of 8-formyl-7-hydroxy-4-methyl-coumarin with 3-amino pyridine. Study performed for IR, H-NMR was referred also microbiological study referred.


Novel transition metal [Cu(II), Ni(II), Zn(II), La(II)] complexes of bidentate Schiff base ligand obtained from 2-hydroxy-3-formylquinoline and substituted p-iodoaniline have been prepared and characterized by physical, spectral and analytical data. The synthesized Schiff base act as bidentate ligand for the complexation reaction with Cu(II), Ni(II), Zn(II) and La(II) ions. The new compounds, possessing the general formula [M(L)2] where [M= Cu(II), Ni(II), Zn(II) and La(II)] show square planar geometry.


Isoniazide can be synthesized by the known literature method. Nicotin-4-carboxylic acid (1) was converted into methyl ester by using methanol in presence of catalytic amount of sulphuric acid. The methyl nicotin-4-carboxylate (2) is converted into isoniazide (3) by the condensation with hydrazine hydrate in DMF. The isoniazide is then condensed with various aldehydes (4a-d) in absolute alcohol in presence of catalytic amount of acetic acid and final product N[(1E)-alkylidene]pyridine-4-carbohydrazide (5a-d) is subjected for further fluorescence study.


A simple, specific and isocratic reversed phase-high performance liquid chromatography (RP-HPLC) method with UV detection at 294 nm was developed and validated for analysis of Moxifloxacin Hydrochloride (MOXI) in
presence of its degradation products. Retention time of the MOXI was found to be 7.8 min. A mobile phase consisting of 10mM sodium phosphate buffer and methanol (60:40 v/v) pH 4.4 at flow rate of 1mL/min was employed in this study. Basics of HPLC method validation and developed is referred from this paper.


An accurate and sensitive novel method was designated chemically for the determination of atenolol in pharmaceutical drugs. The complex formation between copper(II) and atenolol was studied both in aqueous and methanolic media. This reference will be useful for further study of Schiff base method development.


HPLC method development and validation parameters are studied from this research paper in detail. Approach was well understood which will be useful for further study during actual practical work. The method does require only 7 minutes as run time for analysis which prove the adoptability of the method for the routine quality control of the drug.

36) K. Shiva Prasad (2010), Bioinorganic Chemistry and Applications

Four organotin(IV) complexes with 2-(2-hydroxybenzylideneamino)isoindoline-1,3-dione (L1), and 4-(4-hydroxy-3-methoxybenzylideneamino-N-(pyrimidin-2-yl)benzenesulfonamide (L2) were synthesized and well characterized by analytical and spectral studies. The synthesized compounds were tested for antimicrobial activity by disc diffusion method. The DNA binding of the complexes 1 and 3 with CT-DNA has been performed with absorption spectroscopy, which showed that both the complexes are avid binders of CT-DNA. Also the nuclease activity of complexes 1 and 3 with plasmid DNA (pUC19) was studied using agarose gel electrophoresis. In this research HPLC method was not developed and validated so there is a scope for this study.

Basic information about HPLC is very well written in this book. Introduction of HPLC, Principle, instrumentation, apparatus and materials, column efficiency and selectivity, comparision between HPLC and Gas chromatography is read and understood.

38) Eman A. Elzahany and etal (2008), Australian Journal of Basic and Applied Sciences:
The Schiff base ligands (L1) and (HL2) were prepared from the N-amino rhodanine and each of 2-formylindole (L1) and salicylaldehyde (HL2), respectively. Moreover, the ligands were characterized by elemental analysis, IR, mass, 1HNMR and electronic spectra. The Cr(III), Co(II), Ni(II) and Ag(I) complexes of the ligands L1 and HL2 were prepared and characterized by the analytical and spectroscopic methods.

39) Daniel C Harris, (2007), Quantitative Chemical Analysis:
The basics of Liquid chromatography was very well understood in this book. This book will be useful for further determination of the analytical compounds.

40) Patrick Augustijns and Marcus E. Brewster, (2007) Biotechnology – A pharmaceutical approach:
Basic principles of solubility is well understood and are will be applied for further use.