

Review Article



A Clinical Pharmacoepidemiological Evidence-Based Meta-Analysis of the Newer Pharmacotherapeutic Quinolones

Dr. Moumita Hazra*1, 2, 3, 4, 5, 6, 7

¹Medical Director, Consultant Multi-Specialist Clinical Pharmacological Physician, Consultant Clinical Pathologist, Medical Superintendent, Dr. Moumita Hazra's Polyclinic and Diagnostic Centre, Hazra Nursing Home, Hazra Polyclinic and Diagnostic Centre, Medical Academics and Clinical Research Director, Dr. Moumita Hazra's Academic Centre, Dr. Moumita Hazra's Educational Centre, West Bengal, India, World;

²Associate Professor, Head of Department In Charge, Department of Pharmacology, Mamata Medical College and Hospitals, Telangana, India;

³Former Associate Professor, Head of Department In Charge, Department of Pharmacology, Rama Medical College Hospital and Research Centre, Rama University, Uttar Pradesh, India;

⁴Former Resident and Tutor, Departments of Pathology and Pharmacology, J. J. M. Medical College and Hospitals, Chigateri General Hospital, Karnataka, India;

⁶Consultant Pathologist, Laboratory Supervisor, Mahuya Diagnostic Centre and Doctors' Chamber, West Bengal, India;

⁷Medical Appraiser, Medical Examiner, Medical Universities and Examination Boards, India.

*Corresponding author's E-mail: drmoumitahazra.198017thjune@gmail.com

Received: 10-09-2022; **Revised:** 18-11-2022; **Accepted:** 26-11-2022; **Published on:** 15-12-2022.

ABSTRACT

Introduction: The newer fluoroquinolones have broad-spectrum bactericidal activity, excellent oral bioavailability, good tissue penetration and favourable safety and tolerability profiles.

Objectives: The objective of this study was a clinical pharmacoepidemiological evidence-based meta-analysis of the quinolones, with an emphasis on the newer quinolones, the novel pharmacotherapeutics, thus enlightening on the evidence-based analytical quantitation of the expansive spectrum of their clinical indications and pharmacotherapeutic characteristics.

Methods: This study was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) Statement and Guidelines, 2009, described by the Cochrane Collaboration in June, 2016. At first, the steps of identification included the records which were identified through database searching and the additional records which were identified through other sources. This led to the steps of screening, which included the screened records after the duplicates were removed. From these screened records, few records were excluded, as per the exclusion criteria. Then, in the eligibility step, the full text articles were assessed for eligibility, from which few full text articles were excluded, according to the exclusion criteria, with adequate reasons. This led to the final inclusion step, where the studies were included in the qualitative synthesis of a systematic review, according to the inclusion criteria, and ultimately the studies were included in the quantitative synthesis, of a meta-analysis.

Results: This meta-analysis, contributed 4799 refined and relevant medical records, among total 6156 records obtained from the study databases search. It also analytically quantitates the broad spectra criteria of the clinical indications and pharmacotherapeutic characteristics of the quinolones, mostly the newer quinolones, which completes the various quantitative assessments of this meta-analysis.

Conclusions: To conclude, this meta-analysis provided the refined quantitatively synthesised medical records, study literature and databases on quinolones, and specifically on newer quinolones, with well-appraised analytical details.

Keywords: Meta-analysis, quinolones, newer quinolones, clinical indications, pharmacotherapeutic characteristics.

QUICK RESPONSE CODE →

DOI:
10.47583/ijpsrr.2022.v77i02.007



DOI link: <http://dx.doi.org/10.47583/ijpsrr.2022.v77i02.007>

activity, excellent oral bioavailability, good tissue penetration and favourable safety and tolerability profiles.¹⁻¹⁵

This meta-analysis was conducted for revisiting and delving deep into the expansive spectrum of the clinical indications and uses of the quinolones, with an emphasis on the newer quinolones, as well as their elaborate pharmacotherapeutic characteristics, and describing this vast spectrum with thorough explanations and analysis of the study literature and evidence compiled from the innumerable studies conducted, thus validating the growing necessities and efficacy of the newer quinolones, and emphasising their significance, as drugs, essential for multi-dimensional treatment of a wider range of mixed and complicated diseases, disorders and disabilities.

INTRODUCTION

With the advent of quinolones, and later the fluorinated 4-quinolones, the fluoroquinolones, the medical world has enormously progressed in treating innumerable diseases, disorders and disabilities, spanning varying types of worldwide pharmacoepidemiological presentations. The newer fluoroquinolones have broad-spectrum bactericidal



Objectives

The objective of this study was a clinical pharmacoepidemiological evidence-based meta-analysis of the quinolones, with an emphasis on the newer quinolones, the novel pharmacotherapeutics, thus enlightening on the evidence-based analytical quantitation of the expansive spectrum of their clinical indications and pharmacotherapeutic characteristics.

METHODS

The study was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) Statement and Guidelines, 2009, described by the Cochrane Collaboration in June, 2016. At first, the steps of identification included the records which were identified through database searching and the additional records which were identified through other sources. This led to the steps of screening, which included the screened records after the duplicates were removed. From these screened records, few records were excluded, as per the exclusion criteria. Then, in the eligibility step, the full text articles were assessed for eligibility, from which few full text articles were excluded, according to the exclusion criteria, with adequate reasons. This led to the final inclusion step, where the studies were included in the qualitative synthesis of a systematic review, according to the inclusion criteria, and ultimately the studies were included in the quantitative synthesis, of a meta-analysis.

(i) Global Regulatory and Ethical Guidelines, in accordance with:

The study was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) Statement and Guidelines, 2009, described by the Cochrane Collaboration, June, 2016, along with the ethical principles of the Declaration of Helsinki and Good Clinical Practices contained within the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH-E6 and ICH-E17), and in compliance with the global regulatory requirements.¹⁶⁻¹⁷

This study involved almost negligible risk, of any type, to the patients. This study design provided an equal opportunity to all the eligible patients to be included in the study. The patients who were included in the study were kept confidential.

(ii) Database, medical evidence and review literature search methodology:

In this meta-analytical study, any or all types of original research studies, systematic reviews, meta-analyses, case reports, case series, narrative reviews, study series, parallel studies and similar kind of studies or reviews, which were either qualitative, or quantitative, or both qualitative as well as quantitative, in their description of the quinolones, and most specifically, the investigative newer quinolones, like delafloxacin, sitafloxacin, sparfloxacin, zabofloxacin, finafloxacin, garenoxacin,

ozenoxacin, aravofloxacin, merafloxacin, WQ-3810, lascufloxacin and similar newer quinolones. Published medical articles and archival literature, obtained from various global electronic medical search engines and databases like Google Scholar, EMBASE, MEDLINE, Cochrane Library, PubMed, review of proceedings from selected scientific meetings, medical conferences, medical congress, medical summits, clinical trial registries, bibliographies of retrieved citations and reference lists, and expert recommendations, were searched manually, without a language or regional restriction. The comprehensive search was initiated with the titular keywords search, a search using an exploded medical subject headings (MeSH) and textword search, along with the numbered year text search. The recent advances articles on the newer investigative quinolones were searched within the recent publication time-period of mid-2015 to 2022, to derive the current investigative research database, medical evidence and review literature.

(iii) Published articles filtration process, along with determination of methodological quality:

In this meta-analysis, the searched published full text articles, including the abstracts and titles, and medical conference, medical congress, medical summits and scientific meeting abstracts, were collected, thoroughly screened and verified, at first. Duplicate articles were removed. The titles and abstracts of identified citations were appraised, after the duplicates were removed. Bibliographies of identified articles were subsequently reviewed for additional citations. Then, it was assessed to determine if they fulfilled the following study selection criteria, that is the inclusion and the exclusion criteria. Following this, the full text was obtained for the remaining studies, the substantiation of the data derived was validated and compared to the pre-established inclusion criteria, before final inclusion in the analysis.

The study selection criteria were the following:

(a) The inclusion criteria were:

- The published articles on the quinolones, including the newer investigative quinolones, which were based on their expansive and ever-progressive spectrum of clinical indications and uses and which enlighten on their improved anti-microbial spectrum, pharmacokinetic and pharmacodynamic properties, efficacy and safety profiles and pharmacotherapeutic characteristics and qualities, appropriate for their relevance in the multi-dimensional treatment of a wider range of mixed, refractory and complicated diseases, disorders and disabilities.
- The original research studies, systematic reviews, meta-analyses, case reports, case series, narrative reviews, study series, parallel studies and similar kind of studies or reviews, of any or all types, which were either qualitative, or quantitative, or both qualitative as well as quantitative, in their description of the quinolones, and specifically the investigative newer quinolones, were included in this meta-analysis.



- The publication time-frame was chosen to be recent, that is, within a span of the past 5.5 years, emphasising on the well-maintained pharmacogenomic and epigenetic time-frames of evolution.
- Any or all types of observational, descriptive and analytical research studies were included.
- Global, uni-centre and multi-centre studies, belonging to heterogenous pharmacogenomic and epigenetic constitution, of the recent evolutionary time-frame, were included.
- Studies based on either children, adult, pregnant and lactating women, or old patients, or all types of patients, were included.
- Studies based on the treatment of any or all clinically indicated types of diseases were included.
- Studies conducted at any type of small, medium or large medical establishment set-up were included.
- Studies performed on any gender of patients were included.
- Studies performed on any age group of patients were included.
- Studies with any or all routes of drug administration of the newer quinolones were included.

(b) The **exclusion criteria** were:

- The studies which described the procedures of formation, preparation of formulations and interactive handling of the quinolones were filtered, to maintain an already standardised time-bound qualification of the characteristics of the quinolones.
- *In vitro* studies were excluded, to enhance the degree of clinical relevance.
- Studies performed with zoological or botanical subjects were excluded, to enhance the clinical relevance and for appropriate clinical applicability.
- Studies performed on seriously ill patients were excluded.
- Studies performed on patients with co-morbidities or on any concomitant medication were excluded.
- Studies older than 7 years were excluded.

Each study was assessed for allocation concealment, blinding, reporting of losses to follow-up or missing outcome assessments, evidence of important baseline differences between the groups, analysis on an intention-to-treat basis and use of a sample size calculation.

(iv) Methodology of obtaining pertinent medical database, evidence, descriptive and analytical literature, after bias assessment:

After examining the quality of the full articles, the medical data and evidence were independently obtained by the

principal investigator who was simultaneously the author, using a meta-analysis protocol and a pre-structured data collection forms, containing different meta-analysis determinant criteria based on well-defined objectives, which were subsequently reviewed, to refine the medical database and evidence, after assessing and eliminating the study bias. The medical data and evidences extracted from the study resources were of heterogenous qualitative or quantitative nature, or both. Studies with any or all types of study characteristics and outcomes were obtained to derive the pertinent qualitative and quantitative descriptive and analytical literature, the main outcome measures being clinical indications and pharmacotherapeutic uses, chemical drug structure, mechanisms of action, pharmacological actions, pharmacokinetics, pharmacodynamics, medication adverse effects and comparative safety, pharmacotherapeutic efficacy, dosage details, drug interactions, drug contraindications, pharmacogenetic or pharmacogenomic details and newer investigative recent advances. The risk of bias of the studies were also assessed, which included random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias (i.e., design-specific risks of bias, baseline imbalance, blocked randomization in unblinded trials) with the Cochrane Risk of Bias tool and other tools of bias assessment. Methodological quality of the included studies were assessed after independently evaluating each of them in keeping with the Cochrane Collaboration's tool for assessing risk of bias. Using this method, each study was rated as having low, unclear or high risk of bias for domains including "selection bias", which is split into two sub-groups relating to the appropriateness of the randomisation procedure and allocation of participants to study groups. Presence of "performance bias" and "detection bias" relating to the blinding of participants, personnel and outcome assessment was also assessed, in addition to "attrition bias" and "reporting bias" which relate to incomplete outcome data and selective reporting. The domain "other bias" relates to any potential sources of bias which are not covered by the outcome categories, intervention and control groups, or bias arising from particular study designs.

(v) Categorisation and detailing of the different determinant criteria for this meta-analysis:

The categorisation of the refined medical databases and evidences, from the published articles, was made on the basis of the following broad categorisations:

- (1) Meta-Analysis: Assessments related to the study processes
- (2) Meta-Analysis: Assessments related to the clinical indications of the newer quinolones
- (3) Meta-Analysis: Assessments related to the pharmacotherapeutic characteristics



This meta-analysis was performed on the following detailed different determinant criteria under these broad categorisations:

(1) Meta-Analysis: Assessments related to the study processes, based on:

A. Identification:

- (i) Total published articles chosen,
- (ii) a. Total no. of records identified through database searching,
b. Total no. of additional records identified through other sources.

B. Screening:

- (i) No. of records after duplicates removed,
- (ii) No. of records screened,
- (iii) No. of records excluded

C. Eligibility:

- (i) No. of full articles assessed for eligibility,
- (ii) No. of full articles excluded, with reasons,
- (iii) Total number of articles found relevant to the broad categorisations,
- (iv) Total number of articles excluded, based on the exclusion criteria,
- (v) Total number of articles included, based on the inclusion criteria

D. Inclusion:

- (i) Total no. of articles, included in the meta-analysis

E. Analysis:

a. General Analytical Details:

- (i) Total number of articles analysed for the meta-analysis,

b. Advanced Analytical Details:

- (i) Number of articles, based on their nature,
 - (a) qualitative,
 - (b) quantitative,
 - (c) both, qualitative and quantitative
- (ii) Number of articles, based on their types,
 - (a) original research article,
 - (b) review article,
 - (c) systematic review,
 - (d) meta-analysis,
 - (e) case report,
 - (f) case series,

- (g) narrative review,
- (h) study series,
- (i) parallel study,
- (j) mixed study type

(iii) Number of articles, based on the different study designs,

(iv) Assessment of principal accuracy measures, based on: Relative study content quality of the published articles, based on (1) the comprehensive degree of correlation of the articles to the determinant criteria of this meta-analysis, as well as (2) the methodological quality, determined by the total number of included determinant criteria in the studies and the methodological quality assessment, by the key indicators of trial methodological quality, like allocation concealment, blinding, placebo-controlled, analysis by intention-to-treat, baseline imbalance, pre-defined outcomes, loss to follow-up, sample size calculation, keeping in consideration with the Cochrane Collaboration's tools, and (3) the quality of the subjective details of the study literature content, determined by the specificity and the significance of the study literature content

- (a) high quality,
- (b) medium quality,
- (c) low quality

(v) Risk of bias assessment: Relative bias assessment of the studies in the published articles, determined by the total proportionate bias in the studies, including "selection bias", "performance bias", "detection bias", "attrition bias", "reporting bias", and "other bias", keeping in consideration the Cochrane Collaboration's tool and other tools for assessing risk of bias

- (a) high bias,
- (b) medium bias,
- (c) low bias,

(vi) Assessment of applicability: Relative significance of the published articles, determined by the proportionate degree of correlation to the objective of this meta-analysis

- (a) high significance,
- (b) medium significance,
- (c) low significance

(2) Meta-Analysis: Assessments related to the clinical indications of the newer quinolones, based on:

(i) pharmacotherapeutic efficacy

- (a) high
- (b) medium
- (c) low

(ii) pharmacotherapeutic safety



- (a) high
 - (b) medium
 - (c) low
- (iii) total duration of treatment required
- (iv) total duration of recovery
- (v) degree of recovery
- (a) high
 - (b) medium
 - (c) low
- (vi) degree of improvement in recovery confirmation tests and evaluations
- (a) high
 - (b) medium
 - (c) low
- (vi) if any multiorgan involvement, after medication
- (vii) if any concomitant medication required, along with the newer quinolones
- (ix) if any supplementary treatment required, after medication for:
- single, multiple, multi-resistant, concurrent and recurrent infections:
 - bactericidal,
 - anti-viral,
 - anti-fungal,
 - anti-protozoal,
 - drug-resistant tuberculosis,
 - drug-resistant leprosy,
 - coronaviridae – 19,
 - mixed infections,
 - comedolytic or anti-comedogenic
 - anti-inflammatory
 - refractory inflammations
 - immunomodulatory
 - anti-neoplastic or anti-malignant
 - miscellaneous mixed, refractory and complicated diseases, disorders and disabilities

E. Analysis:

b. Advanced Analytical Details

(3) Meta-Analysis: Assessments related to the pharmacotherapeutic characteristics, based on:

- chemical drug structure,

- mechanisms of action,
- pharmacological actions,
- pharmacokinetics,
- pharmacodynamics,
- medication adverse effects and comparative safety,
- comparative pharmacotherapeutic efficacy,
- dosage details,
- drug interactions,
- drug contraindications and suitability,
- pharmacogenetic or pharmacogenomic pharmacotherapeutic suitability,
- newer investigative recent advances.

(vi) The process of refined data and evidence compilation:

The medical databases and evidences were thoroughly reviewed and the compilation of the data was done by selection and categorisation of the published articles, based on the above-mentioned categorisations and the different detailed determinant criteria of the meta-analysis. Then, the study literature was further critically and systematically reviewed; and refined into a standardised, well-structured form of aggregated refined medical data and evidence compilation.

(vii) The process of data and evidence recording:

The refined medical data and evidence obtained were properly recorded manually in a pre-structured analytical proforma. The standardised, well-structured compilation of the study literature was subsequently undertaken for a final analysis.

(viii) The methodology of the final analysis of data and evidence of the meta-analysis:

The final standardised, well-structured compilation of the study literature was then successively synthesised into a sequentially analytical meta-analysis, based on the comprehensive integration of the compiled study literature. This comprehensive integration and synthesis of the compiled study literature was performed by combining the results of the different studies, and describing the integrated study literature, including the description of the variability between the different studies. This process included:

- managing the multiple features of the outcome measures,
- managing the multiple threshold ranges of the study results,
- managing the multiple index assessments, managing the different types of study results, including indeterminate results,



- categorisation and detailing of the extensive study literature, along with comparisons, and managing the different reference standards.¹⁻⁶⁶

RESULTS

(i) The results of this Meta-Analysis:

In accordance with the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) Statement and Guidelines, 2009, described by the Cochrane Collaboration, June, 2016, in identification stage, the study literature search on quinolones, and more specifically on the newer quinolones, contributed a total of 6156 records, among which were 1890 records in PubMed search, 1425 records in EMBASE search, 1795 records in Scopus search,

and 1046 records in additional databases search, identified through other sources. The records, after removing the 426 duplicates, were 5730. In the screening stage, the records screened were 5730, with the exclusion of 553 records, according to the exclusion criteria. In the eligibility stage, the full text articles assessed for eligibility were 5177, with the exclusion of 378 full text articles, according to the exclusion criteria. In the final inclusion stage, the records ultimately included in the qualitative synthesis, according to the inclusion criteria, was 4799. These 4799 records were the refined contributions of this systematic review. Thus, this systematic review contributed 4799 refined and relevant medical records, among total 6156 records obtained from the study databases search, as depicted in Figure 1.

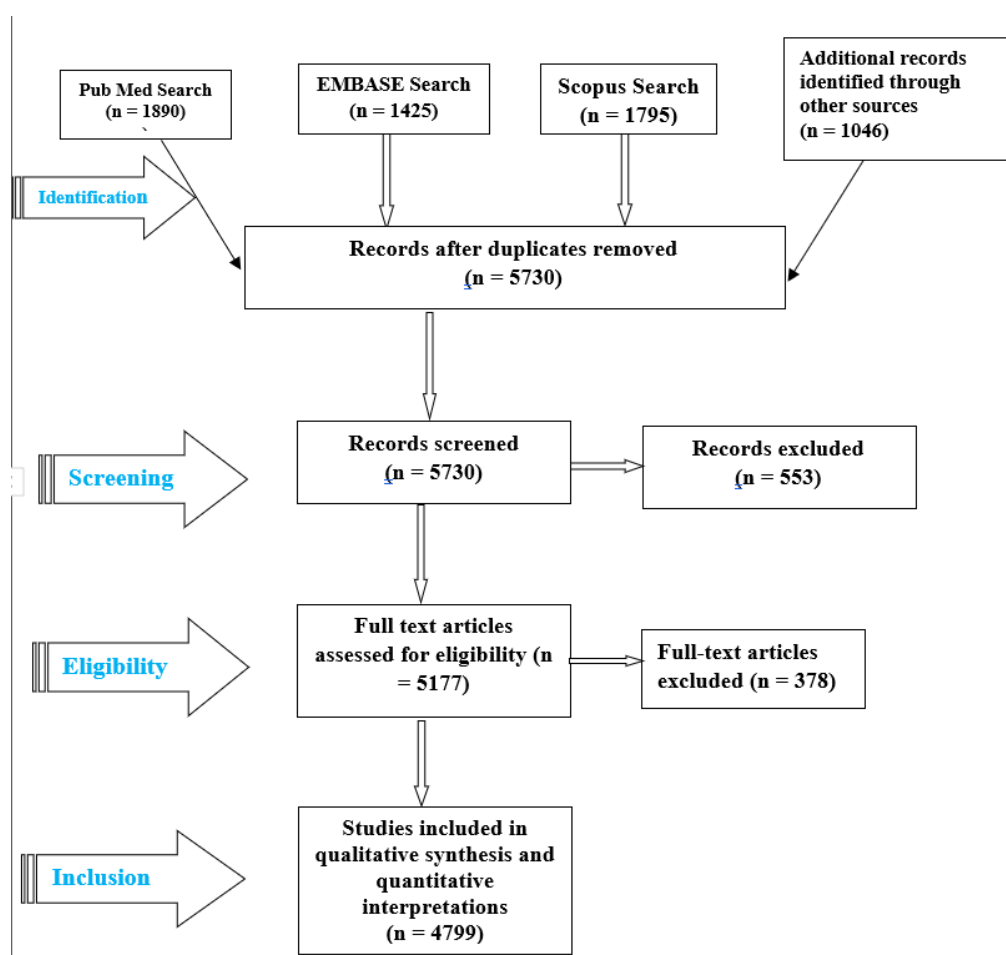


Figure 1: The Stages in PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) Statement and Guidelines, 2009

DISCUSSION

In this study, performed in accordance with the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) Statement and Guidelines, 2009, described by the Cochrane Collaboration, June, 2016, in identification stage, the study literature search on quinolones, and more specifically on the newer quinolones, contributed a total of 6156 records, among which were 1890 records in PubMed search, 1425 records in EMBASE search, 1795 records in

Scopus search, and 1046 records in additional databases search, identified through other sources. The records, after removing the 426 duplicates, were 5730. In the screening stage, the records screened were 5730, with the exclusion of 553 records, according to the exclusion criteria. In the eligibility stage, the full text articles assessed for eligibility were 5177, with the exclusion of 378 full text articles, according to the exclusion criteria. In the final inclusion stage, the records ultimately included in the qualitative synthesis, according to the inclusion criteria, was 4799.



These 4799 records were the refined contributions of this systematic review. Thus, this systematic review contributed 4799 refined and relevant medical records, among total 6156 records obtained from the study databases search.

Newer quinolones are characterized by advantageous pharmacokinetic properties, broad-spectrum bactericidal activity, excellent oral bioavailability, good tissue penetration and favourable safety and tolerability profiles.

The dual inhibitory activity of fluoroquinolones against the bacterial replication enzymes, DNA gyrase and topoisomerase IV, protects them from development of resistance.

Quinolone antibiotics develop from generations to generations to obtain broader activity spectrum by the addition of different substituents into different positions to the core structure.

Quinolones are quite significantly efficacious, for their bactericidal action, through their:

(1) inhibitory action on DNA gyrase, caused by the binding of fluoroquinolones to the A subunits (gyr A), thus inhibiting the replication and transcription of bacterial DNA, responsible for the proper functioning of the cell, and the subsequent change of conformity of DNA gyrase molecule caused by the binding of fluoroquinolones to the DNA binding groove between A (gyr A) and B (gyr B) subunits;

(2) inhibitory action on Par C subunits (par C) and Par E subunits (par E) of DNA topoisomerase IV, thus inhibiting decatenation and relaxation of DNA and segregation of replicating chromosomes or plasmids in bacteria;

(3) inhibitory action on pro-inflammatory cytokines, like interleukins: IL-1 α , IL-6, IL-8, and tumour necrosis factor α ; and,

(4) superinducing effect on IL-2.

Quinolones, the curiously novel pharmacotherapeutics, would always remain pharmacotherapeutically unique, due to the infinite metamorphosis of their extensive spectrum of therapeutic indications, every moment.

This meta-analysis provided the refined quantitatively synthesised medical records, study literature and databases on quinolones, and specifically on newer quinolones, with well-comprehensible evidence-based quantitative analysis, based on a clinical multi-pharmacoepidemiological orientation.¹⁻⁶⁶

CONCLUSION

Therefore, this meta-analysis, performed in accordance with the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) Statement and Guidelines, 2009, described by the Cochrane Collaboration, June, 2016, contributed 4799 refined and relevant medical records, among total 6156 records obtained from the study databases search. This meta-analysis also provided the refined quantitatively synthesised medical records, study literature and databases on quinolones, and specifically on

newer quinolones, with well-appraised analytical details, along with inclusion of the quantitative appraisal of various clinical pharmacoepidemiological aspects.

ACKNOWLEDGEMENTS

My gratitude to the Departments of Pharmacology, Clinical Pharmacology, Molecular Pharmacology, Rational Pharmacotherapeutics, Pharmacovigilance, Clinical Research, Evidence-Based Medicine, and Clinical Medicine, in Dr. Moumita Hazra's Polyclinic And Diagnostic Centre, Hazra Nursing Home, Hazra Polyclinic And Diagnostic Centre, Dr. Moumita Hazra's Academic Centre, Dr. Moumita Hazra's Educational Centre, Rama Medical College Hospital and Research Centre, Rama University, Mamata Medical College, Mamata Hospitals, J. J. M. Medical College and Hospitals, and Chigateri General Hospital, for the successful completion of this research project.

REFERENCES

- Hazra M. A systematic review of the quinolones, the novel pharmacotherapeutics, and the broad spectrum of their clinical indications and pharmacotherapeutic characteristics. *International Journal of Health and Clinical Research*. 2022; 5(2): 517-524.
- Hazra M. A rational pharmacotherapeutic study of comparative safety among topical anti-acne 1% nadifloxacin monotherapy, 0.1% adapalene monotherapy, 0.025% tretinoin monotherapy, 1% nadifloxacin and 0.1% adapalene combination therapy and 1% nadifloxacin and 0.025% tretinoin combination therapy, in mild to moderate acne vulgaris, in tertiary care hospitals. *Int J Basic Clin Pharmacol*. 2019; 8(9): 1959 – 1965.
- Hazra M. A rational pharmacotherapeutic study in pharmacovigilance: a comparative assessment of safety between topical 1% nadifloxacin and 0.1% adapalene combination therapy and topical 1% nadifloxacin and 0.025% tretinoin combination therapy, in mild to moderate acne, in tertiary care hospitals, in India. *J Evid Based Med Healthc*. 2019; 6(35): 2366 - 2371.
- Hazra M, Geetha M, Somashekhar HS, Muruges SB. A comparative study on the efficacy of topical 1% nadifloxacin and 0.1% adapalene combination therapy with 1% clindamycin and 0.1% adapalene combination therapy, in mild to moderate acne, in a tertiary care hospital. *Indian J Pharmacol*. 2014; 46(7 Suppl 1): S73.
- Brar RK, Jyoti U, Patil RK, Patil HC. Fluoroquinolone antibiotics: an overview. *Adesh Univ J Med Sci Res*. 2020; 2(1): 26-30.
- Assar S, Nosratabadi R, Azad HK, Masoumi J, Mohamadi M, Hassanshahi G. A review of immunomodulatory effects of fluoroquinolones. *Immunol Invest*. 2020; 1-20.
- Garcia-Prats AJ, Draper HR, Thee S, Dooley KE, McIleron HM, Seddon JA, Wiesner L, Castel S, Schaaf HS, Hesselring AC. Pharmacokinetics and safety of ofloxacin in children with drug-resistant tuberculosis. *Antimicrob Agents Chemother*. 2015; 59(10): 6073– 6079.
- World Health Organization. Fact sheet: Differences among fluoroquinolones in the treatment of MDR-TB. Geneva, Switzerland: World Health Organisation Archives; 2020. Available at <https://www.archives.who.int>. [Last accessed on 03/03/2022].



9. Yadav V, Talwar P. Repositioning of fluoroquinolones from antibiotic to anti-cancer agents: an underestimated truth. *Biomed Pharmacother.* 2019; 111: 934–946.
10. Idowu T, Schweizer F. Ubiquitous nature of fluoroquinolones: the oscillation between antibacterial and anticancer activities. *Antibiotics.* 2017; 6(4): 26.
11. Gao Y, Shang Q, Li W, Guo W, Stojadinovic A, Mannion C, Man Y-G, Chen T. Antibiotics for cancer treatment: a double-edged sword. *J Cancer.* 2020; 11(17): 5135-5149.
12. Mohammed HHH, Abuo-Rahma GEAA, Abbas SH, Abdelhafez ESMN. Current trends and future directions of fluoroquinolones. *Curr Med Chem.* 2019; 26(17): 3132-3149.
13. Karampela I, Dalamaga M. Could respiratory fluoroquinolones, levofloxacin and moxifloxacin, prove to be beneficial as an adjunct treatment in COVID-19? *Arch Med Res.* 2020; 51(7): 741-742.
14. Pradhan S, Prajna NV. Topical fluoroquinolones: current perspectives. *DJO.* 2015; 25: 267-271.
15. Kasabri V, Arabiyat S, Al-Hiari Y, Zalloum H, Almaliti J, Telfah A, Bustanji YK, Alalawi S. Fluoroquinolones as a potentially novel class of antidiabetes and antiproliferative compounds: synthesis and docking studies. *Can J Chem.* 2020; 98(10): 635-645.
16. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009; 6(7): e1000097.
17. Salameh JP, Bossuyt PM, McGrath TA, Thombs BD, Hyde CJ, Macaskill P, Deeks JJ, Leeftang M, Korevaar DA, Whiting P, Takwoingi Y, Reitsma JB, Cohen JF, Frank RA, Hunt HA, Hooff L, Rutjes AWS, Willis BH, Gatsonis C, Levis B, Moher D, McInnes MDF. Preferred reporting items for systematic review and meta-analysis of diagnostic test accuracy studies (PRISMA-DTA): explanation, elaboration, and checklist. *BMJ.* 2020; 370: m 2632.
18. Bell BG, Schellevis F, Stobberingh E, Goossens H, Pringle M. A systematic review and meta-analysis of the effects of antibiotic consumption on antibiotic resistance. *BMC Infect Dis.* 2014; 14: 13.
19. Liesker JJ, Wijkstra PJ, Ten Hacken NH, Koëter GH, Postma DS, Kerstjens HA. A systematic review of the effects of bronchodilators on exercise capacity in patients with COPD. *Chest.* 2002; 121(2): 597-608.
20. Pavasini R, Camici PG, Crea F, Danchin N, Fox K, Manolis AJ, Marzilli M, Rosano GMC, Lopez-Sendon JL, Pinto F, Balla C, Ferrari R. Anti-anginal drugs: Systematic review and clinical implications. *Int J Cardiol.* 2019; 283: 55-63.
21. Bagshaw SM, Delaney A, Haase M, Ghali WA, Bellomo R. Loop diuretics in the management of acute renal failure: a systematic review and meta-analysis. *Crit Care Resusc.* 2007; 9(1): 60-8.
22. Wargo KA, Banta WM. A comprehensive review of the loop diuretics: should furosemide be first line? *Ann Pharmacother.* 2009; 43(11): 1836-47.
23. Li X, Huang X, Bai C, Qin D, Cao S, Mei Q, Ye Y, Wu J. Efficacy and safety of teneligliptin in patients with type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials. *Front Pharmacol.* 2018; 9: 449.
24. DeCamp LR, Byerley JS, Doshi N, Steiner MJ. Use of antiemetic agents in acute gastroenteritis: a systematic review and meta-analysis. *Arch Pediatr Adolesc Med.* 2008; 162(9): 858-65.
25. Kopsaftis ZA, Sulaiman NS, Mountain OD, Carson-Chahhoud KV, Phillips PA, Smith BJ. Short-acting bronchodilators for the management of acute exacerbations of chronic obstructive pulmonary disease in the hospital setting: systematic review. *Syst Rev.* 2018; 7: 213.
26. Fan KC, Lin J, Yannuzzi NA, Al-Kharsan H, Patel NA, Maestre-Mesa J, Zaidi M, Miller D, Flynn Jr HW. *In vitro* susceptibilities of methicillin-susceptible and resistant staphylococci to traditional antibiotics compared to a novel fluoroquinolone. *J Ophthalmic Inflamm Infect.* 2020; 10(1): 9.
27. Lodise T, Corey R, Hooper D, Cammarata S. Safety of delafloxacin: focus on adverse events of special interest. *Open Forum Infect Dis.* 2018; 5(10): ofy220.
28. Pullman J, Gardovskis J, Farley B, Sun E, Quintas M, Lawrence L, Ling R, Cammarata S, PROCEED Study Group. Efficacy and safety of delafloxacin compared with vancomycin plus aztreonam for acute bacterial skin and skin structure infections: a phase 3, double-blind, randomized study. *J Antimicrob Chemother.* 2017; 72(12): 3471-3480.
29. McCurdy S, Lawrence L, Quintas M, Woosley L, Flamm R, Tseng C, Cammarata S. *In vitro* activity of delafloxacin and microbiological response against fluoroquinolone-susceptible and non-susceptible *Staphylococcus aureus* isolates from two phase 3 studies of acute bacterial skin and skin structure infections. *Antimicrob Agents Chemother.* 2017; 61(9). pii: e00772-17.
30. Mogle BT, Steele JM, Thomas SJ, Bohan KH, Kufel WD. Clinical review of delafloxacin: a novel anionic fluoroquinolone. *J Antimicrob Chemother.* 2018; 73(6): 1439-1451.
31. Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters E, Armstrong DG, Deery HG, Embil JM, Joseph WS, Karchmer AW, Pinzur MS, Senneville E. Executive summary: 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis.* 2012; 54(12): e132-73.
32. Siala W, Mingeot-Leclercq MP, Tulkens PM, Hallin M, Denis O, Van Bambeke F. Comparison of the antibiotic activities of daptomycin, vancomycin, and the investigational fluoroquinolone delafloxacin against biofilms from *Staphylococcus aureus* clinical isolates. *Antimicrob Agents Chemother.* 2014; 58(11): 6385-97.
33. Kutob LF, Justo JA, Bookstaver PB, Kohn J, Albrecht H, Al-Hasan MN. Effectiveness of oral antibiotics for definitive therapy of gram-negative bloodstream infections. *Int J Antimicrob Agents.* 2016; 48(5): 498-503.
34. Shorr AF, Kunkel MJ, Kollef M. Linezolid *versus* vancomycin for *Staphylococcus aureus* bacteraemia: pooled analysis of randomized studies. *J Antimicrob Chemother.* 2005; 56: 923-9.
35. Kingsley J, Mehra P, Lawrence LE, Henry E, Duffy E, Cammarata SK, Pullman J. A randomized, double-blind, phase 2 study to evaluate subjective and objective outcomes in patients with acute bacterial skin and skin structure infections treated with delafloxacin, linezolid or vancomycin. *J Antimicrob Chemother.* 2016; 71: 821–9.
36. Melinta Therapeutics, Inc. Study to compare delafloxacin to moxifloxacin for the treatment of adults with community-acquired bacterial pneumonia (DEFINE-CABP). NCT02679573. <https://clinicaltrials.gov/ct2/show/NCT02679573>. [Last accessed on 03/03/2022].



37. Melinta Therapeutics, Inc. Melinta Therapeutics ceases phase 3 PROCEEDING Study. <http://melinta.com/melinta-therapeutics-ceases-phase-3-proceeding-study/> [Last accessed on 03/03/2022].
38. Center for Drug Evaluation and Research: Delafloxacin NDA Briefing. Reference ID: 4113514. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/208610Orig1s000,208611Orig1s000Approv.pdf.
39. Litwin JS, Benedict MS, Thorn MD, Lawrence LE, Cammarata SK, Sun E. A thorough QT study to evaluate the effects of therapeutic and supratherapeutic doses of delafloxacin on cardiac repolarization. *Antimicrob Agents Chemother.* 2015; 59: 3469–73.
40. Ferguson J, Lawrence L, Paulson S, *et al.* Assessment of phototoxicity potential of delafloxacin in healthy male and female subjects: a phase 1 study. In: Proceedings of the fifty-fifth Interscience Conference on Antimicrobial Agents and Chemotherapy with the International Society of Chemotherapy's International Congress of Chemotherapy and Infection, San Diego, CA, USA, 2015. Poster F-1198a. American Society for Microbiology, Washington, DC, USA.
41. Baxdela (delafloxacin) [Package Insert]. Lincolnshire, IL, USA: Melinta Therapeutics Inc; 2017. https://www.accessdata.fda.gov/drugsatfda_docs/lab/2017/208610s000,208611s000lbl.pdf.
42. Manosuthi W, Wiboonchutikul S. Treatment outcomes of oral sitafloxacin in acute complicated urinary tract infection and pyelonephritis. *Springerplus.* 2016; 5: 410.
43. Shetty N, Wilson AP. Sitafloxacin in the treatment of patients with infections caused by vancomycin-resistant enterococci and methicillin-resistant *Staphylococcus aureus*. *J Antimicrob Chemother.* 2000; 46(4): 633-8.
44. Lubasch A, Erbes R, Mauch H, Lode H. Sparfloxacin in the treatment of drug resistant tuberculosis or intolerance of first line therapy. *Eur Respir J.* 2001; 17(4): 641-6.
45. Park HS, Oh SH, Kim HS, Choi DR, Kwak JH. Antimicrobial activity of zabofloxacin against clinically isolated *Streptococcus pneumoniae*. *Molecules.* 2016; 21(11): 1562.
46. Kocsis B, Domokos J, Szabo D. Chemical structure and pharmacokinetics of novel quinolone agents represented by avarofloxacin, delafloxacin, finafloxacin, zabofloxacin and nemonoxacin. *Ann Clin Microbiol Antimicrob.* 2016; 15(1): 34.
47. Kocsis B, Szabo D. Zabofloxacin for chronic bronchitis. *Drugs Today (Barc).* 2016; 52(9): 495-500.
48. Chalhoub H, Harding SV, Tulkens PM, Van Bambeke F. Influence of pH on the activity of finafloxacin against extracellular and intracellular *Burkholderia thailandensis*, *Yersinia pseudotuberculosis* and *Francisella philomiragia* and on its cellular pharmacokinetics in THP-1 monocytes. *Clin Microbiol Infect.* 2020; 26(9): 1254.e1-1254.e8.
49. McKeage K. Finafloxacin: first global approval. *Drugs.* 2015; 75(6): 687-93.
50. Bartoletti R, Cai T, Perletti G, Wagenlehner FME, Johansen TEB. Finafloxacin for the treatment of urinary tract infections. *Expert Opin Investig Drugs.* 2015; 24(7): 957-63.
51. Rodrigues J, Ramani A, Mondarkar S, Nazareth M, Sobti V, Krishnaprasad KD. Use of garenoxacin: a new generation antibiotic for surgical infections. *Int J Basic Clin Pharmacol.* 2015; 4: 144-147.
52. Pham TDM, Ziora ZM, Blaskovich MAT. Quinolone antibiotics. *MedChemComm.* 2019;10(10): 1719-1739.
53. Wren C, Bell E, Eiland LS. Ozenoxacin: a novel topical quinolone for impetigo. *Ann Pharmacother.* 2018; 52(12): 1233-1237.
54. Hebert AA, Rosen T, Lopez NA, Zsolt I, Masramon X. Safety and efficacy profile of ozenoxacin 1% cream in pediatric patients with impetigo. *Int J Womens Dermatol.* 2020; 6(2): 109-115.
55. Tabara K, Tamura R, Nakamura A, Mori S, Kitano T, Fujikawa K, Fujikawa M, Okamoto K, Kanayama S, Uratsuji H, Ikeda F, Matsumoto T. Anti-inflammatory effects of ozenoxacin, a topical quinolone antimicrobial agent. *J Antibiot.* 2020; 73: 247–254.
56. Farrell DJ, Liverman LC, Biedenbach DJ, Jones RN. JNJ-Q2, a new fluoroquinolone with potent *in vitro* activity against *Staphylococcus aureus*, including methicillin- and fluoroquinolone-resistant strains. *Antimicrob Agents Chemother.* 2011; 55(7): 3631-4.
57. Jones TM, Johnson SW, Di Mondì VP, Wilson DT. Focus on JNJ-Q2, a novel fluoroquinolone, for the management of community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections. *Infect Drug Resis.* 2016; 9: 119-28.
58. Bhatt PR, Scaiola A, Loughran G, Leibundgut M, Kratzel A, Meurs R, Dreos R, O'Connor KM, McMillan A, Bode JW, Thiel V, Gatfield D, Atkins JF, Ban N. Structural basis of ribosomal frameshifting during translation of the SARS-CoV-2 RNA genome. *Science.* 2021; 372 (6548): 1306–1313.
59. Sun Y, Abriola L, Niederer RO, Pedersen SF, Alfajaro MM, Silva Monteiro V, Wilen CB, Ho Y-C, Gilbert WV, Surovtseva YV, Lindenbach BD, Guo JU. Restriction of SARS-CoV-2 replication by targeting programmed -1 ribosomal frameshifting. *Proc Natl Acad Sci USA.* 2021; 118926: e2023051118.
60. Park JH, Yamaguchi T, Ouchi Y, Koide K, Mori S, Kim H, Mukai T, Nakajima C, Suzuki Y. WQ-3810 inhibits DNA gyrase activity in ofloxacin-resistant *Mycobacterium leprae*. *J Infect Chemother.* 2020; 26(4): 335-342.
61. Ouchia Y, Mukai T, Koide K, Yamaguchi T, Park JH, Kim H, Yokoyama K, Tamaru A, Gordon SV, Nakajima C, Suzuki K. WQ-3810: A new fluoroquinolone with a high potential against fluoroquinolone-resistant *Mycobacterium tuberculosis*. *Tuberculosis.* 2020; 120: 101891.
62. Adis Insight. Lascufloxacin – Kyorin Pharmaceutical, 2021. Available from: <https://www.adisinsight.springer.com/drugs/800035339/>. [Last accessed on 03/03/2022].
63. Murata M, Kosai K, Yamauchi S, Sasaki D, Kaku N, Uno N, Morinaga Y, Hasegawa H, Miyazaki T, Izumikawa K, Mukae H, Yanagihara K. *In vitro* activity of lascufloxacin against *Streptococcus pneumoniae* with mutations in the quinolone resistance-determining regions. *Antimicrob Agents Chemother.* 2018; 62(4): e01971-17.
64. Yamagishi Y, Matsukawa Y, Suematsu H, Mikamo H. *In vitro* activity of lascufloxacin, a novel fluoroquinolone antibacterial agent, against various clinical isolates of anaerobes and *Streptococcus anginosus* group. *Anaerobe.* 2018; 54: 61–64.
65. Yan A, Bryant EE. Quinolones. In: Stat Pearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; 2020 Jan; Available from: <https://www.ncbi.nlm.nih.gov/books/NBK557777/>. [Last accessed on 03/03/2022].



66. Dellamonica P, Bernard E, Etesse H, Garraffo R, Drugeon HB. Evaluation of pefloxacin, ofloxacin and ciprofloxacin in the treatment of thirty-nine cases of chronic osteomyelitis. *Eur J Clin Microbiol Infect Dis*. 1989; 8: 1024 – 1030.

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

For any question relates to this article, please reach us at: globalresearchonline@rediffmail.com

New manuscripts for publication can be submitted at: submit@globalresearchonline.net and submit_ijpsrr@rediffmail.com



Corresponding author biography: Dr. Moumita Hazra

Dr. Moumita Hazra is qualified as an MBBS (Medicine), DCP (Clinical Pathology) (Haematology, Cytopathology, Molecular Diagnostics), MD (Pharmacology) (Clinical Pharmacology, Pharmacotherapeutics, Pharmacoepidemiology, Pharmacovigilance, Pharmacogenomics, Evidence Based Medicine, Medical Education, Obstetric and Gynaecological Reproductive Endocrinological Pharmacology, Diabetological Endocrinological Pharmacology, Neonatal Pharmacology, Respiratory Pharmacology, Clinical Medical Pharmacology, Cancer Immunotherapy), MBA (Hospital Management) (Operations Management), PGDCR (Clinical Research) (Medical Research Methods, Clinical Research Ethics); FIAMS (Pathology); Associate MRCP (Clinical Medicine), Associate MRCOG (Obstetrics and Gynaecology); MIPS (Pharmacology), MISRPT (Rational Pharmacotherapeutics, Pharmaco-Haemo-MaterioVigilance), MCCP (Chest Medicine), MIAC (Cytology and Cytopathology), MIAPM (Pathology), MKCIAPM (Pathology), MIMA (Medicine).

Her affiliations include Associate Professor of Pharmacology and Clinical Pharmacology for MBBS, MD, MS, DM, MCh, Dental, MSc, MPhil, PhD, Nursing, Paramedical and Pharmacy students; Associate Professor, Head of Department In Charge, Department of Pharmacology, Former Pharmaco-Haemo-Materio-Vigilance Specialist, Pharmacovigilance Committee, Mamata Medical College and Hospitals; Former Associate Professor, Head of Department In Charge, Department of Pharmacology, Rama Medical College Hospital and Research Centre, Rama University; Former Deputy Medical Superintendent, Department of Medical Administration, Former Assistant Professor, Head of Department In Charge, Department of Pharmacology, Shri Ramkrishna Institute of Medical Sciences and Sanaka Hospitals, Hi-Tech Medical College and Hospital, Gouri Devi Institute of Medical Sciences and Hospital, K.D. Medical College Hospital and Research Center; Former Resident and Tutor, Departments of Pharmacology and Pathology, J. J. M. Medical College and Hospitals, Chigateri General Hospital, Medical and Surgical Departments, Dr. B. R. Ambedkar Medical College and Hospital, K. C. General Hospital; Guest Professor, Head of Department, Department of Pharmacology, Hi-Tech College of Nursing; Consultant Multi-Specialist Clinical Pharmacological Physician, Consultant Clinical Pathologist, Medical Director, Medical Superintendent, Consultant Rational Pharmacotherapeutic Physician, Consultant Drug Safety and Quality Physician, Consultant Fertility and Reproductive Endocrinological Pharmacological Physician, Consultant Clinical Endocrinological Pharmacological Physician, Consultant Respiratory Pharmacological Physician, Consultant Neonatal Pharmacological Physician, Pharmaco-Haemo-Materio-Vigilance Specialist, Pharmacogenomics Specialist, Molecular Pharmacology Specialist, Cytopathologist, Molecular Diagnostics Specialist, Medical Academics and Clinical Research Director, Managing Director, Hazra Nursing Home, Hazra Polyclinic And Diagnostic Centre, Dr. Moumita Hazra's Polyclinic And Diagnostic Centre, Academic Centre, Educational Centre, and World Enterprises; Consultant Pathologist, Laboratory Director, Mahuya Diagnostic Centre and Doctors' Chamber, Indus Nursing Home and Indus Diagnostic Centres, General Patho Clinic, Medilab Pathological Laboratory; Medical Editor-In-Chief, Medical Editorial and Advisory Board Member, Medical Editor, Medical Reviewer and Medical Author in many National and International Publications; Former Manager, Clinical Excellence and Quality Management, Fortis Hospitals; Former Assistant Medical Director, Medical Editor, GIOSTAR IRM Institutes, Hospitals and Laboratories, New Delhi, India, USA, World; Medical Examinations Appraiser, Medical Examinations Assessor, Medical Invigilator, Medical Examiner, Medical Universities and Examination Boards, India; Medical Fellow and Member, Medical Associations, Academies and Colleges, India, UK; Former Academic Scholar and Research Scientist, Medical and Science Universities, India, USA, UK, World; with a professional experience in Medical Sciences, for 42-43 years.

She has authored and co-authored almost 100 ongoing and published medical articles in national and international journal publications. She has authored and edited almost 32 ongoing and published medical books. She has presented numerous medical posters and medical papers as speaker in many national and international conferences. She has significant literary contributions in: Pharmacology, Clinical Pharmacology, Molecular Pharmacology, Pharmaco-Haemo-Materio-Vigilance, Rational Pharmacotherapeutics, Evidence Based Medicine, Pharmacological Quality and Safety, Pharmacology and Clinical Pharmacology undergraduate, postgraduate, doctorate and postdoctorate Professing, Pharmacology and Clinical Pharmacology Education, Medical undergraduate, postgraduate, doctorate and postdoctorate Professing, Medical Education, Medical Advisory Board and Faculty, Competency Based Medical Education: Competencies, Objectives, Teaching Learning Methods, Alignment and Integration in Medical Education, Assessment Methods, Aligned and Integrated Assessment Methods, Pharmacology Professing Methods, Clinical Pharmacology Professing Methods, Medical Professing Methods, Medical Academic and Education Management, Academic Directorialship, Pharmacology Research Methods, Clinical Pharmacology Research Methods, Clinical Research Methods, Pharmacology Education Research Methods, Clinical Pharmacology Education Research Methods, Medical Education Research Methods, Dermatopharmacology, Respiratory Pharmacology, Drug Delivery Systems, Pharmacology of Antibiotics, Pharmacology of Retinoids, Ocular Pharmacology, Gynaecological and Obstetric Pharmacology, Endocrine Pharmacology, Endocrine Onco-Pharmacology, Reproductive Endocrinology, Pharmacology of Vitamins and Antioxidants, Onco-Molecular Pharmacology, Therapeutic Onco-Vaccines, Pharmaco-Immuno-Onco-Therapeutics, Molecular Therapeutics, Pharmacogenetics, Pharmacogenomics, Epigenetics, Pharmacoepidemiology, Pharmacoconomics, Pharmacodynamics, Pharmacokinetics, Personalised Medicine, Clinical Medicine, Stem Cell Therapeutics and Research, Regenerative Medicine, Haematology, Haemato-Oncology, Endocrine Onco-Pathology, Onco-Molecular Pathology, Cytopathology, Cytology, Molecular Diagnostics, Medical Directorship, Hospital Management, Hospital Administration, Medical Administration, Medical Directorship of Global Medical Universities, Institutions, Hospitals and Laboratories, Management of Government Universities, Institutions and Hospital Establishments, Corporate Strategies, Planning and Advisory, Brand Management, Corporate Project Improvisation, Clinical Research, Clinical Research Methods, Clinical Research Authorship and Reviewing, Clinical Research Publications Editing, Medical Editing, Clinical Trials Management, Medical and Clinical Research Directorship.

