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Research Article

Trends in Research on The Effects of Nutritional Supplements Against Nephrotoxicity; A Bibliometric Study

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Abstract:

Aim: Over the years, publications investigating the potential of various nutritional supplements, such as antioxidants, probiotics, and phytochemicals, to improve drug-induced nephrotoxicity have increased both qualitatively and quantitatively. This bibliometric analysis evaluated 100 highly cited articles on the protective effects of nutritional supplements against nephrotoxicity published between 2010 and 2023.
Method: Articles published in these 13 years were evaluated through a structured search in Scopus and Web of Science databases. Statistics and visualization techniques were done using VOSviewer and RStudio software.
Results: The increase rate of articles published on this subject was found to be %450. The average h-index of selected studies was calculated as 60. A total of 534 authors and a citation rate of 86.95 were determined. The total citation mean was defined as 9 per year. The top 3 supplements were curcumin (n=7), melatonin, and probiotics (n=5) in the trends. Cisplatin and gentamicin are used as toxic agents in 34% of the top 100 articles we researched, and they continue to be a trend.
Conclusion: Curcumin, melatonin, berberine, quercetin, and probiotics are trending and effective supplements in this field. Based on our investigations, we think that the synergy between the effective bioactive ingredients and probiotics and/or other functional foods suggests future novel approaches based on interactions involving microbiota, oxidative, and inflammatory stress.

1. Introduction

Kidneys are organs that can be heavily exposed to toxic substances due to their urination mechanism to remove waste products from the blood and their very high blood perfusion capacity. Because of these properties, nephrotoxicity (acute renal failure, acute kidney injury) may develop, especially because of heavy drug consumption, high doses, and/or long-term exposure to toxic components. As it progresses, chronic renal failure may develop, leading to organ loss and even mortality [1–3]. Drugs frequently used by patients, like chemotherapeutic agents, non-steroidal analgesics, and radiopharmaceuticals, have potential dangers that may cause nephrotoxicity in cases such as careless use and incorrect dosage calculation. In many studies on laboratory animals, experimental nephrotoxicity is created, and research is carried out that can protect the kidney tissue against toxic substances and prevent or treat damage [4]. Since it is very difficult to carry out such experimental studies on humans, most of the projects developed in this field are animal experiments to a considerable extent. Experimental animals are supplemented with agents such as functional foods, plant chemicals, vitamins, and microorganisms at rates and doses, especially in fields such as pharmacology, toxicology, molecular biology, and biochemistry [5,6]. Thus, it aims to contribute to science and humanity by developing protective mechanisms or drugs against pathological conditions such as nephrotoxicity. In Scopus, when the word "Nephrotoxicity" is searched among abstracts, more than 73 thousand documents are listed. When we write in Scopus and search within only abstract page: "Nutritional supplement" OR "functional foods" OR "protective effects" OR "protects" OR "dietary supplement", and associate this with nephrotoxicity or kidney, more than 26 thousand articles are reached, highlighting the importance of this emerging field.

Given the complex pathophysiology of nephrotoxicity involving oxidative stress, inflammation, and apoptosis, compounds with pleiotropic actions like antioxidants, anti-inflammatories, and organelle stabilizers have shown promise [4,7,8]. When it comes to antioxidative properties, plants will, of course, come to mind first. Supplements of plant chemicals and extracts are among the most studied topics due to their high protective-restorative and ameliorative potential against free radicals and oxidative stress [9,10]. There are more than 20 thousand article titles about curcumin, which has high protective effects alone in this context.

Several nutritional supplements derived from foods and plants have demonstrated nephroprotective potential in clinical and/or preclinical studies [11]. These include curcumin, melatonin, quercetin, vitamin C, lycopene, ginger, berry polyphenols, fatty acids, probiotics, bioactive peptides, etc. [12–16]. Proposed mechanisms include scavenging reactive oxygen species, suppressing inflammatory cytokines and infiltrating leukocytes, inhibiting apoptosis, and preserving mitochondrial structure and function [17]. Such supplements are especially attractive nephroprotective agents given their safety, low cost, and accessibility. However, translation from bench to bedside requires more rigorous validation. Systematically analyzing global research trends can help identify key gaps and promising directions that will advance the field. The discussion highlights the need for more research on therapeutic and ameliorative effects after toxicity has occurred to mimic clinical scenarios better.

This study aims to conduct a comprehensive bibliometric analysis of global research trends on the protective, therapeutic, and ameliorative effects of supplements on nephrotoxicity from 2010–2023. Our main specific aim is to determine articles with high impact value that research the protective effects constituting one-third of all publications in the scope of nephrotoxicity. Through these articles, we have determined we are able to reveal which authors, which countries, which collaborations are effective, and which articles would be more beneficial for those who want to work in this field to read. In addition, we are to determine the scopes, such as which toxic substances and which protective supplements are more remarkable and which keywords should be used when planning a high-impact value research.

2. Material and Methods

2.1. Data Source

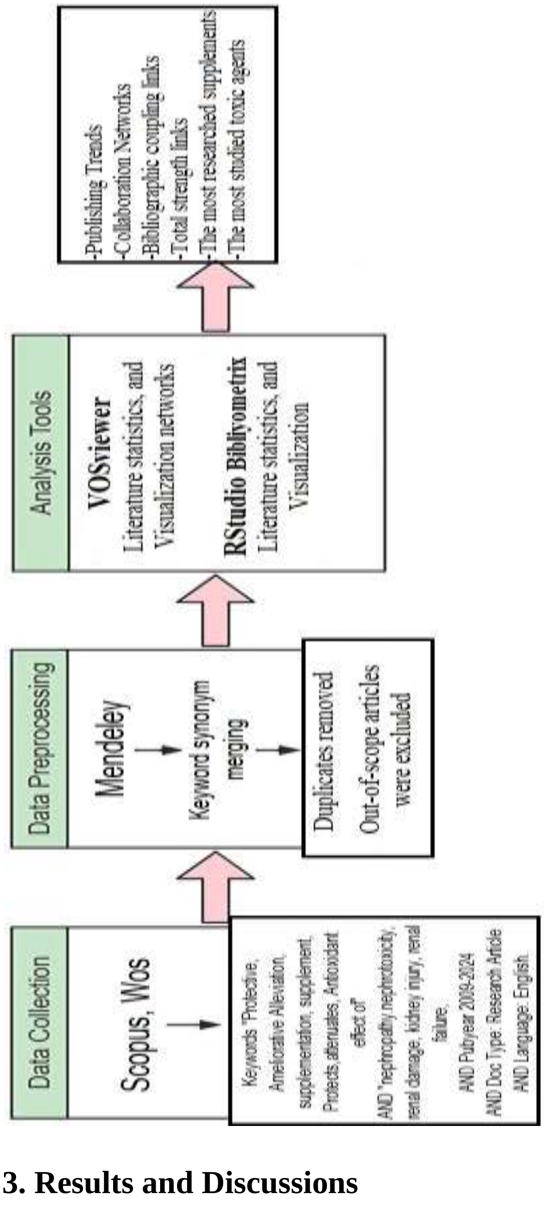
The data source for this bibliometric analysis consisted of scholarly publications from Scopus and Web of Science Core Collection. The Web of Science Core Collection provides access to over 21,000 peer-reviewed, high-quality journals across 250 sciences. It enables comprehensive citation analysis and includes the Science Citation Index Expanded (SCIE), Conference Proceedings Citation Index-Science (CPCI-S), Book Citation Index-Science (BKCI-S), and Emerging Sources Citation Index (ESCI). By searching the Web of Science and Scopus, this analysis ensured comprehensive coverage of the literature on nutritional supplements and nephrotoxicity spanning science, medicine, biochemistry, pharmacology, toxicology, and complementary or alternative medicine domains.

2.2. Search Strategy

The search strategy employed a combination of relevant keywords pertaining to the key concepts of nephrotoxicity and protective, therapeutic, and ameliorative effects. For nephrotoxicity, search terms included "nephrotoxicity". The protective, therapeutic, and ameliorative effects were captured using the keywords “protective effects on nephrotoxicity,” “therapeutic effects,” “ameliorative effects,” “protect,” and "ameliorate." The search combined these groups of keywords to retrieve relevant papers. Additional filters were applied to limit the results to English-language articles published from 2010 to 2023. Among the 901 research articles accessed, the 100 most cited articles were selected according to the year they were published. The query is as given below;

(TITLE-ABS-KEY ("Protective" OR "Ameliorative" OR "Alleviation of " "dietary" OR "supplementation" OR "supplement" "Protects" OR "attenuates" OR "Antioxidants" OR "Antioxidant effect of") AND ALL ("nephropathy" OR "nephrotoxicity" OR "renal damage" OR "induced nephrotoxicity" OR "kidney injury" OR "renal failure")) AND PUBYEAR >2009 AND PUBYEAR<2024 AND (LIMIT-TO (DOCTYPE,"ar")) AND (LIMIT-TO (EXACTKEYWORD, "Article")) AND (LIMIT-TO (LANGUAGE,"English")).

The records retrieved from the database search were imported into Mendeley, and duplicates were removed. The articles were then screened manually based on title, abstract, and full-text review to confirm they examined the protective, therapeutic, and ameliorative effects against drug- or toxin-induced nephrotoxicity. Exclusion criteria eliminated papers that were not original experimental research articles (e.g., meta-analyses, reviews, letters, editorials, and conference abstracts), did not have full text available, or involved nephroprotection by medications, plant extracts, or chemical compounds rather than defined nutritional supplements. After applying these screening criteria, the final set of eligible publications was imported into VOSviewer (version 1.6.20, Nees Jan van Eck and Ludo Waltman, Leiden University, Netherlands), RStudio Bibliyometrix 2024 and Excel tools for in-depth bibliometric analysis. A framework flow diagram is schematized below.



3. Results and Discussions

3.1. General results

The analysis conducted on the screened publications aimed to assess research productivity, impact, collaborations, intellectual structure, and emerging frontiers within this domain.

This bibliometric analysis compiled 100 research articles on the protective effects of nutritional supplements against nephrotoxicity published between 2010 and 2023. The dataset encompassed articles investigating a diverse range of supplements using different study models and methodologies. An overview of publication trends showed increasing research interest in this domain over the past decade. The number of publications rose steadily from 32 in 2010 to 176 articles in 2023. The Increase rate was found to be 450% (Figure 1).

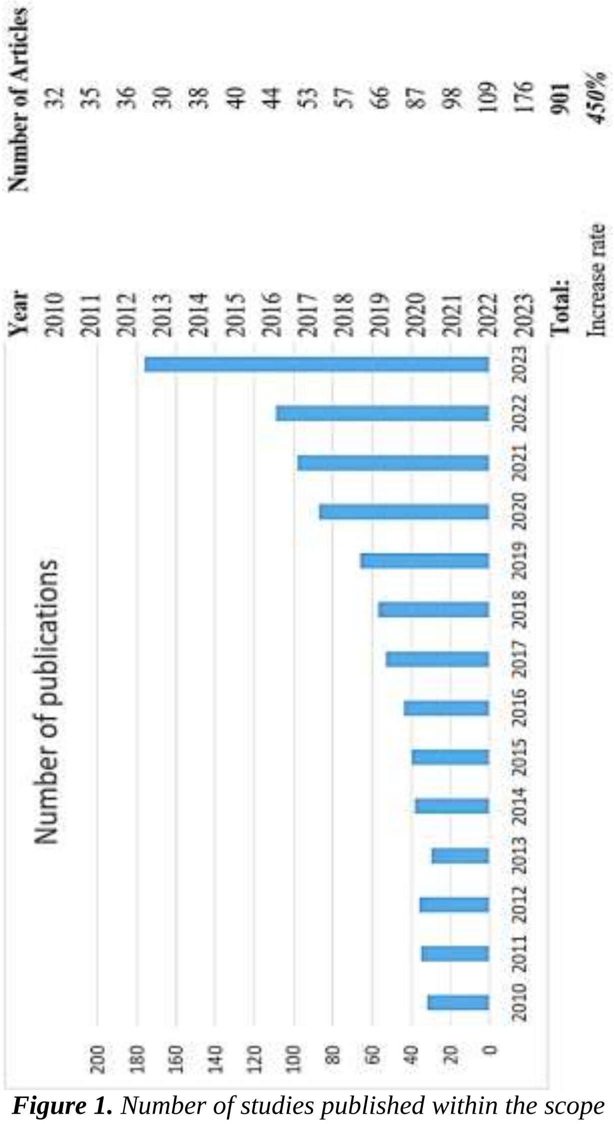


Figure 1. *Number of studies published within the scope of our concept.*

Graphic enabled the examination of temporal publication volume and growth patterns over the past decade. The graph can point to potential surges in research interest or productivity within certain periods.

We carefully selected 100 studies throughout 2010–2023 conducted across the Web of Science, examining the protective, therapeutic, and ameliorative effects on nephrotoxicity that were most cited according to the years they were published, and that fit our concept. Analysis of temporal publication trends showed the output has grown steadily over the past decade. An overview of citations related to our selected Top 100 cited studies is given in Figure 2.

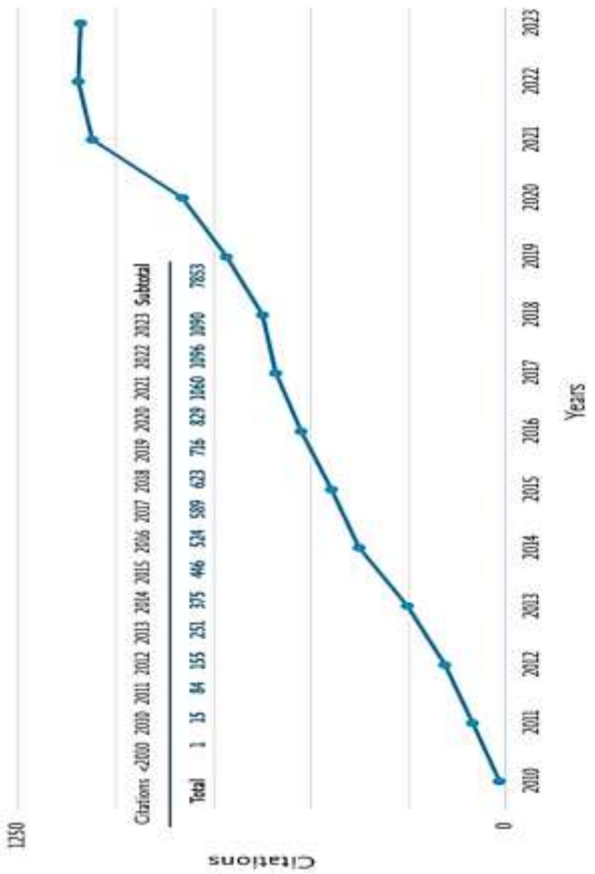


Figure 2. *Overview of citations related to our selected Top 100 studies.*

The average h-index of selected studies was calculated as 60. In 2023, 1128 citations were made slightly behind 2022, thus creating a peak at the top.

Table 1. *Main information of the 100-research article*

Information Data	Value
Timespan	2010:2023
Documents	100
Sources	65
Annual growth rate	7.09
Authors	534
Single-authored doc	1
International Co-Authorship	21%
Co-Authors per doc	5.96
Author’s keywords	243
References	5096
Document average age	8.6
Average citations per doc	86.95

A total of 534 authors and a citation rate of 86.95 were determined. The other main information of the 100 research articles of our study is as follows (Table 1). This publication trajectory aligns with recognizing nutritional supplements as a promising avenue for mitigating drug- or toxin-induced kidney injury. The accumulated preliminary evidence has spurred greater research interest to further validate and expand on earlier findings. If the current growth rate is raised, publication output looks poised to surpass hundreds of articles in 2030. This ascending tendency foreshadows an intensifying research focus on elucidating nephroprotective supplements and mechanisms to enable translation to clinical application.

Table 2*. Top ten journals*

Journals	Articles	IF
Chemico-Biological Interactions	7	5.1
Food And Chemical Toxicology	5	4.3
Ecotoxicology and Environmental Safety	4	6.8
Experimental and Toxicologic Pathology	4	2.6
Scientific Reports	4	4.6
Bmc Complementary and Alternative Medicine	3	3.9
Pharmaceutical Biology	3	3.8
Toxicology Mechanisms and Methods	3	3.2
Biological Trace Element Research	2	3.9
Biomedicine and Pharmacotherapy	2	7.5

*(**IF**; 2-year Impact Factor)*

Table 3. *Mean total citation per article and mean total citation per year.*

Year	Mean TC/Art	*n*	Mean TC/Year	Citable Years
2010	134	13	8,9	15
2011	144	9	10,3	14
2012	95	12	7,3	13
2013	117	5	9,8	12
2014	95	10	8,6	11
2015	72	7	7,3	10
2016	85	5	9,5	9
2017	75	7	9,4	8
2018	67	3	9,6	7
2019	79	6	13,2	6
2020	69	8	13,9	5
2021	32	5	8,0	4
2022	16	5	5,4	3
2023	7	5	3,5	2
Mean	**79,7**	100	**9,0**	

The list and issue of the 10 journals where articles are most frequently published are below (Table 2).In addition, the mean total citation per article (MeanTC/Art) and mean total citation per year rates (MeanTC/Year) of the top 100 articles in our study are below (Table 3).
As can be seen from the mean total citation per year rates data, articles were balanced according to the years they were published.

3.2. Top Contributing Countries and Authors

The publications were categorized based on the country affiliation of the corresponding author to determine the top 10 countries with the greatest research output. The number of publications for these productive countries was visualized using a bar chart in descending order. This analysis delineates the leading countries driving research in this field. The top 10 authors were identified based on the number of publications for which they were either the first or corresponding author. A bar chart displayed the ranking of these 10 prolific authors. This helps distinguish researchers who are making significant contributions (Table 4).

Table 4. *Country and author productions.*

Country	Freq	Authors	Articles	TC
Turkey	69	Kandemir FM	7	426
China	61	Caglayan C	6	413
Egypt	46	Kucukler S	6	407
India	25	Yildirim S	4	310
Saudi Arabia	14	Zhang J	4	224
Iran	11	Abdel M AE	3	194
Tunisia	11	Chen C	3	248
Pakistan	10	Li Jl	3	258
Japan	9	Li W	3	248
Netherlands	7	Wang Z	3	248

The screened articles represented authorship from a broad collection of countries spanning six continents: Asia, Europe, North America, South America, Africa, and Australia. In total, 29 different countries have contributed to this research domain over the past decade. The wider international distribution underscores the global relevance of nutritional supplements for nephroprotection across diverse geographic regions. Further analysis ranked the countries by their total publications to identify the top 10 most productive nations shown in Table 4, Figure 3.
The fact that developing countries like China, Turkey, India, Iran, and Egypt emerged as major contributors is unsurprising, as the affordability and accessibility of nutritional interventions make them especially valuable in resource-limited settings. Investigating traditional medicines in these countries also provided clues on bioactive compounds with nephroprotective potential worth pursuing further. On the other hand, the lack of North American and European nations at the top is notable, given their prominence in biomedical research overall. This presents an opportunity for more studies in Western contexts to facilitate translation. However, the wide range of productive countries signifies that nephroprotection using nutritional supplements has truly become a global research priority. In addition, the richness of the traditional culinary culture and the depth of their historical agricultural background in these countries are the underlying facts that they have a society that uses functional foods much more and reflects this to science.

3.3. Highly Cited Articles

The articles were sorted by their Scopus citation count to identify the top 10 most highly cited papers. These were compiled into a table listing each article's first author, year, journal, DOI, total number of citations (TC), and TC/per-year rates. This table delineates the foundational studies that have been hugely impactful (Table 5).

Table 5. *Top 10 cited papers.*

Article	DOI	TC	TC/ Year
Grams Me, *2011, Clin J Am Soc Nephrol*	10.2215/CJN.08781010	305	21,8
Leoncini M, *2014, J Am Coll Cardiol*	10.1016/j.jacc.2013.04.105	231	21,0
Mansour Sa, *2010, Pestic Biochem Physiol*	10.1016/j.pestbp.2009.08.008	230	15,3
Yousef Mi, *2010, Food Chem Toxicol*	10.1016/j.fct.2010.08.034	213	14,2
Heerspink Hjl, *2012, Kidney Int*	10.1038/ki.2012.74	202	15,5
Latha R, *2011, Chem-Biol Interact*	10.1016/j.cbi.2010.11.005	200	14,3
Li Y, *2011, Biomaterials*	10.1016/j.biomaterials.2011.08.001	200	14,3
Xie K, *2010, Shock*	10.1097/SHK.0b013e3181cdc4ae	200	13,3
Sahin K, *2010, Life Sci*	10.1016/j.lfs.2010.06.014	190	12,7
Khan Ra, 2012, Bmc Complement Med-A	10.1186/1472-6882-12-178	169	13,0

First author, year, journal, DOI, total of citations (TC) and TC/Per year rates on top 10 cited papers. [1,11,14,18–24]

3.4. Collaboration Network Visualization

Bibliometric mapping was conducted using VOSviewer software to visualize research collaborations between countries, institutions, and authors. VOSviewer extracts and analyzes bibliographic data to construct networks based on co-authorship linkages. Each network graph presents nodes representing the entities connected by edges

denoting relationships between nodes. For this analysis, three collaboration networks were generated.
Country collaboration network: The network map illustrates connections between countries whose researchers have co-authored papers, providing insights into cross-country collaborative partnerships and knowledge exchange driving this research field. Egypt was found to be the leader with 1242 strength links (Figure 3).

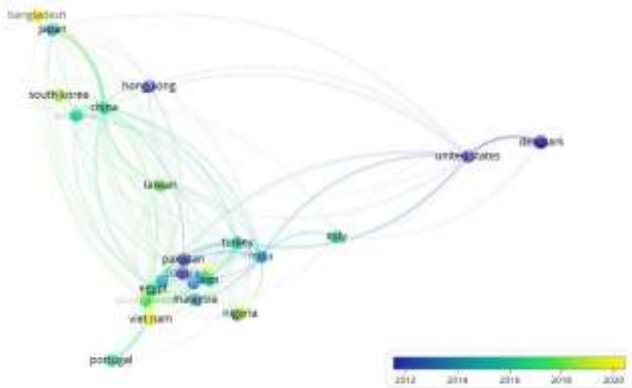


Figure 3. *The total strength of the bibliographic coupling links with author countries.*

Author collaboration network: The network graph maps links between authors who have co-authored papers, revealing key authors leading collaborative initiatives and the relationships between them. A minimum number of articles of an author, at least two, are visualized (Figure 4).

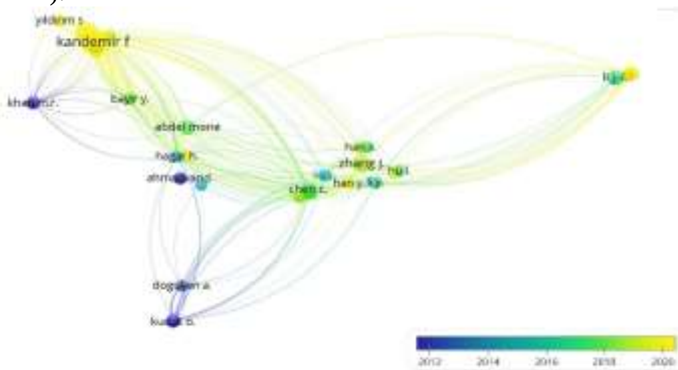


Figure 4*. The total strength of the citation links with other authors.*

3.5. Trend Topics

Topic bursts were identified using RStudio to detect research trend topics that have rapidly grown in popularity. This points to emerging frontiers and knowledge surges. RStudio extracts noun phrases from titles, abstracts, and keywords to construct a co-occurrence map linking related topics based on shared terminology. Each topic is assigned a strength metric, indicating its burst intensity. Strong bursts reveal research hotspots gaining momentum (Figure 5). Analysis of high-frequency noun phrases in article titles, abstracts, and keywords over 2010–2023 revealed several topic bursts: Curcumin gained momentum, as indicated by seven publications investigating its nephroprotective

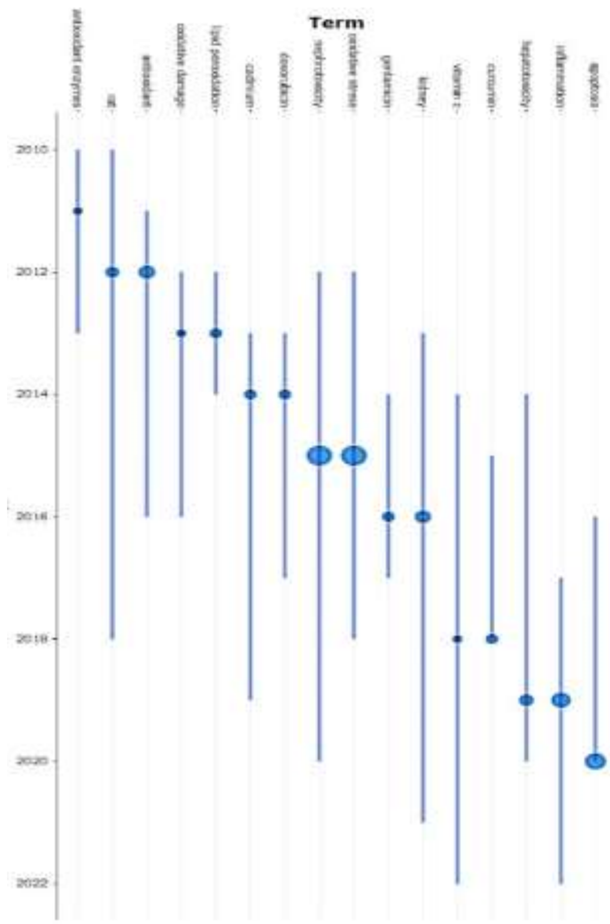


Figure 5. *Trend topics of 100 articles*

mechanisms and efficacy against toxicity from drugs like cisplatin, doxorubicin, gentamicin, and methotrexate [14,25–30]. Melatonin burst onto the scene with five articles examining its protective effects against nephrotoxicity like cadmium and mechanisms involving mitophagy [31–35]. Probiotics emerged in 5 studies. They generally used *Lactobacillus rhamnosus* and demonstrated that probiotics exhibit protective effects on kidney tissue by reducing the negative effects of factors such as gut-derived uremic toxins and inflammatory cytokines [9,13,36–38].
Several papers pointed to Nrf2 signaling as a mechanism for supplements like lycopene, curcumin, and tannic acid to mitigate nephrotoxicity from drugs like cisplatin and metals like cadmium [11,12,30,39]. The burst of dietary supplements of functional foods highlighted its attenuation of toxicity from cisplatin and other agents by modulating anti-inflammatory, anti-apoptotic, and antioxidant systems [40,41]. Autophagy arose as a protective mechanism that could be modulated by supplements like ginsenoside Rb3 and curcumin [30,42,43]. Cisplatin was the most used toxic agent by far [22,38,42,44,45]. These rising topic bursts indicate nascent areas of inquiry that have gained traction over the past decade within this research domain.
Below is the strength link keywords visualization prepared with Vosviewer; the most used supplements, toxic agents (Table 6), and strength keywords link connections are listed in Figure 6. Also, created Worldcloud via RStudio (Figure 7).

Table 6. *The most researched supplements and toxic agents in 100 articles.*

Supplement	Freq	Supplement	Freq
Curcumin	7		
Melatonin	5	Hesperidin	2
Probiotics	5	Hydrogen sulfide	2
Berberine	4	Ferulic Acid	2
Quercetin	4	Flavonoids	2
Kaempferol	3	Mangiferin	2
Naringin	3	Metformin	2
Resveratrol	3	*Moringa oleifera*	2
Rutin	3	N-Acetylcysteine	2
Ascorbic acid	2	*Nigella sativa*	2
Atorvastatin	2	*Rosmarinus officinalis*	2
Beatin	2	Rosuvastatin	2
Carotenoids	2	Salidroside	2
Chlorogenic acid	2	Selenium	2
Chrysin	2	Silymarin	2
Crocin	2	Thymoquinone	2
Toxic Agents	**Freq**	**Toxic Agents**	**Freq**
Cisplatin	24	Methotrexate	3
Gentamicin	10	Paracetamol	3
Doxorubicin	6	Acetaminophen	2
Arsenic	5	Acrylamide	2
Cadmium	3	Cyclophosphamide	2

Other Supplements; 6-gingerol, *Abroma augusta*, Acetylsalicylic acid, *Aloe vera*, Alpha-tocopherol, American ginseng berry extract, Black cumin, Carnosic acid, *Cichorium intybus*, Cinnamon, Ellagic Acid, Estradiol, Flaxseed oil, Formononetin, Gallic acid propyl ester, Ginsenoside Rg5, Ginsenoside Rh, Grape Seed, Proanthocyanidin, İfosfamide, Indoxyl Sulfate, Kaempferols, Turmeric, Leonurine, Losartan, Luteolin, Lycopene, Magnesium, Milk Thistle, Mincle, Morin, *Nigella sativa* oil, Nuciferine, Occludin, Paeoniflorin, Pamidronate, Parkin, *Parthenium hysterophorus*, Polymyxin E, Polyphenols, S-Sulfhydration, *Salvia miltiorrhiza*, Vancomycin, Vinpocetine, Vitamin C, Vitamin D, Vitamin E, Zingerone.

3.6. Discussion

This bibliometric analysis quantitatively delineated publication patterns, leading countries, institutions, and authors, impactful studies, collaborations, and research fronts that have shaped the domain of nutritional supplements for nephroprotection from 2010 to 2023. Several major findings emerge from synthesizing these scient metric insights that carry meaningful implications for strategizing future research directions in this field. The major findings can be summarized along dimensions of research growth, global productivity distribution, intellectual structure mapped through visual knowledge networking, high-impact foundation layers, and rising popularity bursts that point to emerging frontiers. The publications we selected were determined to be highly influential publications in the year they were published. We believe that interest in this field is increasing and that it will

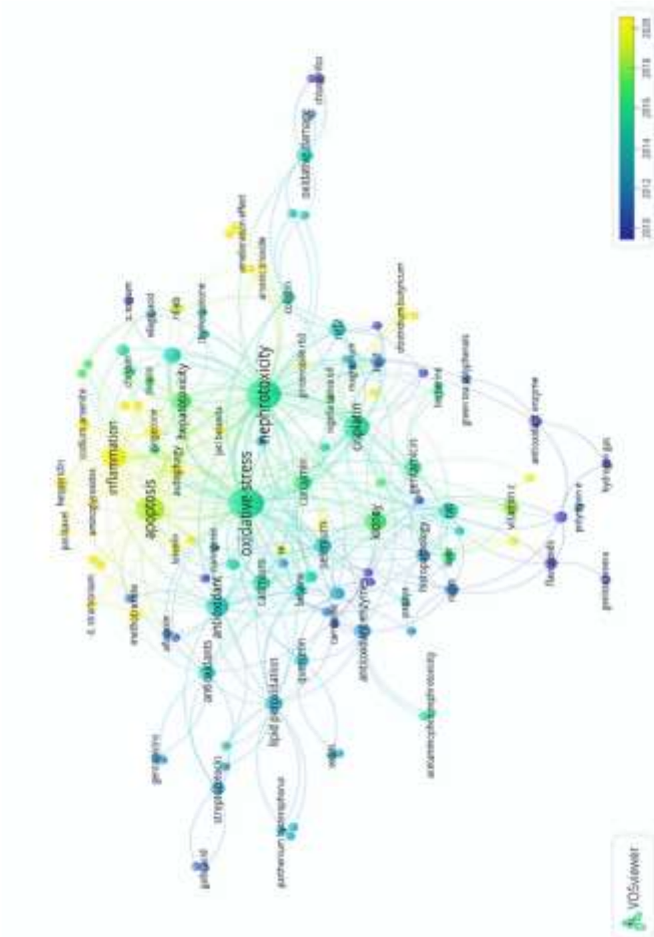


Figure 6. *The strength keywords link to 100 articles.*

Figure 7. *Word cloud of top 100 articles. (Produced via RStudio)*

continue to be at the center of new research (Figure 1,2) [18,46,47]. Up to 300 publications can be reached in 2030 if the current publication momentum continues. However, it is also noteworthy that as of 2020, the citations to the articles we selected have peaked and displayed a horizontal graph (Figure 2). This may be due to the economic problems experienced around the world and the focus of researchers on different topics due to the COVID-19 pandemic. Perhaps the very close citation rates in the last 3 years have now reached an average standard level on this subject.

China, Turkey, Egypt, India, and Iran led the global landscape of contributor nations. Highlighting productivity from developing regions where low-cost, accessible interventions hold appeal (Figure 3.). However, the involvement of Western powerhouses on the scale of the U.S., U.K., and Germany could accelerate translation to clinical adoption. A wide array spanning 29 countries does indicate widespread relevance across continents, though, from Asia to the Middle East and South America. This sets the stage for cross-pollination through expanded international collaborations. Analysis of highly cited publications that represent the field's intellectual cornerstones showed foundational layers along antioxidative, anti-inflammatory, and anti-apoptotic mechanisms have gained acceptance [19,48]. Other emerging topics like autophagy, mitophagy, and metal chelation signify supplementary protective pathways gaining mechanistic footing [30,49].

Visualization of country collaborations revealed small localized clusters within nations and regions but minimal cross-pollination globally (Figure 3) [27,50]. This suggests untapped synergies that expanded worldwide partnerships could unlock by combining global expertise. The total strength of the citation links with other authors and connections between prolific authors were also limited, pointing to opportunities through joint initiatives aligning top contributors (Figure 4). Analysis of high-frequency noun phrases denoted rising interest in particular supplements like curcumin, melatonin, tannic acid, resveratrol, berberine, quercetin, etc., and upstream processes like anti-apoptotic pathways or Nrf2 signaling (Table 6) [11,46,51–55].

The bursts around selective compounds forecast their consolidation as leading chemo-preventative contenders, backed by accrued validation. Other less-studied nutraceuticals may gain similar momentum if initial publications elucidate their nephroprotective utility. Continued uncovering of modulated cellular processes can shape mechanistic frameworks. However, research fields ranging from gene expression to in vivo testing remain underpopulated, signaling avenues for exploration. The analysis revealed a growing focus beyond just protective effects toward investigating therapeutic and ameliorative effects to mitigate existing nephrotoxicity.

Because of the concerning implications of research trends, the scientific metric insights carry strategic implications for enabling the next phase of progress through constructive research practices, expanded collaborations, and emphasizing underexplored directions. The overarching implication is that firm foundations have solidified our conceptual grasp of nutritional regimens' multimodal protective actions against kidney injury. However, translation remains stunted without more rigorous verification in preclinical models and clinical studies. Findings predominately based on rat experiments require replication in higher organisms and humans to demonstrate translational validity [41,56]. Most studies also employed co-treatment protocols for nephro-protectants rather than post-treatment scenarios resembling actual overdose scenarios. Testing real-world administration conditions can build applicability. Conflicting outcomes also need resolution through well-powered multi-lab studies. Registering, standardizing, and collating experiments across institutions via shared databases can limit duplication and enable meta-analyses clarifying consensus mechanisms or optimum dosing regimens.

According to Scopus data, in the last 15 years, there have been more than 20,000 articles titled curcumin and more than 26,000 articles titled cisplatin. Gentamicin, cisplatin's closest follower, has been used in almost 5,000 article titles. Cisplatin and gentamicin are used as toxic agents, as mentioned in 34% of the titles of the top 100 articles we researched, and they continue to be a trend in the light of literature data.

When it comes to the kidney, of course, the most examined parameters were found to be blood urea nitrogen and creatinine. Clusterin or cystatin-c was not included in any of the articles. However, it has been considered an important parameter, especially in recent years [57]. Multi-omics approaches to tracking genetic, protein, and metabolic responses can illuminate perturbed pathways. Systems biology integration can structurally model pathways, distinguishing key regulatory nodes for targeting. In vitro experiments dissecting proximal tubule cells can isolate functioning, but more holistic tissue, organoid, and computational models better capture complex system dynamics. More significant linkage with clinical specimens and data to confirm in situ mechanism concordance with more extensive phenotyping can also enhance external validity.

Highly cited cornerstones centered on antioxidative and anti-inflammatory mechanisms provide firm etiological grounding, while supplements like curcumin, quercetin, probiotics, vitamins, and resveratrol show particular promise through accrued evidence bursts. However, research fields remain around novel compounds, pathways, and technologies sparsely populated despite nephroprotective signals, presenting opportunities for exploration. Also, if there are more than 40 thousand research articles on curcumin, why are people not volunteering enough to consume curcumin? These questions are considered important question marks for this bibliographic analysis.

On the other hand, there are deficiencies in determining metabolic pathways in the studies; there are few human clinical studies, and it may be more valuable to focus on innovative synergistic effects such as probiotic supplements as well as the natural protective effects of antioxidant properties. It is well known in the literature that many functional foods or complex herbs have antioxidant properties. In our research, many publications are within the scope of "we applied and protected". Rather than such studies, the hypothesis through which metabolic pathways the protective effects occur should be explained. Many studies claim the same thing: antioxidant, anti-apoptotic, anti-inflammatory. This may not be an adequate approach. Pharmacokinetic interactions and signaling pathways should be discussed to obtain realistic quantitative evidence to explore supplements against nephrotoxicity, especially for patients receiving heavy drug therapy.

3.7. Limitations

While this bibliometric analysis provided a comprehensive quantitative mapping of research progress on protective, therapeutic, and ameliorative effects on nephrotoxicity, limitations must be acknowledged. The literature search and screening may have missed relevant publications that were not properly indexed or tagged with the specified keywords. The dynamic nature of bibliographic databases also means new records are continually added, so updated searches closer to publication should capture the latest material. Different results can be obtained by using different databases such as Pubmed and Google Scholar.

No matter how many different keyword combinations we used, we could not reach the top 100 high-citation lists because many systematic studies are listed as original research articles. That is why we had to try to collect items by eliminating them impartially.

On the other hand, including articles that were highly cited according to the year they were published caused a disproportion between years. However, rather than a publication published in 2010 and receiving 90 citations, a study published in 2023 and receiving eight citations was found to be more valuable by us and was included. We created the current concept impartially, trying to bring a formula to this situation.

In fact, in bibliometric analysis, co-author relationships, author-citation relationships, and institution-citation relationships are examined in more depth. However, our focus was different. We did not include such bibliographic data in our study. Additionally, we did not use a rote data download system. We read the abstracts of 100 articles one by one, made eligibility checks, then included them in the study.

4. Conclusions

The bibliometric analysis provided vital insights into emerging focuses like therapeutic and ameliorative effects, in addition to traditional protective effects for mitigating nephrotoxicity. Key observations can inform strategic directions to enable further advancement. Ascendant productivity trajectories, though still below maturity, confirm escalating investment aligned with initial supportive preclinical findings. Geographic emphases in leading developing nations spotlight the value of low-cost, accessible interventions but underscore the imperative for broader validation across Western settings and humans to hasten translation.

Over the past 14 years, the popularity of functional foods researched against nephrotoxicity has been increasing. Trending and effective supplements in this field are curcumin, melatonin, probiotics, berberine, and quercetin, which attract attention with their protective properties in nephrotoxicity studies. However, to create toxic effects, cisplatin is by far the leader, followed by gentamicin. There may be manipulative data records in this regard. In our research, we encountered more than 20 titles of "cisplatin-induced nephrotoxicity" in articles written by only 1 author. However, nephrotoxicity is a health problem caused by a much wider range of chemical factors, and examining this problem only through 2 chemical agents such as gentamicin and cisplatin, may not make healthy contributions to the literature.

As a result of our bibliographic analysis, we concluded that producing articles that adopt innovative approaches or include more evidence-based innovative ideas and explore pharmacodynamic mechanisms focused on synergistic effects between the effective bioactive ingredients with probiotics suggest future novel approaches based on interactions involving microbiota, oxidative and inflammatory stress. However, more animal and clinical studies are needed in order to strengthen evidence.

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- **Ethical approval:** The conducted research is not related to either human or animal use.
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References

[1] Leoncini, M., Toso, A., Maioli, M., Tropeano, F., Villani, S., and Bellandi, F., (2014). Early High-Dose Rosuvastatin for Contrast-Induced Nephropathy Prevention in Acute Coronary Syndrome: Results from the PRATO-ACS Study (Protective Effect of Rosuvastatin and Antiplatelet Therapy on Contrast-Induced Acute Kidney Injury and Myocardial Damage in Patients with Acute Coronary Syndrome), *Journal of the American College of Cardiology*, 63(1);71–79. https://doi.org/10.1016/j.jacc.2013.04.105

[2] Sinanoglu, O., Yener, A. N., Ekici, S., Midi, A., and Aksungar, F. B., (2012). The Protective Effects of Spirulina in Cyclophosphamide Induced Nephrotoxicity and Urotoxicity in Rats, *Urology*, 80(6);1392.e1-1392.e6. https://doi.org/10.1016/j.urology.2012.06.053

[3] Altınkaynak, Y., Kural, B., Akcan, B. A., Bodur, A., Özer, S., Yuluğ, E., Munğan, S., Kaya, C., and Örem, A., (2018). Protective Effects of L-Theanine against Doxorubicin-Induced Nephrotoxicity in Rats, *Biomedicine and Pharmacotherapy*, 108;1524–1534. https://doi.org/10.1016/j.biopha.2018.09.171

[4] Kellum, J. A., Romagnani, P., Ashuntantang, G., Ronco, C., Zarbock, A., and Anders, H. J., (2021). Acute Kidney Injury, *Nature Reviews Disease Primers*. 7(52). https://doi.org/10.1038/s41572-021-00284-z

[5] Mirabelli, M., Chiefari, E., Arcidiacono, B., Corigliano, D. M., Brunetti, F. S., Maggisano, V., Russo, D., Foti, D. P., and Brunetti, A., (2020). Mediterranean Diet Nutrients to Turn the Tide against Insulin Resistance and Related Diseases. *Nutrients* 12(4), 1066 https://doi.org/10.3390/nu12041066

[6] Zółkiewicz, J. ˙, Marzec, A., Ruszczy´nski, M., Ruszczy´nski, R., and Feleszko, W., (2020), Postbiotics-A Step Beyond Pre-and Probiotics. *Nutrients* 12(8), 2189; https://doi.org/10.3390/nu12082189

[7] Farooqui, Z., Ahmed, F., Rizwan, S., Shahid, F., Khan, A. A., and Khan, F., (2017) Protective Effect of Nigella Sativa Oil on Cisplatin Induced Nephrotoxicity and Oxidative Damage in Rat Kidney, *Biomedicine and Pharmacotherapy*, 85;7–15. https://doi.org/10.1016/j.biopha.2016.11.110

[8] Song, C., Fu, B., Zhang, J., Zhao, J., Yuan, M., Peng, W., Zhang, Y., and Wu, H., (2017) Sodium Fluoride Induces Nephrotoxicity via Oxidative Stress-Regulated Mitochondrial SIRT3 Signaling Pathway, *Scientific Reports*, 7(1). https://doi.org/10.1038/s41598-017-00796-3

[9] Tungsanga, S., Katavetin, P., Panpetch, W., Udompornpitak, K., Saisorn, W., Praditpornsilpa, K., Eiam-Ong, S., Tungsanga, K., Tumwasorn, S., and Leelahavanichkul, A., (2022) Lactobacillus Rhamnosus L34 Attenuates Chronic Kidney Disease Progression in a 5/6 Nephrectomy Mouse Model through the Excretion of Anti-Inflammatory Molecules," *Nephrology Dialysis Transplantation*, 37(8);1429–1442. https://doi.org/10.1093/ndt/gfac032

[10] Caroline de Oliveira Melo, N., Cuevas-Sierra, A., Arellano-Garcia, L., Portillo, M. P., Milton-Laskibar, I., and Alfredo Martinez, J., (2023) Oral Administration of Viable or Heat-Inactivated Lacticaseibacillus Rhamnosus GG Influences on Metabolic Outcomes and Gut Microbiota in Rodents Fed a High-Fat High-Fructose Diet," *Journal of Functional Foods*, 109;105808. https://doi.org/10.1016/J.JFF.2023.105808

[11] Sahin, K., Tuzcu, M., Gencoglu, H., Dogukan, A., Timurkan, M., Sahin, N., Aslan, A., and Kucuk, O., (2010) Epigallocatechin-3-Gallate Activates Nrf2/HO-1 Signaling Pathway in Cisplatin-Induced Nephrotoxicity in Rats, *Life Sciences*, 87(7–8);240–245. https://doi.org/10.1016/j.lfs.2010.06.014

[12] Dai, W., Ruan, C., Zhang, Y., Wang, J., Han, J., Shao, Z., Sun, Y., and Liang, J., (2020) Bioavailability Enhancement of EGCG by Structural Modification and Nano-Delivery: A Review, *Journal of Functional Foods*, 65;103732. https://doi.org/10.1016/J.JFF.2019.103732

[13] Qu, R., Jiang, C., Wu, W., Pang, B., Lei, S., Lian, Z., Shao, D., Jin, M., and Shi, J., (2019) Conversion of DON to 3-Epi-DON in Vitro and Toxicity Reduction of DON in Vivo by Lactobacillus Rhamnosus," *Food & Function*, 10(5);2785–2796. https://doi.org/10.1039/C9FO00234K

[14] Yousef, M. I., Omar, S. A. M., El-Guendi, M. I., and Abdelmegid, L. A., (2010). Potential Protective Effects of Quercetin and Curcumin on Paracetamol-Induced Histological Changes, Oxidative Stress, Impaired Liver and Kidney Functions and Haematotoxicity in Rat, *Food and Chemical Toxicology*, 48(11);3246–3261. https://doi.org/10.1016/j.fct.2010.08.034

[15] Yildiz, H., Ercisli, S., Hegedus, A., Akbulut, M., Topdas, E. F., and Aliman, J., (2014) Bioactive Content and Antioxidant Characteristics of Wild

(Fragaria Vesca L.) and Cultivated Strawberry (Fragaria × Ananassa Duch.) Fruits from Turkey, *Journal of Applied Botany and Food Quality*, 87;274–278. https://doi.org/10.5073/JABFQ.2014.087.038

[16] Raeeszadeh, M., Rezaee, M., Akbari, A., and Khademi, N., (2022). The Comparison of the Effect of Origanum Vulgare L. Extract and Vitamin C on the Gentamycin-Induced Nephrotoxicity in Rats, *Drug and Chemical Toxicology*, 45(5);2031–2038. https://doi.org/10.1080/01480545.2021.1895826

[17] Adil, M., Kandhare, A. D., Dalvi, G., Ghosh, P., Venkata, S., Raygude, K. S., and Bodhankar, S. L., (2016) Ameliorative Effect of Berberine against Gentamicin-Induced Nephrotoxicity in Rats via Attenuation of Oxidative Stress, Inflammation, Apoptosis and Mitochondrial Dysfunction, *Renal Failure* 38(6);996–1006. https://doi.org/10.3109/0886022X.2016.1165120

[18] Grams, M. E., Estrella, M. M., Coresh, J., Brower, R. G., and Liu, K. D., (2011). Fluid Balance, Diuretic Use, and Mortality in Acute Kidney Injury, *Clinical Journal of the American Society of Nephrology* 6(5);966–973. https://doi.org/10.2215/CJN.08781010

[19] Mansour, S. A., and Mossa, A.-T. H., (2010) Oxidative Damage, Biochemical and Histopathological Alterations in Rats Exposed to Chlorpyrifos and the Antioxidant Role of Zinc, *Pesticide Biochemistry and Physiology*, 96(1);14–23. https://doi.org/10.1016/j.pestbp.2009.08.008

[20] Heerspink, H. J. L., Holtkamp, F. A., Parving, H.-H., Navis, G. J., Lewis, J. B., Ritz, E., De Graeff, P. A., and De Zeeuw, D., (2012). Moderation of Dietary Sodium Potentiates the Renal and Cardiovascular Protective Effects of Angiotensin Receptor Blockers, *Kidney International*, 82(3);330–337. https://doi.org/10.1038/ki.2012.74

[21] Latha, R. C. R., and Daisy, P., (2011). Insulin-Secretagogue, Antihyperlipidemic and Other Protective Effects of Gallic Acid Isolated from Terminalia Bellerica Roxb. in Streptozotocin-Induced Diabetic Rats, *Chemico-Biological Interactions*, 189(1–2);112–118. https://doi.org/10.1016/j.cbi.2010.11.005

[22] Li, Y., Li, X., Wong, Y.-S., Chen, T., Zhang, H., Liu, C., and Zheng, W., (2011). he Reversal of Cisplatin-Induced Nephrotoxicity by Selenium Nanoparticles Functionalized with 11-Mercapto-1-Undecanol by Inhibition of ROS-Mediated Apoptosis, *Biomaterials*, 32(34);9068–9076. https://doi.org/10.1016/j.biomaterials.2011.08.001

[23] Xie, K., Yu, Y., Pei, Y., Hou, L., Chen, S., Xiong, L., and Wang, G., (2010) Protective Effects of Hydrogen Gas on Murine Polymicrobial Sepsis via Reducing Oxidative Stress and HMGB1 Release, *Shock*, 34(1);90–97. https://doi.org/10.1097/SHK.0b013e3181cdc4ae

[24] Khan, R. A., Khan, M. R., and Sahreen, S., (2012) CCl4-Induced Hepatotoxicity: Protective Effect of Rutin on P53, CYP2E1 and the Antioxidative Status in Rat," *BMC Complementary and Alternative Medicine*, 12, https://doi.org/10.1186/1472-6882-12-178

[25] Ugur, S., Ulu, R., Dogukan, A., Gurel, A., Yigit, I. P., Gozel, N., Aygen, B., and Ilhan, N., (2015). The Renoprotective Effect of Curcumin in Cisplatin-Induced Nephrotoxicity, *Renal Failure*, 37(2);332–336. https://doi.org/10.3109/0886022X.2014.986005

[26] He, L., Peng, X., Zhu, J., Liu, G., Chen, X., Tang, C., Liu, H., Liu, F., and Peng, Y., (2015). Protective Effects of Curcumin on Acute Gentamicin-Induced Nephrotoxicity in Rats, *Canadian Journal of Physiology and Pharmacology*, 93(4);275–282. https://doi.org/10.1139/cjpp-2014-0459

[27] Edrees, N. E., Galal, A. A. A., Abdel Monaem, A. R., Beheiry, R. R., and Metwally, M. M. M., (2018). Curcumin Alleviates Colistin-Induced Nephrotoxicity and Neurotoxicity in Rats via Attenuation of Oxidative Stress, Inflammation and Apoptosis, *Chemico-Biological Interactions*, 294;56–64. https://doi.org/10.1016/j.cbi.2018.08.012

[28] Laorodphun, P., Cherngwelling, R., Panya, A., and Arjinajarn, P., (2022) Curcumin Protects Rats against Gentamicin-Induced Nephrotoxicity by Amelioration of Oxidative Stress, Endoplasmic Reticulum Stress and Apoptosis, *Pharmaceutical Biology*, 60(1);491–500. https://doi.org/10.1080/13880209.2022.2037663

[29] Benzer, F., Kandemir, F. M., Kucukler, S., Comaklı, S., and Caglayan, C., (2018) Chemoprotective Effects of Curcumin on Doxorubicin-Induced Nephrotoxicity in Wistar Rats: By Modulating Inflammatory Cytokines, Apoptosis, Oxidative Stress and Oxidative DNA Damage, *Archives of Physiology and Biochemistry*, 124(5);448–457. https://doi.org/10.1080/13813455.2017.1422766

[30] Wu, S., Yu, W., Jiang, X., Huang, R., Zhang, X., Lan, J., Zhong, G., Wan, F., Tang, Z., and Hu, L., (2021). Protective Effects of Curcumin on ATO-Induced Nephrotoxicity in Ducks in Relation to Suppressed Autophagy, Apoptosis and Dyslipidemia by Regulating Oxidative Stress, *Ecotoxicology and Environmental Safety*, 219; https://doi.org/10.1016/j.ecoenv.2021.112350

[31] Mahmoud, A. M., Abd El-Ghafar, O. A. M., Alzoghaibi, M. A., and Hassanein, E. H. M., (2021). Agomelatine Prevents Gentamicin Nephrotoxicity by Attenuating Oxidative Stress and TLR-4 Signaling, and Upregulating PPARγ and SIRT1, *Life Sciences*, 278. https://doi.org/10.1016/j.lfs.2021.119600

[32] Kilic, U., Kilic, E., Tuzcu, Z., Tuzcu, M., Ozercan, I. H., Yilmaz, O., Sahin, F., and Sahin, K., (2013). Melatonin Suppresses Cisplatin-Induced Nephrotoxicity via Activation of Nrf-2/HO-1 Pathway, *Nutrition and Metabolism*, 10(1); https://doi.org/10.1186/1743-7075-10-7

[33] Kobroob, A., Peerapanyasut, W., Chattipakorn, N., and Wongmekiat, O., (2018). Damaging Effects of Bisphenol A on the Kidney and the Protection by Melatonin: Emerging Evidences from In Vivo and In Vitro Studies. *Oxidative Medicine and Cellular Longevity* 2018, Article ID 3082438, 15 pages https://doi.org/10.1155/2018/3082438

[34] Goudarzi, M., Khodayar, M. J., Hosseini Tabatabaei, S. M. T., Ghaznavi, H., Fatemi, I., and

Mehrzadi, S., (2017). Pretreatment with Melatonin Protects against Cyclophosphamide-Induced Oxidative Stress and Renal Damage in Mice, *Fundamental and Clinical Pharmacology*, 31(6);625–635. https://doi.org/10.1111/fcp.12303

[35] Dutta, S., Saha, S., Mahalanobish, S., Sadhukhan, P., and Sil, P. C., (2018) Melatonin Attenuates Arsenic Induced Nephropahy via the Regulation of Oxidative Stress and Inflammatory Signaling Cascades in Mice, *Food and Chemical Toxicology*, 118;303–316. https://doi.org/10.1016/j.fct.2018.05.032

[36] Panpetch, W., Visitchanakun, P., Saisorn, W., Sawatpanich, A., Chatthanathon, P., Somboonna, N., Tumwasorn, S., and Leelahavanichkul, A., (2021). Lactobacillus Rhamnosus Attenuates Thai Chili Extracts Induced Gut Inflammation and Dysbiosis despite Capsaicin Bactericidal Effect against the Probiotics, a Possible Toxicity of High Dose Capsaicin, *PLOS ONE*, 16(12);e0261189. https://doi.org/10.1371/JOURNAL.PONE.0261189

[37] Tsai, Y.-S., Chen, Y.-P., Lin, S.-W., Chen, Y.-L., Chen, C.-C., and Huang, G.-J., (2022). Lactobacillus Rhamnosus GKLC1 Ameliorates Cisplatin-Induced Chronic Nephrotoxicity by Inhibiting Cell Inflammation and Apoptosis. *Biomedicine & Pharmacotherapy* 147;112701 https://doi.org/10.1016/j.biopha.2022.112701

[38] Hsiao, Y.-P., Chen, H.-L., Tsai, J.-N., Lin, M.-Y., Liao, J.-W., Wei, M.-S., Ko, J.-L., and Ou, C.-C., (2021). Administration of Lactobacillus Reuteri Combined with Clostridium Butyricum Attenuates Cisplatin-Induced Renal Damage by Gut Microbiota Reconstitution, Increasing Butyric Acid Production, and Suppressing Renal Inflammation, *Nutrients*, 13(8). https://doi.org/10.3390/nu13082792

[39] Sahin, K., Tuzcu, M., Sahin, N., Ali, S., and Kucuk, O., (2010). Nrf2/HO-1 Signaling Pathway May Be the Prime Target for Chemoprevention of Cisplatin-Induced Nephrotoxicity by Lycopene, *Food and Chemical Toxicology*, 48(10);2670–2674. https://doi.org/10.1016/j.fct.2010.06.038

[40] Sahu, B. D., Kalvala, A. K., Koneru, M., Kumar, J. M., Kuncha, M., Rachamalla, S. S., and Sistla, R., (2014). Ameliorative Effect of Fisetin on Cisplatin-Induced Nephrotoxicity in Rats via Modulation of NF-KB Activation and Antioxidant Defence, *PLoS ONE*, 9(9); https://doi.org/10.1371/journal.pone.0105070

[41] Temel, Y., Kucukler, S., Yıldırım, S., Caglayan, C., and Kandemir, F. M., (2020). Protective Effect of Chrysin on Cyclophosphamide-Induced Hepatotoxicity and Nephrotoxicity via the Inhibition of Oxidative Stress, Inflammation, and Apoptosis, *Naunyn-Schmiedeberg's Archives of Pharmacology*, 393(3);325–337. https://doi.org/10.1007/s00210-019-01741-z

[42] Li, J., Gui, Y., Ren, J., Liu, X., Feng, Y., Zeng, Z., He, W., Yang, J., and Dai, C., (2016). Metformin Protects against Cisplatin-Induced Tubular Cell Apoptosis and Acute Kidney Injury via AMPKα-Regulated Autophagy Induction, *Scientific Reports*, 6. https://doi.org/10.1038/srep23975

[43] Xing, J.-J., Hou, J.-G., Ma, Z.-N., Wang, Z., Ren, S., Wang, Y.-P., Liu, W.-C., Chen, C., and Li, W., (2019). Ginsenoside Rb3 Provides Protective Effects against Cisplatin-Induced Nephrotoxicity via Regulation of AMPK-/MTOR-Mediated Autophagy and Inhibition of Apoptosis in Vitro and in Vivo, *Cell Proliferation*, 52(4); https://doi.org/10.1111/cpr.12627

[44] Noori, S., and Mahboob, T., (2010). Antioxidant Effect of Carnosine Pretreatment on Cisplatin-Induced Renal Oxidative Stress in Rats, *Indian Journal of Clinical Biochemistry*, 25(1);86–91. https://doi.org/10.1007/s12291-010-0018-x

[45] Kim, J. Y., Jo, J., Leem, J., and Park, K. K., (2020). Inhibition of P300 by Garcinol Protects against Cisplatin-Induced Acute Kidney Injury through Suppression of Oxidative Stress, Inflammation, and Tubular Cell Death in Mice, *Antioxidants*, 9(12);1–16. https://doi.org/10.3390/antiox9121271

[46] Gur, C., Kandemir, F. M., Caglayan, C., and Satıcı, E., (2022). Chemopreventive Effects of Hesperidin against Paclitaxel-Induced Hepatotoxicity and Nephrotoxicity via Amendment of Nrf2/HO-1 and Caspase-3/Bax/Bcl-2 Signaling Pathways, *Chemico-Biological Interactions*, 365. https://doi.org/10.1016/j.cbi.2022.110073

[47] Tang, Y., Zhao, R., Pu, Q., Jiang, S., Yu, F., Yang, Z., and Han, T., (2023). Investigation of Nephrotoxicity on Mice Exposed to Polystyrene Nanoplastics and the Potential Amelioration Effects of DHA-Enriched Phosphatidylserine, *Science of the Total Environment*, 892 https://doi.org/10.1016/j.scitotenv.2023.164808

[48] El-Mowafy, A. M., Al-Gayyar, M. M., Salem, H. A., El-Mesery, M. E., and Darweish, M. M., (2010). Novel Chemotherapeutic and Renal Protective Effects for the Green Tea (EGCG): Role of Oxidative Stress and Inflammatory-Cytokine Signaling, *Phytomedicine*, 17(14);1067–1075. https://doi.org/10.1016/j.phymed.2010.08.004

[49] Zhang, Q., Zhang, C., Ge, J., Lv, M.-W., Talukder, M., Guo, K., Li, Y.-H., and Li, J.-L., (2020). Ameliorative Effects of Resveratrol against Cadmium-Induced Nephrotoxicity: Via Modulating Nuclear Xenobiotic Receptor Response and PINK1/Parkin-Mediated Mitophagy, *Food and Function*, 11(2);1856–1868. https://doi.org/10.1039/c9fo02287b

[50] Abdul Hamid, Z., Budin, S. B., Wen Jie, N., Hamid, A., Husain, K., and Mohamed, J., (2012). Nephroprotective Effects of Zingiber Zerumbet Smith Ethyl Acetate Extract against Paracetamol-Induced Nephrotoxicity and Oxidative Stress in Rats, *Journal of Zhejiang University: Science B*, 13(3);176–185. https://doi.org/10.1631/jzus.B1100133

[51] Mahmoud, A. M., Hussein, O. E., Abd El-Twab, S. M., and Hozayen, W. G., (2019). Ferulic Acid Protects against Methotrexate Nephrotoxicity: Via Activation of Nrf2/ARE/HO-1 Signaling and PPARγ, and Suppression of NF-KB/NLRP3 Inflammasome Axis, *Food and Function*, 10(8);4593–4607. https://doi.org/10.1039/c9fo00114j

[52] Albarakati, A. J. A., Baty, R. S., Aljoudi, A. M., Habotta, O. A., Elmahallawy, E. K., Kassab, R. B., and Abdel Moneim, A. E., (2020). Luteolin Protects against Lead Acetate-Induced Nephrotoxicity through Antioxidant, Anti-Inflammatory, Anti-Apoptotic, and Nrf2/HO-1 Signaling Pathways *Molecular Biology Reports*, 47(4);2591–2603. https://doi.org/10.1007/s11033-020-05346-1

[53] Elsherbiny, N. M., and El-Sherbiny, M., (2014). Thymoquinone Attenuates Doxorubicin-Induced Nephrotoxicity in Rats: Role of Nrf2 and NOX4, *Chemico-Biological Interactions*, 223;102–108. https://doi.org/10.1016/j.cbi.2014.09.015

[54] Mohamed, M. E., Abduldaium, Y. S., and Younis, N. S., (2020). Ameliorative Effect of Linalool in Cisplatin-Induced Nephrotoxicity: The Role of HMGB1/TLR4/NF-KB and NRF2/HO1 Pathways, *Biomolecules*, 10(11);1–19. https://doi.org/10.3390/biom10111488

[55] Jin, W., Xue, Y., Xue, Y., Han, X., Song, Q., Zhang, J., Li, Z., Cheng, J., Guan, S., Sun, S., and Chu, L., (2020). Tannic Acid Ameliorates Arsenic Trioxide-Induced Nephrotoxicity, Contribution of NF-KB and Nrf2 Pathways, *Biomedicine and Pharmacotherapy*, 126. https://doi.org/10.1016/j.biopha.2020.110047

[56] Turk, E., Kandemir, F. M., Yildirim, S., Caglayan, C., Kucukler, S., and Kuzu, M., (2019) Protective Effect of Hesperidin on Sodium Arsenite-Induced Nephrotoxicity and Hepatotoxicity in Rats, *Biological Trace Element Research*, 189(1);95–108. https://doi.org/10.1007/s12011-018-1443-6

[57] Dieterle, F., Perentes, E., Cordier, A., Roth, D. R., Verdes, P., Grenet, O., Pantano, S., Moulin, P., Wahl, D., Mahl, A., End, P., Staedtler, F., Legay, F., Carl, K., Laurie, D., Chibout, S. D., Vonderscher, J., and Maurer, G., (2010). Urinary Clusterin, Cystatin C, B2-Microglobulin and Total Protein as Markers to Detect Drug-Induced Kidney Injury, *Nature Biotechnology*, 28(5);463–469. https://doi.org/10.1038/nbt.1622