Review Article

Investigating the potential application of organic and non-organic nanoparticles for gastric cancer treatment: An evidence-based review

Moradifar, N[1], Moayyedkazemi, A[1], Mohammadi, HR[1], Ahmadi, S[1], Raziani, Y[2*]

1. *Department of Internal Medicines, Lorestan University of Medical Sciences, Khorramabad, Iran.*
2. *Nursing Department, Al-Mustaqbal University College, 51001 Hillah, Babylon, Iraq.*

How to cite this article: Moradifar N, Moayyedkazemi A, Mohammadi HR, Ahmadi S, Raziani Y. Investigating the potential application of organic and non-organic nanoparticles for gastric cancer treatment: An evidence-based review. Archives of Razi Institute Journal. 2024;79(2):264-271. DOI: 10.32592/ARI.2024.79.2.264

ABSTRACT

Gastric cancer, which is considered a major health concern, is the sixth most frequent cancer and the second leading cause of cancer-related mortality across the globe. The present survey aimed to systematically review the anti-gastric cancer effect of all organic and inorganic nanoparticles (NPs) in *in vitro*, *in vivo*, and clinical trials. The investigation followed the PRISMA guidelines, and the findings were recorded in the CAMARADES-NC3Rs Preclinical Systematic Review and Meta-Analysis Facility database. A detailed search was conducted on various English databases, such as Scopus, Web of Science, EMBASE, PubMed, and Google Scholar, with no specified publication time frame to obtain papers regarding the anti-gastric cancer properties of nanoparticles. The search process was performed using the following terms: "Nanoparticles," "Gastric cancer," "Anti-gastric cancer," "Metal nanoparticles," "Organic nanoparticles," "Inorganic nanoparticles, "*in vitro*," "Clinical," and "*in vivo*,". Out of 11,189 papers, 31 articles, including 19 (45.5%) *in vitro*, 3 (13.6%) *in vivo*, 3 (13.6%) clinical trials, and 6 (27.3%) *in vitro*/*in vivo*, up to 2023, met the inclusion criteria for discussion in this systematic review. The most widely used NPs were found to be organic nanoparticles, such as polylactic acid and poly lactic-co-glycolic acid (16, 80.0%), followed by inorganic nanoparticles, such as silver NPs (13, 41.9.0%). This review study highlighted the high anti-gastric cancer potential of a wide range of organic and non-organic NPs through their activity via some mechanisms, such as the induction of apoptosis, gene therapy, and drug delivery. Nonetheless, further studies, especially in clinical settings, are needed to confirm their anti-gastric effects and accurate mechanisms.

Keywords: Clinical trial, *in vitro*, *in vivo*, Nanomedicine, Nanotechnology, Treatment

Article Info:
Received: 6 August 2023
Accepted: 4 November 2023
Published: 30 April 2024

Corresponding Author's E-Mail:
hegdominik.hug@gmail.com

1. Introduction

Gastric cancer, which is considered a major health concern, is the sixth most common cancer and the second leading cause of cancer-related mortality across the globe [1]. From a histological point of view, this cancer is divided into two categories: diffuse and intestinal. It is categorized as a multifactorial disease, whereas infectious, environmental, and genetic factors have been introduced as risk factors for this disease [2]. The diagnosis of gastric cancer at an early stage increases the chance of a complete cure for the patient. Considering that the symptoms of gastric cancer appear very late, it is crucial to control and measure patients' risk based on their main predisposing components [3, 4]. Although several risk factors, such as age, male gender, cigarette smoking, and race, are described, *Helicobacter pylori* infection and family history are the two main risk factors for gastric cancer [5].

A range of various therapeutic strategies, such as chemotherapy, radiotherapy, surgery, or combinations of these methods, are currently applied for the treatment of cancers [6]. As the favorite surgical resection management for cancer treatment, chemotherapy is recognized as the most reliable therapy for recurring and developed cancer for patients who cannot undergo surgical intervention since they lack the required conditions [6]. Nonetheless, studies have demonstrated that chemotherapy is associated with some side effects, which are generally linked to nonspecific medicine spreading to healthy organs, unselective failure of normal cells, toxicity, and the competency of cancerous cells to produce resistance mechanisms [7]. Recently, the increasing prevalence of cancer deaths, as well as the serious defect of chemotherapy and radiotherapy methods in advanced forms of cancer, has highlighted the necessity of discovering new strategies to control cancer [8]. Targeting anticancer drugs in a way that only affects cancer cells and uses the minimum concentration of drugs seems necessary to reduce the toxic effects of the drug on normal cells [9]. Therefore, to specifically deliver the drug to the cancerous tissue and reduce its side effects, new drug delivery methods to the tissue can be used by nanoparticles (NPs) as a carrier [9]. Nowadays, we are witnessing a widespread use of NPs with a size of 100 nm or less for delivering and targeting diagnostic and pharmacological agents in cancer medical projects [10]. Recently, many NPs have been utilized in targeted drug delivery to malignant tumor cells, including gastric cancer cells, by dropping the systemic toxicity of anticancer drugs [11]. Nanoparticles can be used to improve drug delivery by increasing the drug's solubility, bioavailability, and stability. This allows for lower doses of drugs to be used, reducing the risk of toxicity and side effects [11]. This survey aimed to systematically review the anti-gastric cancer effect of all organic and inorganic NPs in *in vitro, in vivo,* and clinical trials.

2. Context

The investigation followed the PRISMA guidelines, and the findings were recorded in the CAMARADES-NC3Rs Preclinical Systematic Review and Meta-Analysis Facility database. We searched the publications in various English databases, such as Scopus, Web of Science, EMBASE, PubMed, and Google Scholar, with no specified publication time frame to obtain papers regarding the anti-gastric cancer properties of nanoparticles. The search process was performed using the following terms: "Nanoparticles," "Gastric cancer," "Anti-gastric cancer," "Metal nanoparticles," "Organic nanoparticles," "Inorganic nanoparticles, "*in vitro*," "Clinical," and "*in vivo*," (Figure 1). All duplicate papers were removed after importing the selected papers into EndNote X9 software (Thomson Reuters, New York, NY, USA). Independent authors evaluated the titles and abstracts of the papers, and the relevant articles were involved in advanced analysis. After careful reading of the articles, the eligible papers with acceptable inclusion criteria were nominated. In the case of any disagreement between authors, the corresponding author would resolve the problem.The inclusion criteria in this investigation entailed *in vitro, in vivo,* and clinical studies assessing the effects of NPs on gastric cancer treatment. On the other hand, the papers with insufficient data, studies with no full text, inconformity between methods and findings, and incorrect descriptions of the results were excluded from this study. The extracted data from the selected papers included the name of nanoparticles, in combination/loaded with, preparation methods, type of study, and outcome. Out of 11,189 articles, 31 papers, including 19 *in vitro* (45.5%), 3 *in vivo* (13.6%), 3 clinical trials (13.6%), and 6 *in vitro/in vivo* (27.3%), up to 2023, met the inclusion criteria for discussion in this systematic review with the data extracted (Table 1). The most widely used NPs were organic nanoparticles, such as polylactic acid and poly lactic-co-glycolic acid (PLGA) (16, 80.0%), followed by inorganic nanoparticles, such as silver NPs (13, 41.9.0%). Nowadays, it has been established that effective anticancer drugs must be capable of eliminating cancer cells while causing minimal toxicity to normal cells [10]. Consequently, the development of new drugs with minimal side effects on the immune system has emerged as a significant field in advanced biomedicine research. In recent decades, with progress in nanotechnology, the

discovery of proper and effective drugs to treat a broad spectrum of high-impact diseases, such as gastric cancer, is considered one of the primary goals of this medical science. Given the possible anticancer mechanisms of nanoparticles, the induction of apoptosis demonstrated a critical role in determining cellular cytotoxicity subsequent to drug therapy [25, 32]. Recently, Xu et al. (2019) revealed that polyethylene glycol-poly (ε-caprolactone) NPs through inducing cell apoptosis and increasing G2-M arrest in cancer cells, demonstrating the suppression of microtubule synthesis so that the biological and clinical uses of DOC-PEG-PCL-mAb NPs were shown by PD-L1 mAbs for gastric cancer treatment [17]. In another study, Mousavi et al. (2018) demonstrated that silver NPs green synthesized by *Artemisia turcomanica* had a marked effect on gastric cancer cell lines in a dose- and time-dependent response through the induction of apoptosis in treated cells [25]. Tang et al. (2020) pointed out that green synthesized zinc oxide NPs by *Morus nigra* extract through the induction of apoptosis in gastric carcinoma cells acted as a substitute for cell death via reducing matrix metalloproteinase, as well as increasing the level of reactive oxygen species and cytotoxicity in adenocarcinoma gastric cancer cells [33]. Another anticancer mechanism of NPs is gene therapy, which suppresses some key molecules involved in gastric cancer [11]. In this regard, Wu et al. (2010) demonstrated that PEG-modified polyethyleneimine copolymer NPs overwhelmed the activity of CDD4 cells through siRNA delivery, a molecule that is comprised in the development

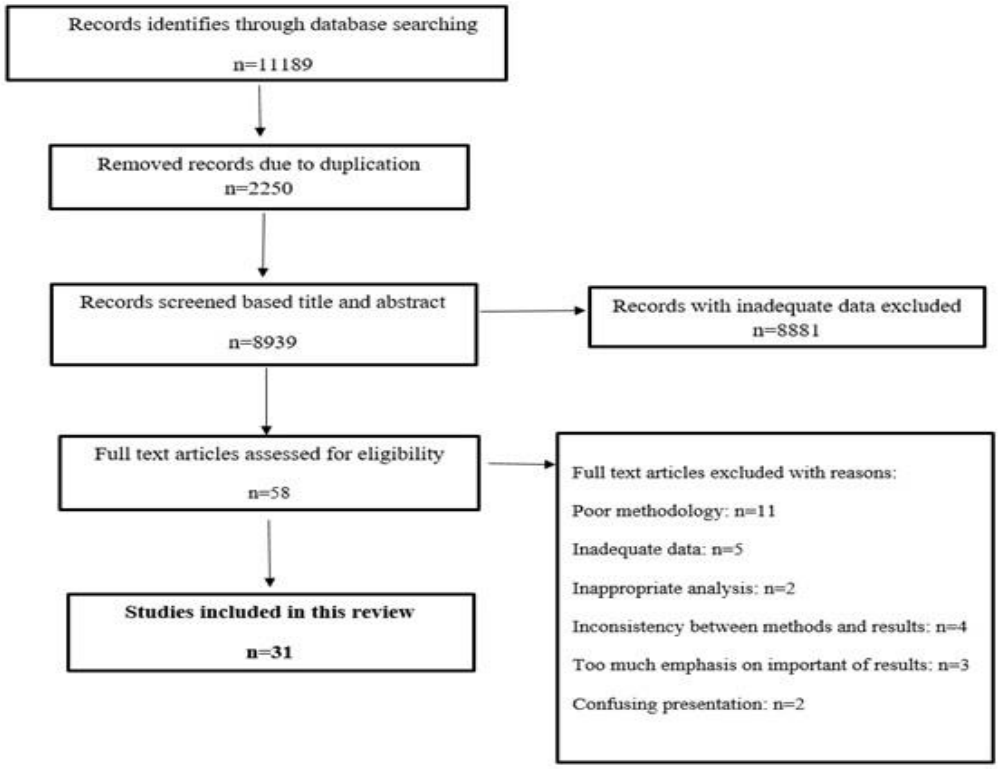

Fig 1. Flowchart describing the study design process

of gastric cancer [32]. In the same vein, Xiao et al. (2016) indicated that cerium oxide NPs (CNPs) improved the expression of DEAH box helicase 15 (DHX15) and its downstream signaling pathways, representing that CNPs could be a promising strategy to inhibit the malignant activity of gastric cancer by enhancing the expression of DHX15 [12]. In another investigation, Mohammadian et al. (2016) exhibited that chrysin-PLGA-PEG NPs inhibited the human gastric cell line by increasing the expression of miR-22, miR-34a, and miR-126 [31]. Currently, the intracellular release of some drugs utilizing NPs is one of the main mechanisms of the anticancer effects of NPs [11]. The results of a study conducted by

Bonelli (2012) revealed that ibuprofen-loaded PLGA NPs had an antiproliferative activity against MKN-45 human gastric adenocarcinoma cells through the intracellular release of ibuprofen from the NPs, indicating that ibuprofen more rapidly encouraged the expression of transcripts complicated in multiplying and invasiveness manners [27].

3. Conclusion

The results of this review study highlighted the high anti-gastric cancer potential of a wide range of organic and non-organic NPs. Therefore, after conducting additional studies, especially on human models, and clarifying all aspects of their effectiveness and toxicity, they can be

Table 1. List of organic and inorganic nanoparticles to treat gastric cancer.

Nanoparticles	In combination /loaded with	Preparation method	Type of study	Outcome	Ref
Cerium oxide nanoparticles (CNPs)	**-**	**Thermal decomposition method**	***In vivo/ in vitro***	**CNPs significantly reduced the movement of gastric cancer cells; moreover, they significantly decreased their proliferation, especially at the dose of 10 µg/mL. CNPs also elevated the DHX15 expression level; thus, is able to overwhelm malignant activity of gastric cancer**	**[12]**
Carbon nanoparticles (CNPs)	**-**	**-**	**Clinical trial**	**CNP with low toxicity might gather more LNs in patients with advanced gastric cancer.**	**[13]**
BCc1 nanomedicine	**Doxil® (liposomal doxorubicin)/Onivyde® (liposomal irinotecan)**	**Nanochelating technology**	**Clinical trial**	**BCc1 nanomedicine represents a potent effect on Quality of life and Total survival with no toxicity in patients with gastric cancer.**	**(14)**
Paclitaxel Liposome (Lipusu®)	**Paclitaxel combined with tegafur &oxaliplation**	**-**	**Clinical trial**	**Lipusu® along withtegafur and oxaliplation have potent therapeutic activity in the advanced gastric cancer.**	**[15]**
Silica nanoparticles (SLN)	**Chlorins e6 (Ce6)/cell membrane (CM) derived from SGC7901 cells**	**Water-in-oil micro-emulsion technique**	***In vitro/in vivo***	**CM/SLN/Ce6 demonstrated the significant *in vitro* and *in vivo* anticancer effects compared to SLN/Ce6. CM/SLN/Ce6 also could be considered as an interesting agent for effective tumors of gastric cancer.**	**[16]**
Polyethylene glycol-poly(ε-caprolactone) NPs (PEG-PCL NPs)	**Docetaxel (DOC)/programmed death-ligand 1 (PD-L1) monoclonal antibody (mAb)**	**Ring opening copolymerization technique**	***In vitro***	**The DOC-PEG-PCL-mAb NPs, through the induction of cell apoptosis and increasing G2-M arrest in cancer cells, demonstrating the suppression of microtubule synthesis.**	**[17]**
Gold nanoparticles (AuNPs)	**Trastuzumab (Tmab)**	**Solution and evaporation technique**	***In vivo***	**T-AuNPs exhibited the significant *in vivo* antitumor activity on NCI-N87 and MKN7 subcutaneous tumors. As a conclude, HER2-targeted AuNPs combined with Tmab is a helpful and novel agent to treat Tmab resistance in gastric cancer**	**[18]**
Folic acid-Targeted Super Paramagnetic Iron Oxide Nanoparticles	**Doxorubicin (Dox)**	**Co-precipitation method**	***In vivo***	**The combination of the Dox combined with iron oxide nanoparticles represents a significant role in increasing the efficacy, and cytotoxic effects of Dox may be considered a nanodrug delivery system for application in clinical uses and treatment of cancer.**	**[19]**
β-casein (β-CN) nanoparticles	**Paclitaxel**	**Aqueous solution**	***In vitro***	**Since the undigested b-CN-encapsulated paclitaxel had no cytotoxicity on gastric cancer cell lines; thus it can probably protect upper GIT regions.**	**[20]**
Novel Fe3O4–carboxymethyl cellulose–5-fluorouracil (Fe3O4–CMC–5FU) nanomedicine	**-**	**High-temperature liquid-phase method**	***In vitro***	**The magnetic nanomedicine significantly reduced the growth rate SGC-7901gastric cells through attacking their mitochondria.**	**[21]**
Polystyrene nanoparticles(PS-NPs)	**-**	**Dyed polystyrene microspheres in water**	***In vitro***	**PS-NPs reduced cell viability, morphology of cells, and the expression of inflammatory genes such as IL-6 and IL-8, as the main cytokines complicated in pathologies of gastric cancer**	**[22]**
5-fluorouracil (5-Fu)NPs	**Chitosan**	**Solution and mixing method**	***In vitro***	**5-Fu nanoparticles considerably reduced the viability of gastric cancer cells through slower**	**[23]**

				drug release	
mPEG-PLA nanoparticles	Gossypol	Emulsion polymerization method	*In vivo/ in vitro*	Through optical molecular imaging, gossypol-loaded nanoparticles have demonstrated the higher antitumor effects and low toxicity effect against gastric cancer cell-bearing mice models.	[24]
Silver nanoparticles (AgNPs)	*Artemisia turcomanica* leaf extract	Sedimentation method	*In vitro*	Synthesized silver nanoparticles through the induction of apoptosis, indicated a relevant effect against gastric cancer cell lines.	[25]
Paclitaxel-loaded nanoparticles (PRNP)	Albumin hydrogel	-	*In vivo/ in vitro*	PRNP is able to release chemotherapeutics in a long-standing and continued way, displayed an improved drug accumulation at tumor place, leads the potent antitumor activity *in vitro* and *in vivo*.	[26]
Poly (lactic-co-glycolic acid) (PLGA) nanoparticles	Ibuprofen	-	*In vitro*	Ibuprofen-loaded PLGA NPs predominantly reduced the cell proliferation of gastric cancer cells through the intracellular release of ibuprofen.	[27]
Oxaliplatin-au-fe3o4-herceptin nanoparticles	-	Decomposing iron pentacarbonyl on the surfaces of Au NPs in the presence of oleic acid and oleylamine	*In vivo*	The results showed that oxaliplatin-Au-Fe3O4-Herceptin has potent effects for concurrent magnetic noticeable and HER2 embattled chemotherapy for treating gastric cancer	[28]
RNA Nanoparticles	-	RNA nanoparticles were dispersed in varied pH buffers for 12h	*In vivo/ in vitro*	After treatment with RNA NPs, the size of gastric tumors remarkably reduced with no injury to the main organs.	[29]
Docetaxel (DOCT)-loaded poly(γ-glutamic acid) (γ-PGA) nanoparticles (NPs)	Monoclonal antibody cetuximab (CET MAb)	Simple polyionic complexation technique	*In vivo/ in vitro*	CET MAb-DOCT-γ-PGA Nps might be considered an alternative to current nonspecific synthetic agents, and, therefore, may become a possible agent for cancer treatment.	[30]
Poly lactic-co-glycolic acid PLGA-PEG-PLGA	Chrysin	Double emulsion method	*In vitro*	The results demonstrated that chrysin-loaded PLGA-PEG through upregulation of miR-34a could be considered a potent anticancer drug delivery system.	[31]
PEG-PEI/siRNA nanoparticles	-	Solution and mixing method	*In vitro*	PEG-PEI/siRNA nanoparticles as a non-viral transporter able to change the gene expression in gastric cancer therapy with some benefits, including low cytotoxicity and high efficacy in the gene transfection.	[32]
Zinc oxide nanoparticles (ZnONPs)	*Morus nigra* (MN) leaf extract	Green chemistry method	*In vitro*	The MN-ZnONPs exhibited *in vitro* anticancer activity by increasing the ROS and subsequently inducing apoptosis, increasing lipid peroxidation, reduced antioxidants, and promoting cell cycle stops.	[33]
ZnO nanoparticles	Curcumin	Solution and mixing method	*In vitro*	ZnO NPs induce significant cell death in human gastric adenocarcinoma (AGS) cell line with IC50 of ~0.05 µg mL-1 ,	[34]
Silver nanoparticles	*Teucrium polium* leaf extract	Green synthesize	*In vitro*	The IC_{50} value of *T. polium*-AgNPs against MNK45 human gastric cancer cell line was 68.2 mg/ml after 48 h incubation.	[35]
Silver nanoparticles	*Dysosma pleiantha* rhizome extract	Green synthesize	*In vitro*	Green synthesized AgNPs significantly reduced the viability of AGS gastric cancer cell viability with an IC_{50} value of 7.14 µM/mL.	[36]
Silver nanoparticles	*Artemisia Ciniformis* leaf extract	Green synthesize	*In vitro*	AgNPs inhibit AGS gastric cancer cell proliferation (especially at the concentration of 100 µg/mL) through	[37]

				apoptosis.	
Silver nanoparticles	***Satureja Rechingeri* extract**	**Green synthesize**	***In vitro***	**Green synthesized AgNPs significantly reduced the viability of AGS gastric cancer cell viability with an IC50 value of 4.84 µg/mL after 24 h.**	**[38]**
Titanium Dioxide Nanoparticles	**Polyethylene glycol**	**-**	***In vitro***	**TiO_2 NPs inhibits human gastric cancer cell line MKN-45 proliferation by inducing apoptosis and inhibition of invasion, especially at 40 µg/mL for 72 hours.**	**[39]**
Golden nanoparticles	***Vetex negundo* extract**	**Green synthesize**	***In vitro***	**AgNPs inhibit AGS gastric cancer cell proliferation with an IC_{50} value of 15 µg/mL through apoptosis and reactive oxygen species production.**	**[40]**
Copper nanoparticles	**Polyethylene glycol (PEG2000) coated magnetic nanoparticles**	**Precipitation method**	***In vitro***	**Fe3O4/PEG2000/Cu nanocomposite showed significant effect with the IC50 value of were 316 and 131 µg/mL against NCI-N87 and MKN45 gastric cancer cell lines, respectively.**	**[41]**
Titanium Dioxide Nanoparticles	**5-fluorouracil**	**-**	***In vitro***	**The findings exhibited that mixture of TiO2 NP is able to improve the activity of low doses of 5-FU (0.01–1 µM).**	**[42]**

used to cure cancer. Although the possible mechanisms of these anti-gastric cancers are not clearly understood, studies have illustrated that NPs exert their activity through some mechanisms, such as induction of apoptosis, gene therapy, and drug delivery. Nevertheless, further studies are needed to confirm their anti-gastric effects and precise mechanisms, especially in clinical settings.

Acknowledgment
The authors' most profound appreciation goes to Dr. Pegah Shakib for helping with data collection.

Authors' Contribution
Conception and research design: NM and YR. Collection of data: AM, HM, and SA. Supervising and writing the draft of the manuscript: YR. All authors contributed to helpful discussions and approved the final manuscript.

Ethics
Not applicable.

Conflict of Interest
The authors declare that they have no conflict of interest.

Grant Support
None.

References
1. Lyons K, Le LC, Pham YT-H, Borron C, Park JY, Tran CTD, et al. Gastric cancer. Eur J Cancer Prev. 2019;28(5):397–412.
2. Raziani Y, Raziani S. Evaluation of Mental Health of Chemotherapy-Treated Cancer Nurses. Journal of Medicinal and Chemical Sciences. 2021;4(4):351-63.
3. Yusefi AR, Lankarani KB, Bastani P, Radinmanesh M, Kavosi Z. Risk factors for gastric cancer: A systematic review. Asian Pacific J Cancer Prev. 2018;19(3):591–603.
4. Raziani Y, Cheraghipour K, Shakibaie M, Yadegari JG, Mahmoudvand H. High potency of magnetic iron oxide nanoparticles covered by piroctone olamine against cystic echinococcosis. Biomedicine & Pharmacotherapy. 2023;161:114536.
5. Molazem, M., Ramezani, A., Soroori, S., Jafary giv, Z., Shokrpoor, S., Geissbuehler, U. Feasibility of Using Evidence-Based Virtopsy to Answer the Possible Clinical and Post-Mortem Questions, in Veterinary Practice. Iranian Journal of Veterinary Medicine. 2022;16(3):311-336. doi: 10.22059/ijvm.2021.331329.1005197
6. Biagioni A, Skalamera I, Peri S, Schiavone N, Cianchi F, Giommoni E, et al. Update on gastric cancer treatments and gene therapies. Vol. 38, Cancer and Metastasis Reviews. Springer. 2019.p. 537–48.
7. Peidaei, F., Ahari, H., Anvar, S. A. A., Ataee, M. Nanotechnology in Food Packaging and Storage: A Review. Iranian Journal of Veterinary Medicine. 2021;15(2):122-153. doi: 10.22059/ijvm.2021.310466.1005130

8. Jabir NR, Anwar K, Firoz CK, Oves M, Kamal MA, Tabrez S. An overview on the current status of cancer nanomedicines. Vol. 34, Current Medical Research and Opinion. Taylor and Francis Ltd. 2018.p.911–21.
9. Anvar, S. A. A., Nowruzi, B., Afshari, G. A Review of the Application of Nanoparticles Biosynthesized by Microalgae and Cyanobacteria in Medical and Veterinary Sciences. Iranian Journal of Veterinary Medicine. 2023; 17(1): 1-18. doi: 10.22059/ijvm.17.1.1005309
10. Raziani Y, Shakib P, Rashidipour M, Cheraghipour K, Ghasemian Yadegari J, Mahmoudvand H. Green Synthesis, Characterization, and Antiparasitic Effects of Gold Nanoparticles against Echinococcus granulosus Protoscoleces. Tropical Medicine and Infectious Disease. 2023;8(6):313.
11. R. Guerrero A, Oyarzun-Ampuero F, Hassan N, H. Corvalan A, F.G. Quest A, J. Koga Kogan M, et al. Gastric Cancer: Nanoparticles as Tools to Improve Treatment Efficacy.
12. Koohkan, O., Morovvati, H., Taheri Mirghaed, A. Effects of Spirulina platensis on Iron Oxide Nanoparticles Induced-oxidative Stress and Liver Damage in Grey Mullet (Mugil cephalus). Iranian Journal of Veterinary Medicine, 2023; 17(1): 75-86. doi: 10.22059/ijvm.17.1.1005284
13. Li Z, Ao S, Bu Z, Wu A, Wu X, Shan F, et al. Clinical study of harvesting lymph nodes with carbon nanoparticles in advanced gastric cancer: A prospective randomized trial. World J Surg Oncol. 2016;14(1):1–8.
14. Hafizi M, Kalanaky S, Moaiery H, Khayamzadeh M, Noorian S, Kaveh V, et al. A randomized, double-blind, placebo-controlled investigation of BCc1 nanomedicine effect on survival and quality of life in metastatic and non-metastatic gastric cancer patients. J Nanobiotechnology. 2019;17(1):1–19. DOI: 10.1186/s12951-019-0484-0
15. Xu X, Wang L, Xu HQ, Huang XE, Qian YD, Xiang J. Clinical comparison between paclitaxel liposome (Lipusu®) and paclitaxel for treatment of patients with metastatic gastric cancer. Asian Pacific J Cancer Prev. 2013;14(4):2591–4.
16. Yang J, Teng Y, Fu Y, Zhang C. Chlorins e6 loaded silica nanoparticles coated with gastric cancer cell membrane for tumor specific photodynamic therapy of gastric cancer. Int J Nanomedicine. 2019;14:5061–71.
17. Xu S, Cui F, Huang D, Zhang D, Zhu A, Sun X, et al. PD-l1 monoclonal antibody-conjugated nanoparticles enhance drug delivery level and chemotherapy efficacy in gastric cancer cells. Int J Nanomedicine. 2019;14:17–32.
18. Kubota T, Kuroda S, Kanaya N, Morihiro T, Aoyama K, Kakiuchi Y, et al. HER2-targeted gold nanoparticles potentially overcome resistance to trastuzumab in gastric cancer. Nanomedicine Nanotechnology, Biol Med. 2018;14(6):1919–29.
19. Ghanbari M, Asadi A, Rostamzadeh S. Study of the Cytotoxicity Effect of Doxorubicin-loaded/Folic acid-Targeted Super Paramagnetic Iron Oxide Nanoparticles on AGS Cancer Cell Line. J Nanomed Nanotechnol. 2016;7(2):368.
20. Shapira A, Davidson I, Avni N, Assaraf YG, Livney YD. β-Casein nanoparticle-based oral drug delivery system for potential treatment of gastric carcinoma: Stability, target-activated release and cytotoxicity. In: European Journal of Pharmaceutics and Biopharmaceutics. 2012.p.298–305.
21. Liu X, Deng X, Li X, Xue D, Zhang H, Liu T, et al. A visualized investigation at the atomic scale of the antitumor effect of magnetic nanomedicine on gastric cancer cells. Nanomedicine. 2014;9(9):1389–402.
22. Forte M, Iachetta G, Tussellino M, Carotenuto R, Prisco M, De Falco M, et al. Polystyrene nanoparticles internalization in human gastric adenocarcinoma cells. TIV. 2016;31:126–36. DOI: 10.1016/j.tiv.2015.11.006
23. Fan YL, Fan BY, Li Q, Di HX, Meng XY, Ling N. Preparation of 5-fluorouracil-loaded nanoparticles and study of interaction with gastric cancer cells. Asian Pacific J Cancer Prev. 2014;15(18):7611–5.
24. A self-assembling nanoparticles for gossypol delivery in gastric cancer.
25. Mousavi B, Tafvizi F, Zaker Bostanabad S. Green synthesis of silver nanoparticles using *Artemisia turcomanica* leaf extract and the study of anticancer effect and apoptosis induction on gastric cancer cell line (AGS). Artif Cells, Nanomedicine, Biotechnol.2018;46:499–510. doi: 10.1080/21691401.2018.1430697
26. Qian H, Liu Q, Li R, Yu L, Liu B. Delivery of paclitaxel-loaded erythrocytes-based nanoparticles using injectable albumin hydrogel for regional chemotherapy. Ann Oncol. 2017;28:v13.
27. Bonelli P, Tuccillo FM, Federico A, Napolitano M, Borrelli A, Melisi D, et al. Ibuprofen delivered by poly(lactic-co-glycolic acid) (PLGA) nanoparticles to human gastric cancer cells exerts antiproliferative activity at very low concentrations. Int J Nanomedicine.2012;7:5683–91.
28. Liu D, Li X, Chen C, Li C, Zhou C, Zhang W, et al. Target-specific delivery of oxaliplatin to HER2-positive gastric cancer cells in vivo using oxaliplatin-au-fe3o4-herceptin nanoparticles. Oncol Lett. 2018;15(5):8079–87.
29. Cui D, Zhang C, Liu B, Shu Y, Du T. Regression of Gastric Cancer by Systemic Injection of RNA Nanoparticles Carrying Both Ligand and siRNA. 2015; doi: 10.1038/srep10726
30. Sreeranganathan M, Uthaman S, Sarmento B, Mohan CG, Park IK, Jayakumar R. In vivo evaluation of cetuximab-conjugated poly(γ-glutamic acid)-docetaxel nanomedicines in EGFR-overexpressing gastric cancer xenografts. Int J Nanomedicine. 2017;12:7167–82.
31. Mohammadian F, Abhari A, Dariushnejad H, Zarghami F, Nikanfar A, Pilehvar-Soltanahmadi Y, et al. Upregulation of Mir-34a in AGS gastric cancer cells by a PLGA-PEG-PLGA chrysin nano formulation. Asian Pacific J Cancer Prev. 2016;16(18):8259–63.
32. Wu Y, Wang W, Chen Y, Huang K, Shuai X, Chen Q, Li X, Lian G. The investigation of polymer-siRNA nanoparticle for

gene therapy of gastric cancer in vitro. International journal of nanomedicine. 2010;5:129.
33. Tang Q, Xia H, Liang W, Huo X, Wei X. Synthesis and characterization of zinc oxide nanoparticles from Morus nigra and its anticancer activity of AGS gastric cancer cells. Journal of Photochemistry and Photobiology B: Biology. 2020 1;202:111698.
34. Dhivya R, Ranjani J, Rajendhran J, Mayandi J, Annaraj J. Enhancing the anti-gastric cancer activity of curcumin with biocompatible and pH sensitive PMMA-AA/ZnO nanoparticles. Materials Science and Engineering: C. 2018 Jan 1;82:182-9.
35. Hashemi SF, Tasharrofi N, Saber MM. Green synthesis of silver nanoparticles using Teucrium polium leaf extract and assessment of their antitumor effects against MNK45 human gastric cancer cell line. Journal of Molecular structure. 2020;1208:127889.
36. Karuppaiya P, Satheeshkumar E, Tsay HS. Biogenic synthesis of silver nanoparticles using rhizome extract of Dysosma pleiantha and its antiproliferative effect against breast and human gastric cancer cells. Molecular biology reports. 2019;46(5):4725-34.
37. Aslany S, Tafvizi F, Naseh V. Characterization and evaluation of cytotoxic and apoptotic effects of green synthesis of silver nanoparticles using Artemisia Ciniformis on human gastric adenocarcinoma. Materials Today Communications. 2020;24:101011.
38. Ketab RS, Tafvizi F, Khodarahmi P. Biosynthesis and Chemical Characterization of Silver Nanoparticles Using Satureja Rechingeri Jamzad and Their Apoptotic Effects on AGS Gastric Cancer Cells. Journal of Cluster Science.2020:1-1.
39. Nasr R, Hasanzadeh H, Khaleghian A, Moshtaghian A, Emadi A, Moshfegh S. Induction of Apoptosis and Inhibition of Invasion in Gastric Cancer Cells by Titanium Dioxide Nanoparticles. Oman Med J. 2018;33(2):111-117. doi: 10.5001/omj.2018.22. PMID: 29657679; PMCID: PMC5889831.
40. Yun Z, Chinnathambi A, Alharbi SA, Jin Z. Biosynthesis of gold nanoparticles using Vetex negundo and evaluation of pro-apoptotic effect on human gastric cancer cell lines. Journal of Photochemistry and Photobiology B: Biology. 2020;203:111749.
41. Liu Z, Wang K, Wang T, Wang Y, Ge Y. Copper nanoparticles supported on polyethylene glycol-modified magnetic Fe3O4 nanoparticles: Its anti-human gastric cancer investigation. Arabian Journal of Chemistry. 2022;15(1):103523.
42. Azimee S, Rahmati M, Fahimi H, Moosavi MA. TiO2 nanoparticles enhance the chemotherapeutic effects of 5-fluorouracil in human AGS gastric cancer cells via autophagy blockade. Life sciences. 2020;248:117466.
43. Badi N, Fazelipour S, Naji T, Babaei M, Kalantari Hesari A. Histomorphometric and biochemical study of liver and thyroid hormones following administration of MoO3 nanoparticles in female rats. Iranian Journal of Veterinary Medicine. 2022;16(2):188-201.