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Nano-based approaches for diagnosis and therapy of gastric cancer

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Dear Editor,

Cancer is one of the leading causes of death worldwide[1,2]. Gastric adenocarcinoma or gastric cancer (GC) is the third leading cause of cancer-related deaths in the world. Major risk factors associated with the pathogenesis of GC are *Helicobacter pylori* infection, smoking, diet, and chronic gastric mucosal inflammation. Recent data indicates iron deficiencies, high salt intake, and Epstein-Barr virus infection accelerates the progression of gastric carcinogenesis by *H. pylori* virulence. *H. pylori* has been recognized as a class I carcinogen for GC, by WHO. Although more than 50% of the world population is infected with *H. pylori*, only 1%–2% develop GC in their lifetime. Moreover, polymorphism in the proinflammation gene interleukin 1β has been reported as the gastric factor responsible for the progression of GC. TP5 is the frequently mutated gene reported in ~50% of cases of GC[3].

Surgery remains the only curative therapy for GC. However, perioperative, adjuvant chemotherapy, and chemoradiation may improve the outcome of complete resection of cancer and extended lymph node dissection.

The overall efficiency of GC treatment is reduced due to the underlying limitations of conventional chemotherapy including low water solubility and permeability, limited circulation time, toxic effects due to poor drug targeting, and low biodistribution[4]. Therefore, nano-based drug delivery approaches [polymeric nanoparticles (NPs), viral NPs, liposomes, micelles, dendrimers, gold NPs, and inorganic NPs] are being used in GC therapy for achieving enhanced efficiency, high specificity, reduced toxicity, and excellent stability[5].

NP-mediated gene therapy, immunotherapy, oxidation therapy, chemotherapy, phytochemicals delivery, thermotherapy, and phytotherapy are some successfully researched therapeutic approaches for the effective treatment and management of GC. Traditional imaging techniques for the diagnosis of GC in doses include computed tomography (CT), MRI, PET-CT, and single-photon emission computed tomography[6]. The conventional techniques suffer from limitations like poor target distribution, rapid clearance single imaging modality, and other undesirable side effect. NP-designed imaging of GC provides advantages via real-time imaging, superior tumor–background ratio, specific accumulation in tumor metastasis, high sensitivity, and high resolution[7].

NP-based fluorescence imaging, Food and Drug Administration (FDA)-approved fluorophores such as 5-aminolevulinic acid and other cyanide-based fluorophores are employed. Photoacoustic imaging provides high sensitivity and 2-dimensional/3-dimensional resolution imaging. CT with targeting NP contrast agent is used for early-stage diagnosis of GC. MRI, inorganic NP, superparamagnetic iron oxide NPs, and nanoprobes could be employed for improving selectivity for GC[8].

Multidrug resistance (MDR) is the major cause of the failure of chemotherapy for GC. Major factor resulting in MDR may include reduction of intracellular drug concentration, alternation of DNA damage repair, alteration in drug targets, inhibition of autophages and apoptosis pathways, change of tumor microenvironment. Proper understanding of the MDR mechanism and use of novel drug delivery approaches could be useful in better therapeutic outcomes and treatment modalities for managing GC[9].

Nanomaterial-based administration has proven to be a successful technique of administering innovative therapies, particularly for nucleic acids, which are extremely fragile and quickly destroyed in the systemic circulation. This type of genetic therapy uses DNA and RNA-based compounds like small interfering RNA and microRNA[10]. When small interfering RNAs were applied to the surface of NPs as either encapsulated or conjugated molecules. These treatments have frequently been used to target 'undruggable' proteins in GC. In addition, it has been shown that genetic therapies based on nanocarriers have a long-lasting effect due to their increased stability. One such case has been reported in which a suicidal gene named yCDglyTK was delivered to SGC7901 GC cells through calcium phosphate NPs. Its in-vivo experiments were also successful in delivering the NPs to its target site at the GC cells[11].

Advanced research methodologies are required to develop for effective management and treatment of GC. NPs represent a potential method for enhancing the prognosis and treatment options for GC. NPs are helpful for imaging as well as the efficient transportation and delivery of medications to particular target site[12,13]. Therefore, NPs can act as delivery vehicles to improve

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the therapeutic and pharmacological properties of drugs for the treatment of GC. The biodistribution and targeting ability of NPs may differ in preclinical and clinical practices due to degradation/metabolism of NPs in the body and high degree of tumor heterogenicity. Biomimetic and multifunctional NPs maybe endeavored with additional capability may address the challenges associated with stability, degradation, targeting, toxicity, and loading of NPs. Large scale production, reproducibility, regulatory issues, clinical efficiency, toxicity, and stability issues pertaining to NPs requires serious attraction for the effective diagnosis and treatment of GC.

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