



## Review

# Analytical applications of chemiluminescence-detection systems assisted by magnetic microparticles and nanoparticles

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## ABSTRACT

Analytical applications of chemiluminescence detection systems based on magnetic microparticles and nanoparticles (MMP-CL and MNP-CL) have attracted growing interest in research and commercial fields. This article reviews the literature on the analytical applications of MMP-CL and MNP-CL systems, illustrated by different reaction strategies, such as immunoassay and hybridization labels in diverse fields (e.g., clinical and pharmaceutical, environmental or food analysis).

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**Abbreviations:** ABEL, N-(4-aminobutyl)-N-ethylisoluminol; Ab, Antibody; AFP, Alpha-fetoprotein; Ag, Antigen; ALP, Alkaline phosphatase; AMPPD, 4'-methoxy-4-(3-phosphate-phenyl)-spiro-(1,2-dioxetane-3,2'-adamantane); APnEOs, Alkylphenol polyethoxylates; ATP, Adenosine 5'-triphosphate; AuNP, Gold nanoparticle; BMP, Bacterial magnetic particle; BP, Bromophenol blue; CA 125, Carcinoma antigen 125; B-CD, B-cyclodextrin; CL, Chemiluminescence; CEA, Carcinoembryonic antigen; CLIA, Chemiluminescence enzyme immunoassay and chemiluminescence immunoassay; f-MP, Functionalized magnetic particle; DNA, Deoxyribonucleic acid; DPA, Diperoxidate; FITC, Fluorescein isothiocyanate; FT<sub>4</sub>, Free thyroxine; GOx, Glucose oxidase; GPC3, Glypican-3; HRP, Horseradish peroxidase; IgG, Immunoglobulin G; LOD, Limit of detection; MC-LR, Microcystin-LR; MEIA, Microparticle enzyme immunoassay; MIP, Molecularly-imprinted polymer; MMIP, Magnetic molecularly-imprinted polymer; MMP-CL, Magnetic microparticle-based chemiluminescence; MNP-CL, Magnetic nanoparticle-based chemiluminescence; MP, Magnetic particle; MP-CLIA, Magnetic particle-based chemiluminescence immunoassay; LAS, Linear alkylbenzene sulfonate; MFC, Microfabricated cantilever; NSE, Enolase; PEI, Polyethyleneimine; PMT, Photomultiplier; PNIP, Poly(nisopropylacrylamide); QCM, Quartz-crystal microbalance; SCCa, Squamous cell carcinoma antigen; SIA, Sequential injection analysis; SPR, Surface-plasmon resonance; Vg, Vitellogenin; TMPG, 3,4,5-Trimethylphenylglyoxal; TRP, p-Phenol derivative, 4-(1,2,4-triazol-1-yl) phenol; TSH, Thyroid-stimulating hormone.

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## 1. Introduction

Magnetic particles (MPs), which can be readily synthesized in a wide range of sizes (from nm to a few  $\mu\text{m}$ ), possess remarkable merits, including large ratio of surface area to volume, low cost of synthesis, magnetic susceptibility, low toxicity and compatibility with biomaterials. Because of these features, MPs have found a plethora of applications in a wide variety of scientific fields [1]. General applications of MPs are presented in Fig. 1. In this regard, the use of MPs as biomolecule carriers in analytical chemistry is promising, because they can be easily manipulated by using an external magnetic field and matrix effects are almost eliminated because of the improved washing steps. Also, unlike conventional purification methods, exploitation of MP-based techniques eliminates the need for sample pretreatment by centrifugation or chromatography, therefore shortening the time needed. Indeed, the molecules, which are immobilized on MPs, can be readily separated or dispersed in solution by an external magnetic field [2]. It is noteworthy that immobilization of enzymes, including horseradish peroxidase (HRP), onto magnetic nanoparticles (MNPs) efficiently increased the activity and the stability of the enzyme and allowed its reuse in chemical operations [3].

Combining MPs with immunoassay has made screening faster and easier than conventional immunoassay because, in such a homogenous system, the mass-transfer distance of analytes and reagents to the immobilized antibody (Ab) on the MPs is significantly decreased. The Ab–antigen (Ag)-binding equilibrium can therefore be provided faster than that with antibodies coated on the planar surface, including in micro-plate wells, so reducing the incubation time [4]. Besides, MNPs possess intrinsic peroxidase-like activity similar to that found in natural peroxidases [5–7]. Based on this finding, analytical applications of MPs have been extended to determination of various species involved in the oxidase-mimicking activities of MPs [7].

CL is generally defined as the emission of light (ultraviolet, visible, or infrared) during the process of a chemical reaction [8,9]. The CL reactions have high potential for a great variety of analytical applications due to their high sensitivity, wide linear range and cost-effective apparatus because there is no need for an excitation light source and a spectral resolving system [10,11].

Recently, Iranifam [12] reviewed the state-of-the-art in flow-CL techniques for pharmaceutical analysis. However, CL analysis sometimes suffers from drawbacks, such as poor selectivity because of existing species in the solution that can alter analytical signals. The relatively low emission intensity of some CL reactions, due to possessing very low efficiency in transforming chemical energy into light, is another possible shortcoming of CL-detection systems [13].

Indeed, the current classical CL systems generally need to enhance emission intensity and to improve selectivity for quantitative analysis in samples with complex matrices, including biological and environmental samples.

In this context, coupling magnetic microparticles (MMPs) and MNPs with CL methods could meet two requirements: high sensitivity and selectivity, in which MPs can participate in the CL reactions as catalyst, biomolecule carrier and separation tool. Due to these properties, analytical applications of MP–CL systems have attracted much attention of researchers, so they deserve a comprehensive review on the findings of published studies in this topic, as intended in this review.

## 2. Magnetic particle-based chemiluminescence immunoassays (MP-CLIA)

Antibodies (Abs) are large Y-shaped proteins produced by the immune systems of animals and humans, when the body detects the presence of allochthonous substances (Ags). Abs have a high

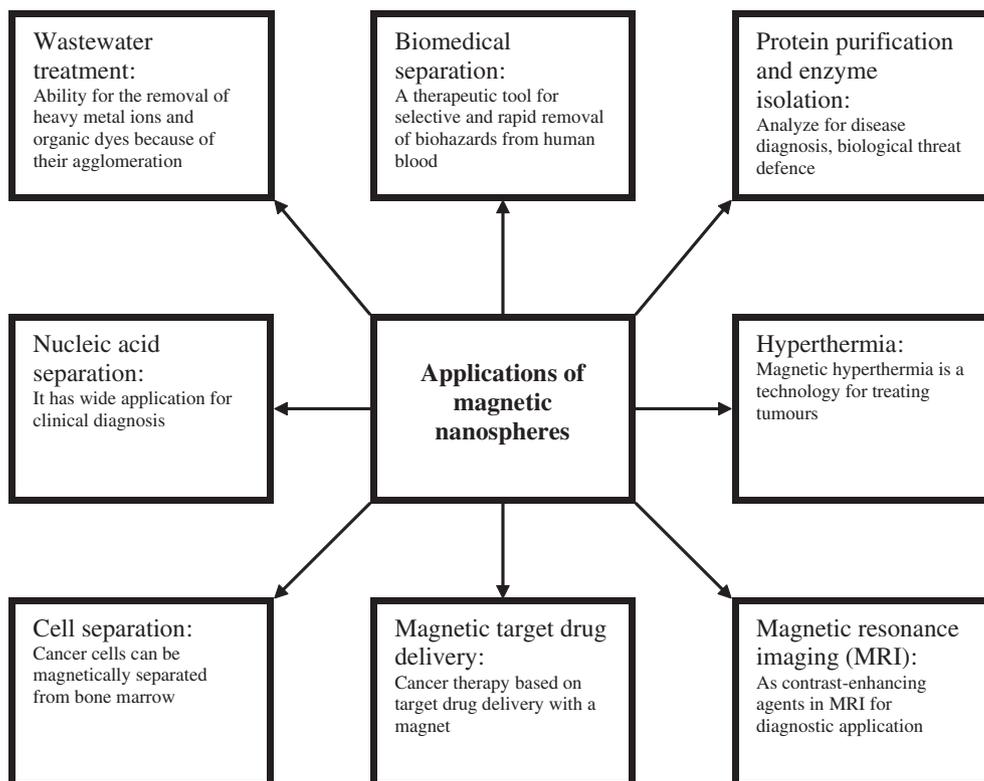


Fig. 1. General applications of magnetic nanoparticles (MNPs) [1].

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