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# Electromagnetic induction detector for capillary electrophoresis and its application in pharmaceutical analysis

Xiu-juan Yang, Zuan-guang Chen*, Cui Liu, Ou-lian Li

*School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou, Guangdong 510006, PR China*

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ABSTRACT

A new electromagnetic induction detector for capillary electrophoresis and its application are described. The detector is consisted of an inductor, a resistor, a high-frequency signal generator and a high-frequency millivoltmeter. The conditions affecting the response of the detector, including dimension of the magnetic ring, position of the capillary, number of coil turns, frequency, excitation voltage and value of the resistor were examined and optimized. The feasibility of the proposed detector was evaluated by detection of inorganic ions and separation of amino aids. Its quantification applicability was investigated by determination of aspirin and paracetamol in pharmaceutical preparation (Akafen powder). The primary factors affecting separation efficiency, which include variety of buffer, buffer concentration, injection time and injection height and separation voltage, were researched. Experimental results demonstrated that this new detector showed a well-defined correlation between sample concentrations and responses ($r = 0.997–0.999$), with detection limits of 30 μmol $L^{-1}$ for aspirin and 10 μmol $L^{-1}$ for paracetamol, as well as good reproducibility and stability. Compared with currently available detection techniques, this new detector has several advantages, such as simple construction, no complicated elements, ease of assembly and operation, and potential for universal applications. It can be an alternative to the traditional methods in the quality control of the pharmaceutical preparations.



## 1. Introduction

As one of the fast growing analytical techniques, CE has many advantages such as high separation efficiency, short analysis time, low operation cost, and minimum consumption of sample and reagents. It has rapidly become an important analytical tool for separation of a large variety of compounds, ranging from small inorganic ions [1] to large biological molecules [2] and has been widely applied to biomedical and pharmaceutical analysis [3], food analysis [4], clinical diagnostics [5], environmental monitoring [6], and forensic investigations [7]. Detection technique is one of the key techniques in CE and it has been extensively investigated by many research groups from various directions. Typical detection techniques such as ultraviolet–visible (UV–vis) spectrophotometry [8], laser-induced fluorescence (LIF) [9], chemiluminescence (CL) [10], electrochemical detection (including conductometry [11–13], amperometry [14], and potentiometry [15]) and mass spectrometry (MS) [16], etc., have been employed successfully in CE.

Spectrophotometric detection based on UV–vis absorption is the most commonly used detection technique up to now. However, limited by the short path-length through the column, the sensitivity of this detection method is far from satisfactory. Moreover, it is not suitable for the most inorganic ions because very few of these ions exhibit significant direct absorbance in the UV–vis wavelength range [1]. Indirect photometric detection, aiming to overcome this disadvantage, has been developed and has become a kind of rather better detection method because of its universal character [17]. Also, the use of highly absorbing probes [18] has allowed the detection limits to be significantly reduced.

The combination of LIF detection with CE was introduced by Gassman et al. in 1985 [19]. LIF is considered as one of the most sensitive detection schemes available for CE, and it has been shown to be uniquely suited for the detection of individual particles and organelles [20]. Laser beams emit highly collimated light which is adequate for focusing the light onto the small diameter of the capillary. By increasing the fluorescence intensity and reducing the optical noise, including the reflecting and scattering light from the capillary wall and optical system, the limit of detection can be greatly improved [21]. However, large size, high cost, limited lifetime and high power consumption are some drawbacks that hinder its widespread application.

*Abbreviations:* Arg, arginine; His, histidine.

* Corresponding author. Tel.: +86 20 3994 3044; fax: +86 20 3994 3071.
*E-mail address:* chenzg@mail.sysu.edu.cn (Z.-g. Chen).

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Light-emitting diode (LED) has become a more and more attractive alternative light source for fluorescence detection, due to its inherent features such as high stability, small size, low cost, a variety of wavelengths ranging from near-UV to near-IR and very long lifetime [22,23]. It has been applied in CE analyses of inorganic ions, amino acids [24], proteins [25] and pharmaceuticals. Higher sensitivity can be achieved by using higher-intensity LEDs, multifarious filters and improved focusing optics. What is more, deep-UV-LEDs, reported by Macka and co-workers [26], extend the use of LEDs as light sources for photometric detection in CE.

Chemiluminescence (CL) has also been considered to be an alternative detection scheme for CE which is characterized by simple optical systems without an excitation light source, low or even no background, high sensitivity and low cost [27]. However, the lack of CL reactions for many compounds is the main drawback in the use of CL detection for CE.

Electrochemical detection including conductometry, amperometry and potentiometry, offers potentially universal detection of all inorganic cations and anions. It is sensitive, inexpensive, portable and easy to be integrated. Moreover, the measuring procedures and required instrumentation are simple. However, one weak point is that separation voltage interferes with detection signal strongly in this kind of detection techniques.

Since the hyphenation of CE with MS was first reported by Smith and co-workers in 1987 [28], large numbers of original research papers and reviews articles on this technique and its application, have been published. With its high resolving power, high detection sensitivity and high compound identification capability, CE-MS is an extremely valuable analytical technique for the analysis of complex mixtures [29]. It has become an essential bioanalytical tool in the fields of life, pharmaceutical, food, environmental and forensic sciences [30]. But CE-MS still requires relatively expensive instrumentation and experienced operation.

Besides the detection methods mentioned above, there is still need to find some new ones which are easy to fabricate, simple to operate, low cost and of wide application. In the previous work of our research group headed by Chen, we have reported a new kind of method, electromagnetic induction detection with vertical coil for CE and microfluidic chip [31]. In this work, another novel electromagnetic induction detector was developed. There are two main differences between the previous one and this one. First, the principle of electric circuit is different. The voltage difference between the inductor and the resistor instead of that between the two uniform inductors is sensed by a high-frequency millivoltmeter. Therefore, the instrumentation is easier to fabricate for this one because it is rather difficult to make two strictly uniform inductors in the previous one. Second, the construction of the inductors is different. The previous one is made by winding enameled wire onto a magnetic core while this one is made by winding enameled wire onto a magnetic ring.

In this work, an inductor, located at the detection zone of separation capillary, with a resistor in series is connected to a high-frequency signal generator. As the analytes are driven through the detection zone, the electromagnetic field changes according to the electrical and/or magnetic properties of the components, which results in the alteration of the inductance value of the inductor. This alteration causes a variation of the voltage distribution between the inductor and the resistor. The change of the voltage in the resistor is sensed by a high-frequency millivoltmeter and further enhanced by an amplifier. Compared with those current detection techniques, this new detector has its own distinguished features such as easy to assemble, simple and convenient to operate and low cost. The feasibility of the proposed detector was evaluated by detection of inorganic ions, analysis of amino acids, and determination of aspirin and paracetamol in Akafen powder, which implied that it might have great potential for universal application.

## 2. Materials and methods

### 2.1. Reagents

All reagents used in this investigation were of analytical grade. Standard aspirin and paracetamol were purchased from National Institute for the Control of Pharmaceutical and Biological Products (Beijing, China). Akafen powder was produced by Baiyunshan Pharmaceutical Co. Ltd. (Guangzhou, China). Histidine (His), arginine (Arg) and cetyltrimethylammonium bromide (CTAB) were purchased from Shanghai Bio Life Science & Technology Co. Ltd. (Shanghai, China). Tris(hydroxymethyl)aminomethane (Tris) was obtained from Shanghai Sangon Biological Engineering Technology & Services Co. Ltd. (Shanghai, China). Other reagents were purchased from Guangzhou Chemical Reagent Co. Ltd. (Guangzhou, China).

### 2.2. Solutions

All kinds of buffer solutions were prepared with redistilled water in a concentration of 0.1 mol $L^{-1}$ and were diluted in suitable concentration prior to use. Stock sample solutions of inorganic ions and amino acids were prepared in a concentration of 10 mmol $L^{-1}$ with redistilled water. Stock standard solutions of aspirin and paracetamol were prepared with redistilled water containing 20% (v/v) of ethanol to a concentration of 10 mmol $L^{-1}$ and stored in the refrigerator (4 °C). Operating standard solutions were prepared from the stock solutions by appropriate dilution in running buffer solution immediately before use. All the solutions were degassed in an ultrasonic bath and filtered through 0.22-μm nylon filters before use.

### 2.3. Samples preparation

A pack of Akafen powder containing 230 mg aspirin and 126 mg paracetamol was put into a centrifuge tube, then, 50.0 mL of the solvent mixture (redistilled water containing 20% of ethanol) was added to the tube. After shaking, it was agitated for 15 min on an ultrasonic bath and then centrifuged for 15 min at 3000 rpm. Subsequently, 10.0 mL of the clear supernatant was transferred into a 100-mL volumetric flask. The volume was adjusted to 100.0 mL with the same solvent mixture. This stock sample solution was stored in the refrigerator at 4 °C. The operating sample solution was 10 times diluted from the stock sample solution by running buffer solutions immediately and filtered through 0.22-μm nylon filters before injection.

### 2.4. Apparatus

The homemade capillary electrophoresis system consisted of a high voltage supplier and an electromagnetic induction detector. The high voltage supplier was made of piezoelectric ceramics, to provide a potential of constant direct current or pulse of 0.5–50 kV for separation, as described in detail in previous literature [32]. The electromagnetic induction detector was consisted of a high-frequency signal generator (DG1011; Rigol Technologies Inc., sine wave was employed), a high-frequency millivoltmeter (WY2271; Shanghai Wuyi Electronics Co., Ltd.), a resistor (60 kΩ) and an inductor. As shown in Fig. 1, the inductor, which was located at the detection zone of separation capillary, with a resistor in series was connected to a high-frequency signal generator. Both ends of the resistor were linked up to the input of the high-frequency millivoltmeter. The output voltage of the high-frequency millivoltmeter was magnified by an amplifier (TI 081). Data acquisition and processing was carried out by commercial chromatography software (CT-22 USB, Qianpu Co., Ltd., Shanghai, China). An uncoated

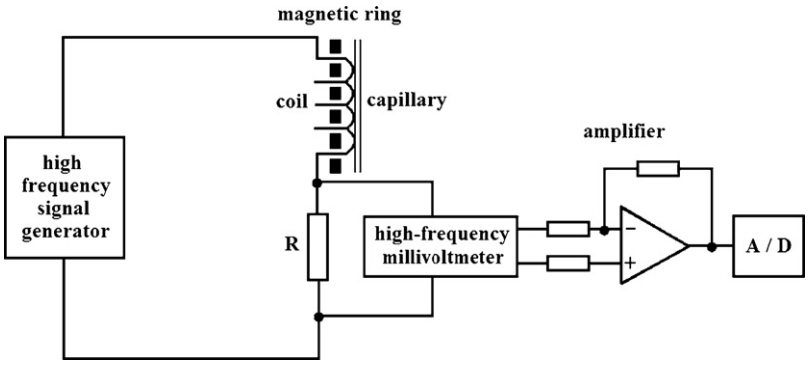


**Fig. 1.** The electric circuit of the electromagnetic induction detector.

fused-silica capillary of 75 cm (60 cm to the detector) and 150 μm id (Reafine Chromatography Ltd., Hebei, China) was employed for sample separation.

As shown in Fig. 2, a part of an unabridged magnetic ring (made from non-magnetized ferrate, with the dimension of 5 mm in inner diameter, 9 mm in outer diameter, 3 mm in thickness) was cut flat, and a gap (1 mm) was made in the middle of the flat surface. Then, two edges were sharpened. Enameled wire (copper wire, insulated with lacquer on the surface, 0.1 mm in diameter) was wound onto the magnetic ring. A capillary went straight through the gap of the flat surface of the magnetic ring which was just the detection zone. The magnetic ring and enameled wires were purchased from Meizhou Magnetic Co., Ltd., Guangdong, China. The detector was located in a shielded box to prevent interference from external electromagnetic fields.

The working principle of this electromagnetic induction detector could be explained as following. The equivalent circuit of the detector is shown in Fig. 3, the inductor ($L$) and the resistor ($R$) are connected in series and then connect with the high-frequency signal generator. There exists a capacitor beside the inductor. The inductor and the capacitor are connected in parallel to form a parallel $LC$ circuit. According to the principles of analog electronics, the impedance of the parallel $LC$ circuit is:

$$Z = \frac{(1/j\omega C)(r + j\omega L)}{(1/j\omega C) + (r + j\omega L)} = \frac{r + j\omega L}{1 + j\omega rC - \omega^2 LC} \quad (1)$$

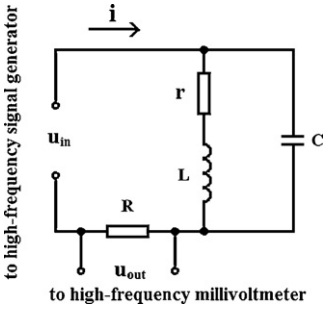


**Fig. 3.** The equivalent circuit of the electromagnetic induction detector.

where $L$ is inductance value of the inductor, $r$ is the internal resistance of the inductor itself, $C$ is the capacitance of the capacitor, $\omega$ is the radian frequency of input signal, and $j = \sqrt{-1}$.

Because $r$, the internal resistance of the inductor, is very small, the impedance of the parallel $LC$ circuit can be expressed as:

$$Z \approx \frac{j\omega L}{1 + j\omega rC - \omega^2 LC} = \frac{1}{(rC/L) + j(\omega C - (1/\omega L))} \quad (2)$$

when the frequency of the input signal is adjusted to resonance frequency, $\omega_0 = (1/\sqrt{LC})\sqrt{1 - (C/L)r^2}$ or $f_0 = (1/2\pi\sqrt{LC})\sqrt{1 - (C/L)r^2}$, the $LC$ circuit occurs resonance. The

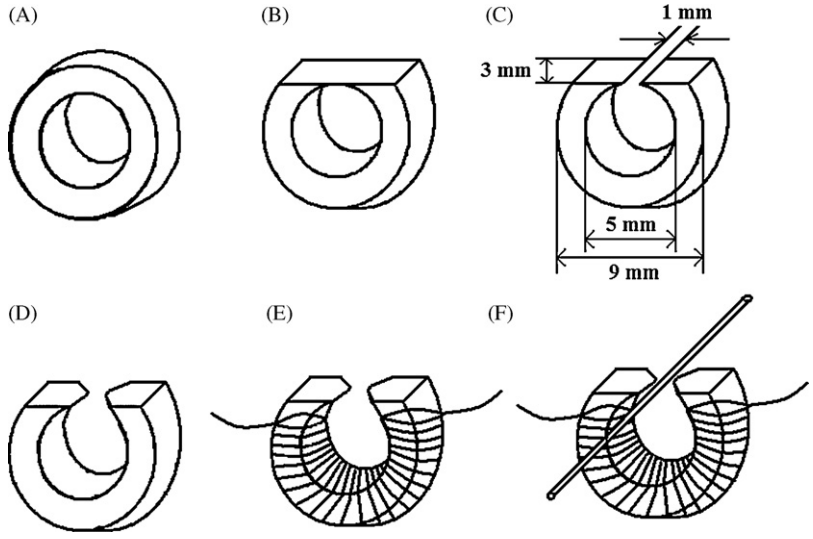


**Fig. 2.** The procedures for making an electromagnetic inductor. (A) An unabridged magnetic ring; (B) a part of the ring was cut flat; (C) a gap (1 mm) was made in the middle of the flat surface; (D) two edges were sharpened; (E) enameled wire was wound onto the ring; (F) a capillary was placed in the gap of the flat surface.

impedance of the parallel *LC* circuit reaches maximum:

$$Z_0 = Z_{max} = \frac{L}{rC} \quad (3)$$

Therefore, the current ($i$) flowing through the circuit reaches minimum at resonance frequency, and the voltage ($u_{out}$) in the resistor ($R$) also comes to minimum.

The inductance value of the inductor would be altered when the analyte in running buffer passes the detection zone of the capillary channel. This alteration leads to a deviation from the resonance state. Then, it results in a decrease of the total impedance of the circuit. Meanwhile, the current ($i$) flowing through the circuit increases, and the voltage in the resistor ($u_{out}$) also increases. So, analytes passing the detection zone will cause alteration of the voltage in the resistor. This voltage alteration is sensed by a high-frequency millivoltmeter and amplified further, then recorded by the chromatography working station. Chromatographic peaks of these analytes can be obtained.

### 2.5. Electrophoresis procedures

A new separation capillary should be pretreated with 1.0 mol $L^{-1}$ sodium hydroxide solution and redistilled water for 30 min. Before starting experiments every day, the separation capillary was flushed with 0.1 mol $L^{-1}$ sodium hydroxide solution for 10 min, followed by redistilled water for 10 min, and then with the corresponding running buffer for 15 min. Sample injection was performed by hydrodynamic mode. The separation was carried out with a negative applied voltage. After each analysis run, the capillary was treated sequentially with 0.1 mol $L^{-1}$ sodium hydroxide solution for 5 min, redistilled water for 5 min and corresponding running buffer for 5 min. This was done to equilibrate the capillary and to maintain the reproducibility of the analysis. At the end of the day, the channel was filled with redistill water so as to prevent clogging of the capillary.

## 3. Results and discussion

### 3.1. The optimization of the operating parameters

#### 3.1.1. The dimension of the magnetic ring

Different size of magnetic rings was investigated: inner diameter (i.d.) 3 mm and outer diameter (o.d.) 5 mm, i.d. 5 mm and o.d. 9 mm, i.d. 6 mm and o.d. 10 mm, i.d. 9 mm and o.d. 17 mm. It was found that when the ring was too small (i.d. 3 mm and o.d. 5 mm), the inductance value of the inductor was too low and the magnetic field was too weak, there was no response for any analyte passing through the capillary. However, when the ring was too large (i.d. 9 mm and o.d. 17 mm), baseline noise rising and peak broadening were observed. Taking response and peak shape into consideration, magnetic ring of i.d. 5 mm and o.d. 9 mm was chosen in the following experiments.

#### 3.1.2. The position of the capillary

The position of the capillary is also an important parameter which needs to be carefully studied, because the response of the same analyte might be quite different by keeping the capillary in different position inside the magnetic ring. In this experiment, three alignments of the capillary were tested (Fig. 4): in the gap of the flat surface, over the gap of the flat surface (1 mm higher) and under the gap of the flat surface (1 mm lower). The results showed that when the capillary was in the gap of the flat surface, the response was stronger than that while it was over or under the gap of the flat surface. Therefore, the capillary just was just kept in the gap of the flat surface.

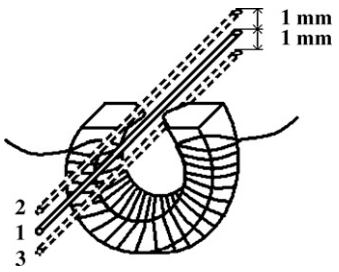


**Fig. 4.** Three different positions of the capillary: (1) in the gap of the flat surface; (2) 1 mm over the gap of the flat surface; (3) 1 mm under the gap of the flat surface.

#### 3.1.3. The number of turns

Winding enameled wire onto a magnetic ring to make a coil, the number of turns of the coil was essential to the whole detection system. Fig. 5A shows the influence of the number of turns (50, 100, 200, 500, 700, 800, 850, 900, 950, 1000, and 1200) of the coil on the detector response for an analysis of 500 μmol $L^{-1}$ manganese ions. It was recorded at their optimal frequency and excitation voltage. As we can see that when the number of the turns was less than 50, there was no response for any running buffer or samples, which might be attributed to the low inductance value of the coil and the weak magnetic field. The response increased gradually with increasing the number of the turns. While the number of the turns was from 800 to 950, the peak height retained stably. A decrease of peak height was observed when it was over 950. Thus, the number of the turns of the coil was adjusted to 800–950.

#### 3.1.4. Frequency

As expected, the response of the detector highly depended on the frequencies applied. Fig. 5B shows the curves of the signal-to-noise ratio (S/N) and peak height for the detection of manganese ion (1 m mol $L^{-1}$) in three kinds of coils (500, 800 and 900 turns), which were recorded at the frequencies from 100 kHz to 1 MHz and under a constant excitation voltage of 700 mV (effective voltage). When the frequencies were lower than 100 kHz, there was no response for any running buffer or samples. When the frequencies were higher than 1 MHz, it was too hard to distinguish the signal from the noise. When the frequencies were from 100 kHz to 1 MHz, there existed a peak response value for each coil. The S/N for the 900-turn coil increased slowly between 100 and 220 kHz and then increased dramatically to a maximum at 285 kHz, before declining rapidly. Afterwards, the S/N fluctuated within a small range. The S/N for the 800-turn coil was similar to that of the 900-turn coil while the peak response was recorded at 472 kHz. The S/N for the 500-turn coil initially fluctuated within a small range between 100 and 610 kHz and then increased sharply, reached a maximum at 750 kHz, and subsequently decreased significantly. The curves of peak height got the same tendency as that of S/N in three kinds of coils. Analyzing the optimal frequency for each kind of coil (285 kHz for the coil of 900 turns, 472 kHz for the coil of 800 turns, 750 kHz for the coil of 500 turns), the result indicates that the more turns of coil, the larger the inductance value is, and the lower optimal frequency is.

#### 3.1.5. Excitation voltage

The S/N and peak height for three kinds of coils (500 turns, 800 turns and 900 turns) versus the excitation voltage in the range from 200 mV to 1000 mV (effective voltage) at their optimal frequency were plotted (Fig. 5C). The S/N and peak height for manganese ion (1 mmol $L^{-1}$) increased gradually with the excitation voltage amplitude from 200 mV to 500 mV in each kind of coil. Then, the S/N reached the peak (700 mV for the coil of 900 turns, 650 mV for the coil of 800 turns, 550 mV for the coil of 500 turns). After that, the

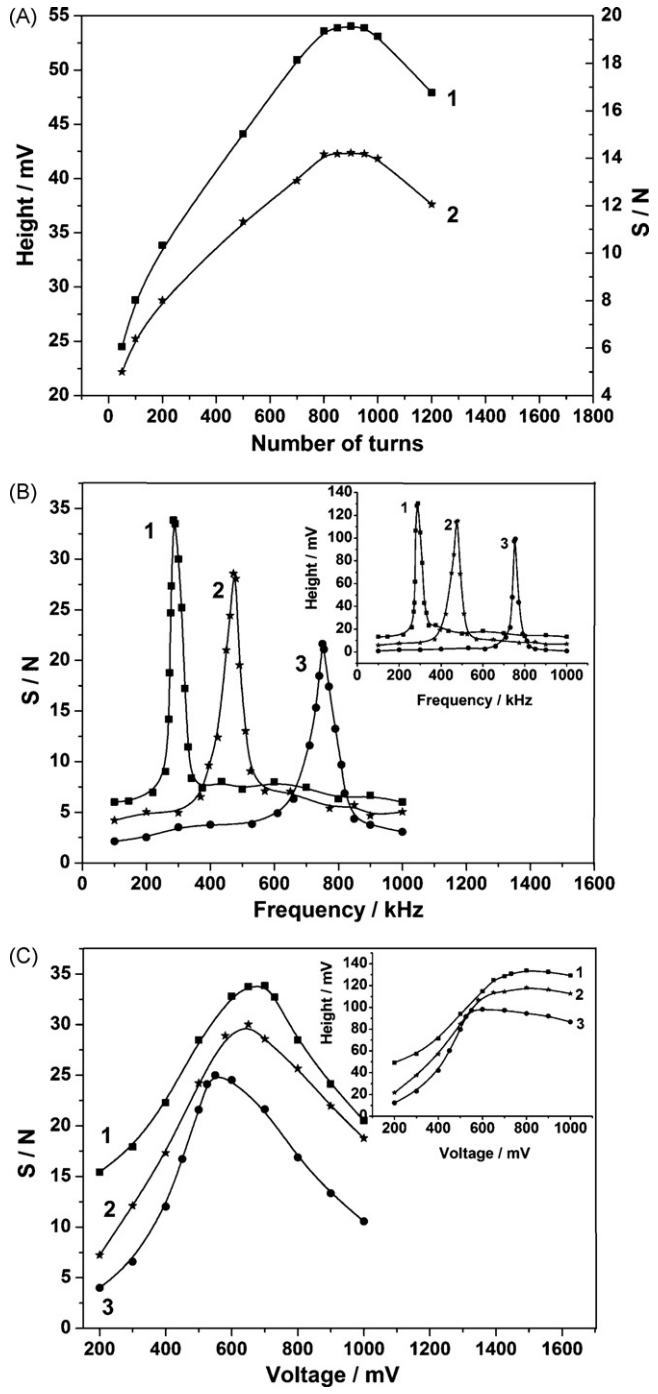


**Fig. 5.** (A) Influence of coil turns on peak height (1) and S/N (2) upon the response for 500 μmol $L^{-1}$ manganese ion. (B) Influence of frequency on S/N and peak height (in the inset) at a constant excitation voltage of 700 mV (effective voltage) for coils of 900 turns (1), 800 turns (2) and 500 turns (3). (C) Influence of the excitation voltage on S/N and peak height (in the inset) at a constant frequency of 285 kHz for a coil of 900 turns (1), 472 kHz for a coil of 800 turns (2) and 750 kHz for a coil of 500 turns (3).

peak height rose slowly while the S/N declined due to the increasing of baseline noise. Therefore, S/N must be taken into consideration while choosing the best excitation voltage amplitude. Also, it can be found that each kind of coils has its own optimal excitation voltage.

### 3.1.6. The value of the resistor

When different samples in the running buffer passed through the inductive zone of the capillary channel, it might cause an alteration of the inductance value of the inductor, which might result in a change of voltage distribution between the inductor and the resistor. Thus, the value of the resistor is also an essential parameter. The influence of employing resistors of different value (1, 2, 5, 10, 20, 40, 50, 60, 80 and 100 kΩ) on response for 1 mmol $L^{-1}$ manganese ions was investigated. There was no response when using 1, 2 and 5 kΩ; low response was observed when using 10, 20 and 40 kΩ; Good response was obtained when using 50, 60, 80 and 100 kΩ. A 60 kΩ resistor was adopted at last due to best S/N ratio was achieved.

## 3.2. Electrophoresis conditions

### 3.2.1. Composition, concentration and pH of buffer

The electrophoretic mobilities of aspirin and paracetamol were examined in different kinds of buffer solutions, such as HAc–NaAc, MES–His, Tris–$H_3BO_3$, sodium borate, etc. The experimental results showed that the current in buffer HAc–NaAc was too strong, which led to baseline noise rising and peak tailing. Such experiment phenomenon was also observed in buffer sodium borate. There were responses in buffer MES–His, as well as in Tris–$H_3BO_3$. But in comparison with buffer MES–His, buffer Tris–$H_3BO_3$ offered better peak shape and resolution together with higher stabilization of the basic line. Therefore, buffer Tris–$H_3BO_3$ was chosen to be the running buffer solution in this experiment.

Buffer pH value usually becomes a key parameter in separation of the analytes, as it determines the extent of ionization of each individual solute. It may also affect mobility and electroosmotic flow (EOF) by changing the dissociation constant of analyte and Si–OH groups on the capillary [33]. The effect of variation in pH on the resolution and migration time of the analytes was examined within pH 7.0–9.0. The mixture of aspirin and paracetamol standards was separated at pH 8.0. As pH increased from 8.0 to 8.8, the separation efficiency improved. Also, due to a general increase of EOF, a decrease of migration times was observed. However, when the pH was over 9.0, there was a co-migrated tendency between the two analytes. Therefore, the best resolution and suitable migration time for aspirin and paracetamol was obtained at pH 8.8.

Besides, the concentration of the buffer solution is another key parameter in CE separation. The increase in buffer concentration may lead to the increase of ionic strength, which can change the buffer capacity obviously and reduce the interactions between the analytes, also between the analytes and the capillary wall [34]. Therefore, in many cases, with the increasing of the buffer concentration, the resolution is better. However, high concentration may result in strong current and high Joule heating. Different concentrations of Tris (5–35 mmol $L^{-1}$) mixed with different concentrations of $H_3BO_3$ (5–35 mmol $L^{-1}$) were investigated in this research. Raising the concentration of Tris increased the resolution and obtained better peak shape, while increasing the concentration of $H_3BO_3$, peaks broadening were observed. A 40 mmol $L^{-1}$ buffer concentration (32 mmol $L^{-1}$ Tris + 8 mmol $L^{-1}$ $H_3BO_3$, pH 8.8) was finally chosen due to best separation efficiency as well as elegant peak shapes and stable baseline was obtained.

Reversal of EOF in capillary electrophoresis can be achieved by the addition of cationic surfactants to the electrophoretic buffer. This reversal of flow is caused by the formation of a bilayer or hemimicelle at the walls of the capillary, effectively making the wall charge positive [35]. CTAB (cetyltrimethylammonium bromide), as one kind of the cationic surfactants, was employed in this experiment. The addition of 0.05, 0.1, 0.2, 0.3 and 0.4 mmol $L^{-1}$ CTAB was studied in seeking an optimal concentration. Experimental results showed that when the concentration of CTAB was 0.05 mmol $L^{-1}$, it was not sufficient to reverse the EOF. Using 0.1 mmol $L^{-1}$ CTAB, reversal of the EOF could be obtained. Upon raising the concentration of CTAB, the residence time of the samples decreased. However,

**Table 1**
Comparison of LOQ and precision of some methods used in the determination of aspirin and paracetamol.

| Methods | Quantification limit (mol $L^{-1}$) | Precision | | References |
|---|---|---|---|---|
| | | Intra-day | Inter-day | |
| HPTLC | | | | |
| Aspirin | – | 0.2–1.0 | – | [36] |
| Paracetamol | – | 0.5–0.6 | – | |
| Flow-through sensor with UV detection | | | | |
| Aspirin | $1.50 \times 10^{-5}$ | 3.4 | – | [37] |
| Paracetamol | $1.12 \times 10^{-5}$ | 1.9 | – | |
| Capillary electrochromatography | | | | |
| Aspirin | $1.66 \times 10^{-5}$ | 1.2–1.7 | 2.2–2.8 | [38] |
| Paracetamol | $1.98 \times 10^{-5}$ | 1.4–1.9 | 2.1–2.9 | |
| Reversed-phase sequential injection chromatography | | | | |
| Aspirin | $5.55 \times 10^{-6}$ | 1.1–3.6 | – | [39] |
| Paracetamol | $1.06 \times 10^{-5}$ | 1.3–2.4 | – | |
| Graphical transform methods | | | | |
| Aspirin | – | 0.5–3.5 | – | [40] |
| Paracetamol | – | 1.4–3.7 | – | |
| Solid-phase molecular fluorescence | | | | |
| Aspirin | – | 0.5–3.9 | – | [41] |
| Paracetamol | – | 1.2–4.8 | – | |
| HPLC | | | | |
| Aspirin | $8.67 \times 10^{-5}$ | 1.3–2.6 | 3.7 | [42] |
| Paracetamol | $6.46 \times 10^{-6}$ | 0.9–1.6 | 2.5–3.9 | |
| CE with electromagnetic induction detector | | | | |
| Aspirin | $6.0 \times 10^{-5}$ | 1.3–1.7 | 2.0–2.5 | Our work |
| Paracetamol | $2.0 \times 10^{-5}$ | 1.5–1.9 | 2.2–2.8 | |

with the concentration of 0.3 and 0.4 mmol $L^{-1}$, the noise of the baseline increased and an unexpected overlapping of peaks was observed. Thus, the intermediate concentration of 0.2 mmol $L^{-1}$ was adopted.

Therefore, the buffer solution used in the following experiments was 32 mmol $L^{-1}$ Tris + 8 mmol $L^{-1}$ $H_3BO_3$ + 0.2 mmol $L^{-1}$ CTAB (pH 8.8).

### 3.2.2. Injection time and injection height

For CE, the injection volume, which is determined by the sample injection time and injection height, is a parameter that cannot be ignored. Different injection time (from 5 s to 15 s) was tested. It was found that the longer the injection time was, the higher the peak height was. The same phenomenon was observed in the different injection height (from 20 cm to 35 cm). However, when the injection time was more than 10 s, or the injection height was higher than 30 cm, it resulted in the tailing and broadening of peaks and the decreasing of the separation efficiency. Therefore, an injection height of 30 cm and an injection time of 10 s were considered to be optimal.

### 3.2.3. Separation voltage and temperature

Under the selected buffer solution and injection system, separation voltage (from 12 kV to 28 kV) was also tested in this research. It was observed that the separation efficiency improved and the retention time shortened with increasing the separation voltage. But when it was over 20 kV, deterioration of the baseline noise and distortion of the peaks were observed, which might be attributed to higher Joule heat it produced. Therefore, taking good peak pattern, resolution as well as reproducibility into consideration, 20 kV was the appropriate separation voltage for this system.

Column temperature affects not only the viscosity of the background electrolyte solution, but also the ion mobility and band broadening. Different column temperatures (21 °C, 23 °C, 25 °C, 27 °C and 29 °C) were investigated during sample analysis. At low temperatures the migration time became longer while high temperatures led to decrease in separation efficiency. Hence, 25 °C (close to room temperature) was adopted for analysis.

After a careful study on the effect of the above several parameters, the conditions of the electromagnetic induction detector for the determination of samples were selected as following: running buffer, 32 mmol $L^{-1}$ Tris + 8 mmol $L^{-1}$ $H_3BO_3$ + 0.2 mmol $L^{-1}$ CTAB (pH 8.8); injection time, 10 s; injection height, 30 cm; separation voltage, 20.0 kV; frequency (sine wave), 285 kHz; excitation voltage, 700 mV (effective voltage); turns of the coil, 900.

### 3.3. Application in pharmaceutical analysis

The performance of this newly developed electromagnetic induction detector was first evaluated by analyzing amino acids. A mixture of 500 μmol $L^{-1}$ histidine (His) and 500 μmol $L^{-1}$ arginine (Arg) was separated under the optimal conditions (Fig. 6A-1), then a further separation of a mixture of 800 μmol $L^{-1}$ His and 500 μmol $L^{-1}$ Arg was carried out for comparison (Fig. 6A-2). As we can see from the electropherogram, His and Arg were easily separated within 8 min and the peak area of 800 μmol $L^{-1}$ His was larger than the peak area of 500 μmol $L^{-1}$ His obviously. Therefore, this new detector is suitable for qualitative analysis.

Aspirin and paracetamol are most frequently and widely used drugs in daily life and lots of different methods have been used for the determination of them (Table 1). The quantification applicability of this novel detector was further demonstrated by the determination of aspirin and paracetamol in Akafen powder. As shown in Fig. 6B, good separation efficiency, as well as peak shapes for aspirin and paracetamol, was achieved under the optimal conditions. Calibration curves were acquired and the linearities were studied by testing a series of standard solutions of aspirin and paracetamol. The regression equations and the linear correlation coefficients listed in Table 2 reveal good linear relationship between the peak area and analyte concentration. The LODs based on the S/N of 3 for aspirin and paracetamol were 30 μmol $L^{-1}$ and 10 μmol $L^{-1}$, and the LOQ based on the S/N of 10 for them were 60 μmol $L^{-1}$ and 20 μmol $L^{-1}$. Intra-day precisions were investigated by injecting a standard mixture solution of aspirin and paracetamol six times within the same day at two different concentrations (a low level of 200 μmol $L^{-1}$ and a high level of 600 μmol $L^{-1}$) and inter-day precisions were assessed by the same

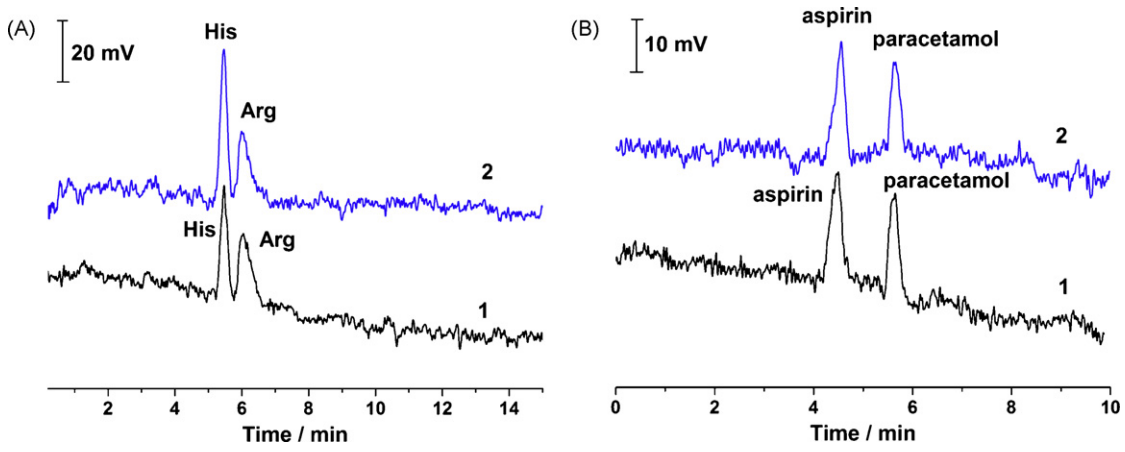


**Fig. 6.** (A) Electropherogram of the capillary electrophoresis of a mixture of 500 μmol $L^{-1}$ His and 500 μmol $L^{-1}$ Arg (1), 800 μmol $L^{-1}$ His and 500 μmol $L^{-1}$ Arg (2), detected by electromagnetic induction. (B) Electropherogram of the capillary electrophoresis of a mixture standard solution of aspirin and paracetamol (1, 200 μmol $L^{-1}$ each) and sample solution (2, determination of aspirin and paracetamol in Akafen powder), detected by electromagnetic induction. *Conditions*: running buffer, 32 mmol $L^{-1}$ Tris + 8 mmol $L^{-1}$ $H_3BO_3$ + 0.2 mmol $L^{-1}$ CTAB (pH 8.8); injection time, 10 s; injection height, 30 cm; separation voltage, 20.0 kV; frequency (sine wave), 285 kHz; excitation voltage, 700 mV (effective voltage); turns of the coil, 900.

**Table 2**
Statistical results for linearity, LOD, LOQ, regression analysis, precision, and sample determination.

| Parameters | Aspirin | Paracetamol |
|---|---|---|
| Calibration range ($\times10^{-5}$ mol $L^{-1}$) | 8.0–120 | 5.0–100 |
| Limit of detection (LOD) ($\times10^{-5}$ mol $L^{-1}$) | 3.0 | 1.0 |
| Limit of quantitation (LOQ) ($\times10^{-5}$ mol $L^{-1}$) | 6.0 | 2.0 |
| Regression equation[a] | | |
| Slope (B) | 20.88 | 7.16 |
| Intercept (A) | −180.1 | 170.3 |
| Correlation coefficient, *r* | 0.999 | 0.997 |
| Confidence limit of slope[b] | 20.88 ± 0.16 | 7.16 ± 0.10 |
| Confidence limit of intercept[b] | −180.1 ± 1.7 | 170.3 ± 2.1 |
| Intra-day RSD | 1.3[c]–1.7[d] | 1.5[c]–1.9[d] |
| Inter-day RSD | 2.0[c]–2.5[d] | 2.2[c]–2.8[d] |
| Sample | | |
| Label claim (mg) | 230 | 126 |
| Amount found (mg) | 228 ± 4.5 | 125 ± 2.5 |

[a] The regression equation was $Y = A + BX$ ($Y$ was peak area, $X$ was the concentration (μmol $L^{-1}$)).
[b] 95% confidence limit.
[c] Concentration level of 600 μmol $L^{-1}$.
[d] Concentration level of 200 μmol $L^{-1}$.

standard mixture solution over 6 days (Table 2). For comparison, it can be seen from Table 1 that the LOQ and the precision of this method are close to those of currently used methods, and even better than one of them (LOQ of aspirin by HPLC). Moreover, the quantitative ability and reproducibility of this method will be greatly improved after all the elements of the detector (including the inductor, the resistor, the signal generator and the millivoltmeter) integrated into a circuit board. Therefore, it could be an alternative to the traditional methods. The determination results of sample were listed in Table 2, which suggested that about 99.1% and 99.2% of the labeled amount of aspirin and paracetamol were found. The recovery test was carried out by spiking three known amounts of standard solutions of aspirin and paracetamol into the sample solution and satisfactory recoveries were obtained, ranging from 96.9% to 101.5% (Table 3).

## 4. Concluding remarks

A novel electromagnetic induction detector has been developed for CE. Its working conditions have been investigated and optimized. Its application in detection of inorganic ions, analysis of amino acids, and determination of aspirin and paracetamol in Akafen powder have also been demonstrated in this article.

As we can see, it is a good alternative to exiting detection methods for CE. Quite different from optical detection, which contains lots of complex optical elements, the construction of this electromagnetic induction detector is quite simple. It just consists of an inductor, a resistor, a high-frequency signal generator and a high-frequency millivoltmeter. Electrochemical detectors require precise alignment of electrodes, while in this new detector, the capillary only needs to place in the gap of the flat surface of the magnetic ring. What's more, the operation of this detection system is easy, which suggests its potential for extensive popularization and application.

Some improvements of the detector are under research. First, due to the construction of the detector is simple, it can be expected all these elements could be integrated into a circuit board, which might result in the enhancing of the sensitivity. Second, as the size of the detector could be greatly reduced after integration, it would be easier to apply this detector to microchip CE. Third, the application of this detector would be fully expanded. Further research may focus on applying this new detector to analysis of Chinese herbal medicines and level assay in biological fluids.

**Table 3**
Recoveries of standard addition ($n = 6$).

| Components | Background ($\times10^{-4}$ mol $L^{-1}$) | Added ($\times10^{-4}$ mol $L^{-1}$) | Found ($\times10^{-4}$ mol $L^{-1}$) | Recovery (%) | RSD (%, $n = 6$) |
|---|---|---|---|---|---|
| Aspirin | 2.53 | 1.00 | 3.51 | 99.4 | 1.1 |
| | | 3.00 | 5.42 | 98.0 | 1.9 |
| | | 7.00 | 9.27 | 97.3 | 1.5 |
| Paracetamol | 1.65 | 1.00 | 2.63 | 99.2 | 1.4 |
| | | 3.00 | 4.72 | 101.5 | 2.3 |
| | | 7.00 | 8.38 | 96.9 | 2.0 |

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