Design of a Fiber-optic Sensor for Monitoring Duodenogastric Reflux *

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Abstract A fiber-optic sensor for monitoring of duodenogastric reflux is fabricated. The sensing system, based on the principle of double-beam compensation, includes two diodes for light sources, blue at 470 nm as signal light and yellow at the wavelength of 595 nm as reference one, and a Y model fiber optic bundle for transmitting light. The sensor performs on detection of spectrophotometric absorption of bilirubin always present in enterogastric reflux at 470 nm and 595 nm. A general evaluation of the sensor about factors affecting its detection is discussed in detail: Wavelength choice, pH, scattering effect resulting from gastric precipitates and others. The sensor shows a good excellent performance with a dynamic linear range of up to 10 mg/dl. The in-vitro experiment shows it can be used in clinical analysis of DGR.

Keywords Fiber optic sensor; Bilirubin; Duodenogastric reflux (DGR)
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0 Introduction

Duodenogastric reflux (DGR), the regurgitation of alkaline duodenal juice into the stomach is a normal physiological phenomenon during the early hour of the morning or postprandial period[1]. But the excessive reflux is believed to be related with gastritis, gastric ulcer, gastric cancer, Barrett's esophagus and other pathological changes in digestive tract. A method suitable to accomplish continuous and in-vivo monitoring of DGR is crucial for clinical diagnosis.

Bechi et al reported a portable fiber optic sensor capable of monitoring of DGR, the Bilitec optoelectronic device[2]. The sensor mainly detects the absorbance of bilirubin present in duodenogastric reflux. The technique arises great interest in physicians and a great deal of research efforts has been devoted to develop the sensor for its clinical diagnosis. However no conception about the sensor is given in technical aspect. In this paper a new design of the fiber optic sensor is given. The sensor exhibits a better performance with a dynamic linear range of up to 10 mg/dl. Wavelength choice, the influences of pH, scattering effect and other factors affecting absorbance detected by the sensor are presented.

1 Configuration of the fiber optic sensor

The fiber optic sensor monitors DGR is spectrophotometrically based on the characteristic absorption of bilirubin present in DGR. According to Beer's law, the absorbance (A) is proportional to the concentration of absorbing analyte (c) and the optical path (l).

$$A = \varepsilon cl \quad (1)$$

Here ε is the molar absorbtivity with units of L mol^{-1} cm^{-1}. In this case the optical length (l) and the molar absorbtivity (ε) can be considered as constants. The working curve of absorbance vs. known concentration is established by measuring a series of standard solutions of known concentration using a fiber optic sensor device. Then quantitative determination of sample of unknown concentration can be done from the working curve.

The optoelectronic device contains two light-emitted diodes (LEDs) emitted alternatively as light sources in the sensor system (Fig. 1). One is green centered at 595 nm as reference light and the other is blue at the wavelength of 470 nm used as signal light, which is corresponding to the absorption peak at the absorption-wavelength graph of bilirubin and bile sample. Two optical filters (centered at 470 nm and 600 nm) are positioned in front of the signal LED and reference LED respectively to get more monochromatic

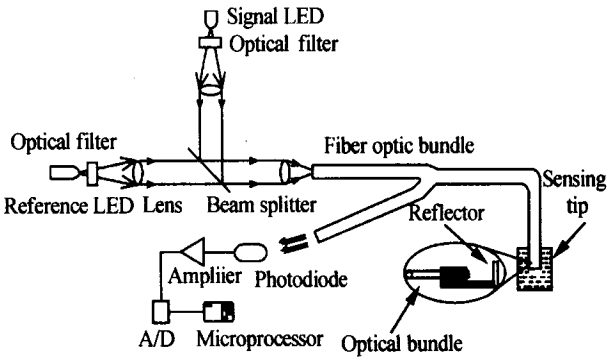

Fig. 1 Block diagram of experimental set-up of the fiber optic sensor for analysis of DGR

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lights. The filtered lights travel to a special beam-splitter, by which the signal light is reflected and the reference light is transmitted.

Finally the lights are coupled to one arm of a Y fiber optic bundle consisting of 50 plastic fibers with 300/350 μm of core/cladding diameter and then transported to the sensing probe. The lights are modulated by the analyte (bilirubin and bile sample) in the sensing tip and reflected back to the other arm of the optic bundle. The modulated lights are finally converted into electronic signal by a simple photodiode. The electronic signals are then amplified by an operational amplifier and processed by a microprocessor for further signal process. As for the sensor, the relation between concentration and absorbance is changed as follows

$$M = A_s - A_r = (\varepsilon_s - \varepsilon_r)\, cl \qquad (2)$$

where M is the difference between the absorbances of signal light and reference light, ε_s, ε_r are the molar absorbtivities corresponding to the signal and reference light respectively. A_r, A_s are the absorbances of the two lights.

2 Evaluation of the measurement system

Fig. 2 shows the response of the fiber optic sensor in bilirubin solution at pH 1.26 and 7.46 respectively. The dynamic linear range comes up to 10 mg/dl, which is better than that reported by P. Bechi et al[2]. The standard solution contains bilirubin purchased from Shanghai Institute of Biological Products in lyophilized form (10 mg/dl, 1.71×10^{-4} mol/l). The pH measurement is performed by a REX pHS-3C meter. The lower concentration of bilirubin solution is obtained by careful dilution with 1 mol/l HCl solution. The analysis is carried out in the dark due to light-induced oxidization.

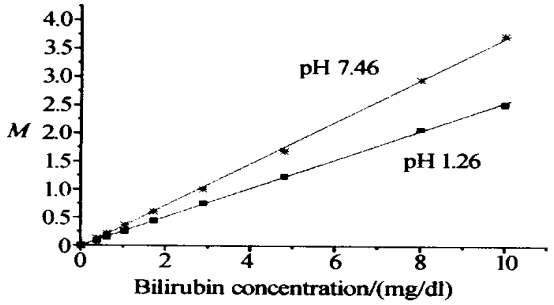

Fig. 2 Calibration curves of the fiber optic sensor in standard bilirubin solutions at pH 1.26 and 7.46 respectively

Fig. 3 shows the dynamic response of in vitro measurement of bile sample. Bilirubin concentration is determined by the Van der Berg method. As can be seen in the figure, the response increases with the concentration increment up to about 10 mg/dl and then begins to saturate gradually. The linear dynamic range is on the whole accordant to that of the standard calibration obtained above. The sensor shows good accuracy and sensitivity.

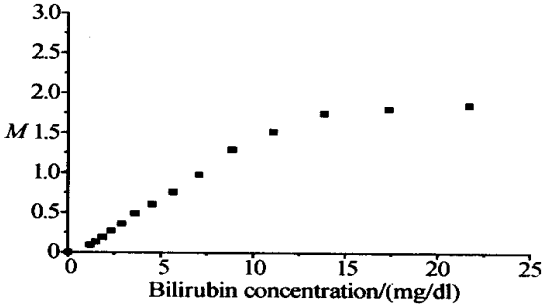

Fig. 3 In vitro analysis of bilirubin in bile sample by the fiber optic sensor

However the measurement by the sensor is still merely the approximation to the true values. The clinical analysis is involved in many factors that cannot be avoided. To evaluate the detection performance of the sensor can be significantly helpful for diagnosis of DGR and useful for physician to take measures to improve the dynamic response of the sensor.

2.1 Effect of optic source wavelength

One of the most important prerequisites to apply Lambert-Beer law (Eqs. (1)) is the monochromatic light. However the LEDs used in the sensing system are found to contain a wide spectrum. The measured absorbance by the fiber optic sensor becomes a sum of that at all wavelengths emitted from the signal and reference LEDs. Eqs. (2) is then converted into the following equation Eqs. (3)[3]

$$M = A_s - A_r = \log\left[\frac{\int I_0(\lambda)\,d\lambda}{\int I(\lambda)\,d\lambda}\right]_{\lambda_{sig}} - \log\left[\frac{\int I_0(\lambda)\,d\lambda}{\int I(\lambda)\,d\lambda}\right]_{\lambda_{ref}} \qquad (3)$$

where I_0, I are the intensities of the initial light and the light after passing through the sample solution respectively. Here we choose two wavelengths λ_1, λ_2 for further study: I_{01} is the intensity of the wavelength λ_1 corresponding to the absorption peak and I_{02} is that of stray light near wavelength of λ_1 (Fig. 4).

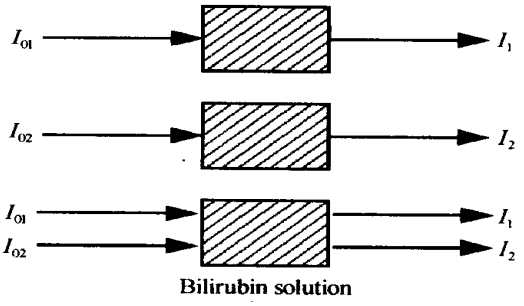

Fig. 4 Diagram showing absorption of polychromatic light through the sample solution

$$A_2 = \log\frac{I_{02}}{I_2} = \varepsilon_2 cl \quad \frac{I_{02}}{I_2} = 10^{\varepsilon_2 cl} \qquad (4)$$

$$A_1 = \log \frac{I_{01}}{I_1} = \varepsilon_1 cl \quad \frac{I_{01}}{I_1} = 10^{\varepsilon_1 cl} \tag{5}$$

$$A_3 = \log \frac{I_{01} + I_{02}}{I_1 + I_2} = \log \left[\frac{I_{01} + I_{02}}{I_{01}10^{-\varepsilon_1 cl} + I_{02}10^{-\varepsilon_2 cl}} \right] =$$

$$A_1 + \log \left[\frac{1 + I_{02}/I_{01}}{1 + (I_{02}/I_{01})10^{-(\varepsilon_2 - \varepsilon_1)cl}} \right] \tag{6}$$

A_1, A_2 are the absorbances of monochromatic light λ_1, λ_2 respectively. A_3 is the absorbance corresponding to polychromatic light including λ_1 and λ_2. I_1, I_2 are the intensities of light after passing through the sample solution. ε_1, ε_2 are the molar absorbtivity for monochromatic light λ_1, λ_2 respectively. It can be seen from Eqs. (6) that, as for $I_{02} \ll I_{01}$ or $\varepsilon_1 \approx \varepsilon_2$, A_3 is much closer to A_1 and the interference radiation almost can be neglected. Otherwise the measurement by the sensor may deviate from Lambert-Beer law. The higher the concentration of bilirubin in DGR, the higher the offset deviated from the law (Generally $\varepsilon_1 > \varepsilon_2$). Although a monochromator can be used to generate a narrower monochromatic light, it is not suitable for an ambulatory sensor with low cost for long-term monitoring. Here the optical filters with narrower bandwidth of a few nms are used to enhance its dynamic response.

2.2 pH effect

pH value of gastric juice is normally between 1-2. But as for the patients with DGR disease, pH of gastric juice mixed with duodenal contents or medications may vary in the wide pH range about 1.0～8.0. So it is necessary to study pH effect on DGR estimation when the fiber-optic sensors are applied in clinical analysis.

The dependence of absorbance on pH of bilirubin standard solution is described in Fig. 5 using the fiber optic sensor. It is obviously demonstrated that the relative error of the response signal in acidic solution (the relative error for 4.8 mg/dl increasing from 5.5% at pH 6.76 to 12.7% at pH 3.17) is much smaller than that in alkaline solution (26% at pH 7.46). The result was consistent with other reports[4,5]. The tendency with pH may be attributed to the N-B transformation of albumin conformation[6], in which a red shift of about 25 nm for the absorption peak is observed over the 1.0～8.0 pH range, and the shoulders become narrower or relative narrower as pH increases. Another possible explanation about this trend at low pH values (especially less than pH 3.5) seems to be related with conversion from bilirubin monomers to bilirubin dimmers, both of which have different absorption peaks and the molar absorbtivities, thus causing much underestimation[7].

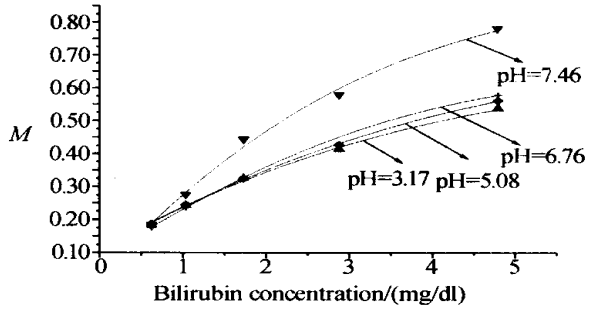

Fig. 5　Dynamic responses of the fiber optic sensor in the different pH bilirubin solutions

2.3 Scattering effect of precipitates in gastric juice

In derivation of Lambert-Beer law, light traveling through an absorbing solution is only absorbed and transmitted without consideration of scattering effect. That means that the sum of absorbance and transmission equals 1. However the gastric juice mixed with mucus and chyme is often full of small precipitates. Moreover the main form of bilirubin in DGR is (di- or mono-) glucoronide bilirubin whose pKa is more than 4.0. Then the pigment containing bilirubin in the gastric pH range may become insoluble. The beam of light penetrating the mixture with precipitates can be scattered randomly in all directions. Only some of scattered light and the transmitted light can be checked by the detector. Then the results may deviate from Lambert-Beer law and cause estimation error. The precipitates in gastric juice move randomly. The intensity of light detected by the sensor then changes irregularly. Then the sampled data fluctuate greatly in the absorbance-time graph.

2.4 Other factors

There are other factors that can affect the application of the fiber optic sensor in diagnosis of DGR. The sensor is more prone to interference from other substances due to lack of its selectivity. If the analytical sample is mixed with colorful components with an absorption peak in the visible range, then the absorbance detected by the sensor becomes the sum of all absorbers present in DGR. The sensor may give false information about DGR. So colorful food, such as apples, bananas, orange and so on is especially avoided before application.

Due to unavailability of (di- or mono-) glucoronide bilirubin, BDT (Bilirubin Ditaurate) with a pKa close to 1 is often used to set up standard curves. Although glucoronide bilirubin and BDT are found to share almost the same total bilirubin standard curves at neutral pH[8], there is no proof showing their spectrum superposition in the gastric pH range. BDT is always soluble in the pH > 1.0 while the glucoronide bilirubin becomes insoluble below 3.0. Furthermore glucoronide bilirubin is apt to oxidize to biliverdin, which has a completely different spectrum below pH 4.5[5]. This can give rise to more complexity to the spectrum of analyte in clinical analysis.

The application of the fiber optic sensor is complicated by the fact that binding to bile salts or phospholips can significantly affect the absorbance of bilirubin glucuorides or unconjugated bilirubin[5]. This factor cannot be minimized and there is no control over it.

3 Conclusion

A fiber optic sensor for clinical analysis of DGR is developed and an excellent performance is achieved with a dynamic linear range of up to 10 mg/dl. As reviewed in this paper the following factors are found to affect its application: optic wavelength, pH of gastric juice, interference from other colorful components in DGR, the feature of bile, etc.

Fortunately the fiber sensor is still applicable and helpful for clinical monitoring DGR regardless of these effects. The physicians do not in fact care too much for the accurate concentration of bilirubin in DGR. They seem to be more attentive to whether DGR happens and the relationship between DGR and gastro-oesophageal reflux diseases and their concerned complications. So the sensor is now under development and will be applied in clinical diagnosis.

References

1 Keane F B, Dimagno E P, Malagelada J R. Duodenogastric reflux in humans: Its relationship to fasting antroduodenal motility and gastric, pancreatic, and biliary secretion. *Gastroenterology*, 1981, **81**: 726～731

2 Bechi P, Falciai R, Baldini F, *et al*. A new fiber optic sensor for ambulatory entero-gastric reflux detection, In: A Katzir, (ed) Proceedings of Fiber Optic Medical and Fluorescent Sensors and Applications, 1992, Bellingham, Washington: *SPIE*, 1992, **1648**: 130～135

3 Baldini F, Bechi P, Cianchi F, *et al*. Analysis of the optical properties of bile. *Journal of Biomedical Optics*, 2000, **5**(3): 321～329

4 Champion G, Richter J E, Vaezi M F, *et al*. Duodenogastroesophageal Reflux: Relationship to pH and Importance in Barrett's Esophagus. *Gastroenterology*, 1994, **107**: 747～754

5 Kauer W K H, Burdiles P, Ireland A P, *et al*. Does Duodenal Juice Reflux Into the Esophagus of Patients With Complicated GERD? Evaluation of a Fiberoptic Sensor for Bilirubin. *American Journal of Surgery*, 1995, **169**: 98～104

6 Heirwegh K P M, Brown S B. Bilirubin (translated into Chinese by Shen Tao & Zhang Naijian). Beijing: Union Publisher of Beijing Medical University and China Xiehe Medical University, 1991. 102～107

7 Vaezi M F, Lacamera R G, Richter J E. Validation studies of Bilitec 2000: an ambulatory duodenogastric reflux monitoring system. *American Journal of Physiology*, 1994, **267**: G1050～1057

8 Guo Y B, Guan M, Du Z L, *et al*. Using Purified Conjugated Bilirubin as a Calibrator for Bilirubin Measurement. *Journal of West China Medical University*, 2002, **33**(1): 129～131

一种检测十二指肠胃返流光纤传感器的研制

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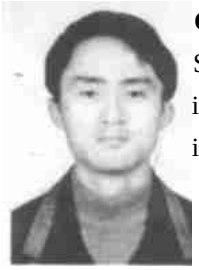
摘 要 设计了可检测十二指肠胃返流的光纤传感器,该传感器由 470 nm 的信号光、595 nm 参考光和光纤束构成,主要检测十二指肠返流物中的胆红素在 470 nm 与 595 nm 的吸光度,本文还对影响传感器检测的因素,诸如波长、pH、胃液中悬浮颗粒造成的散射作用以及其他的因素,做了详细评价. 传感器可以达到 10 mg/dl 优良的动态响应范围,离体实验结果表明,该传感器可以作为临床动态检测手段.

关键词 光纤传感器;胆红素;十二指肠胃返流(DGR)



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