POTENTIOMETRIC DETERMINATION OF SALICYLATE BY USING ZINC ALUMINIUM 4(2,4-DICHLOROPHENOXY)BUTYRATE NANOCOMPOSITE AS ION SELECTIVE ELECTRODE

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ABSTRACT

This study describes the construction and characterisation of zinc aluminium layered double hydroxides-4(2,4-dichlorophenoxy)butyrate (Zn/Al-DPBA) nanocomposite membrane electrode for determination of salicylate. The best performance of the membrane electrode was shown by having compositions Zn/Al-DPBA : PVC : 2-NPOE : NaTPB at 7 : 33 : 60 : 3 The sensitivity, selectivity, response time, working range and detection limit of the membrane sensor depends on the ionophore and the pH value of the solution. The best Nernstian slope for the membrane sensor is 58.8 ± 1.0 mV per decade in the concentration range of 1.0 x 10^{-5} to 1.0 x 10^{-1} M with a detection limit of 3.9 x 10^{-6} M. The potentiometric response is independent of the pH of the solution in the pH range 4.0 to 12.0 at temperature 25.0 ± 1.0 ºC. The proposed sensor was easy to develop, low cost, fast response time (11-35 seconds) and shows a good stability for at least 4 months without significant change in its performance characteristics. The selectivity coefficients were determined by the mixed solution method with fixed interference. Good selectivity towards salicylate ion in the presence of other ions was obtained.

PENENTUAN POTENSIOMETRIK SALISILAT DENGAN MENGGUNAKAN NANOKOMPOSIT ZINK ALUMINIUM 4(2,4-DIKLOROFENOKSI)BUTIRAT SEBAGAI ELEKTROD PEMILIH ION

ABSTRAK

Kajian ini menghuraikan pembinaan dan pencirian elektrod membrane nanokomposit lapisan berganda zink aluminium-4(2,4-diklorofenoksi)butirat (Zn/Al-DPBA) bagi penentuan salisilat. Keupayaan terbaik elektrod membran telah ditunjukkan dengan mempunyai komposisi Zn/Al-DPBA : PVC : 2-NPOE : NaTPB pada 7 : 33 : 60 : 3. Kepekaan, kepilihan, masa gerak balas, julat bekerja dan had pengesanan membran bergantung kepada ionofor dan nilai pH larutan. Kecerunan Nernstian terbaik bagi pengesan membran ialah 58.8 ± 1.0 mV per dekad dalam julat kepekatan 1.0 x 10^{-5} hingga 1.0 x 10^{-1} M dengan had pengesanan 3.9 x 10^{-6} M. Gerak balas potensiometrik tidak bergantung kepada pH larutan dalam julat pH 4.0 hingga 12.0 pada suhu 25.0 ± 1.0 ^{o}C. Pengesan yang dicadangkan mudah dibina, murah, masa gerak balas yang cepat (11- 35 saat) dan menunjukkan kestabilan yang baik sekurang-kurangnya 4 bulan tanpa perubahan yang bermakna dalam ciri-ciri keupayaannya. Pekali kepilihan telah ditentukan melalui kaedah larutan bercampur dengan menetapkan gangguan. Kepilihan yang baik terhadap ion salisilat dalam kehadiran ion-ion lain telah diperolehi.

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ASA	Acetylsalicylic acid
BA	Benzyl acetate
BBPA	Bis(1-butyl-pentyl) adipate
BEHA	Bis(2-ethylhexyl) adipate
EMF	Electromotive force
FIA	Flow injection analysis
FTIR	Fourier transform infrared
HPLC	High performance liquid chromatography
HT	Hydrotalcite
ISEs	Ion selective electrodes
IUPAC	International union of pure and applied chemistry
KTpClPB	Potassium tetrakis(4-chlorophenyl)borate
LC	Liquid chromatography
LDH	Layered double hydroxides
2-NPOE	2- nitrophenyloctyl ether
NaSal	Sodium salicylate
NaTPB	Sodium tetraphenyl borate
OA	Oleic acid
o-NPOE	o-nitrophenyloctyl ether
PVC	Poly(vinyl) chloride
RE	Reference electrode
SA	Salicylic acid
Sal^-	Salicylate ion

SIA	Sequential injection analysis
SPE	Solid phase extraction
SSM	Separated solution method
T_g	Glass transition temperature
THF	Tetrahydrofuran
TOMACl	Trioctylphenoxylpolyrthoxy ethanol
Zn/Al-DPBA	Zinc aluminium-4(2,4-dichlorophenoxyl)butyrate

CHAPTER 1

INTRODUCTION

1.1 Introduction to Salicylate

Salicylic acid (SA) is a biological substance that acts as a phytohormone and plays an important role to signal transduction in plants. It involves in the regulation of many physiological processes such as flowering, heat production, seed germination, stomatal closure, membrane permeability and ion absorption (Wang, Ai, Xu, Yang, Yu, Huang, et al., 2010). SA is also widely used in chemical and pharmaceutical industries. Thus, several derivatives have been synthesized, in particular, the esters obtained by reaction of the carboxylic group with alcohols or of the phenolic group with organic acids (Gualandi, Scavetta, Zappoli, & Tonelli, 2011).

Salicylate and its derivatives, including acetylsalicylate (Aspirin), are widely used as an analgesic and inflammatory agent. Salicylate, including acetylsalicylate (aspirin), is available to the public in a wide variety of formulation. The free acid is widely used as an antiseptic and a preservative of food. Nowadays, aspirin is widely used to treat cardiovascular complications (Ardakani, Pourhakkak, & Salavati-Niasari, 2007). Hydrolysis of this compound produces salicylic acid, which circulates blood in its ionized form. Monitoring the plasma salicylate concentration is important to control the dose and frequency of aspirin administrations.

Salicylate, acetylsalicylic acid and their derivatives have been used as fungicidal and antimicrobial agents in pharmaceuticals preparations (external use) as well as in the treatment of inflammatory processes as antipyretic and analgesic drugs (internal use). Salicylate has been used in beverages and foods for preservation, but it hasbeen forbidden since in the sixties in several countries due to its toxicity (Rainsford, 2004; Thiessen, 1992). After the aspirin ingestion, this compound hydrolyses into salicylic acid and circulates the blood in an ionized form as salicylate. When the salicylate concentration in the blood is higher than 2.2×10^{-3} mol L^{-1}(300 mg L^{-1}), it becomes toxic, requiring control and monitoring of the salicylate level in the serum. The effective therapeutic range is between 1.1 and 2.2×10^{-3} mol L^{-1}(150–300 mg L^{-1}), which is very close to the toxicity stage. Salicylate concentration values higher than 4.3×10^{-3}mol L^{-1}(600 mg L^{-1}) is regarded as lethal (Thiessen, 1992; Nietsch, 1989). Salicylate is the main aspirin metabolite in the body, reaching its maximal level in the blood serum two hour after aspirin hydrolyses. Other aspirin metabolites analogous to salicylate, such as gentisic acid (2,5-dihydroxybenzoic acid) and salicyluric acid are present in the blood, but at minor levels. Paracetamol (acetaminophen) is another compound with analgesic effects similar to the aspirin as pain relief and can be presented in plasma at relatively high concentrations (Nietsch, 1989).

1.1.1 Structure of Salicylate

Salicylic acids is a monohydroxybenzoic acid. It is an important part to produce the acetyl salicylic acid, salicyluric acid, salicylic acyl glucuronide, salicylic phenol glucuronide and gentisic acid. Figure 1.1, shows the derivative of salicylate.

1.2 Introduction to Layered Double Hydroxides (LDH)

Layered double hydroxides (LDH), also referred to as hydrotalcite like compounds (HT) or anionic clays, is an important class of ionic lamellar solids (Cavani, Trifiro, & Vaccari, 1991). Its' important applications include LDH as heat stabilizers in PVC (Ferreira, De Moraes, Duran, Cornejo, & Alvez, 2006), or as flame retardant additives in plastic (Wang, Zhang, Evans, & Duan, 2005). Furthermore, LDH can also be used as sorbents for purification of wastewater in order to remove phosphate or heavy metal such as chromate (Ferreira, De Moraes, Duran, Cornejo, & Alvez, 2006) LDH can be used as a host for the formation of LDH-intercallated or the so- called the host guest type materials. This type of material attracted intense research interest lately due

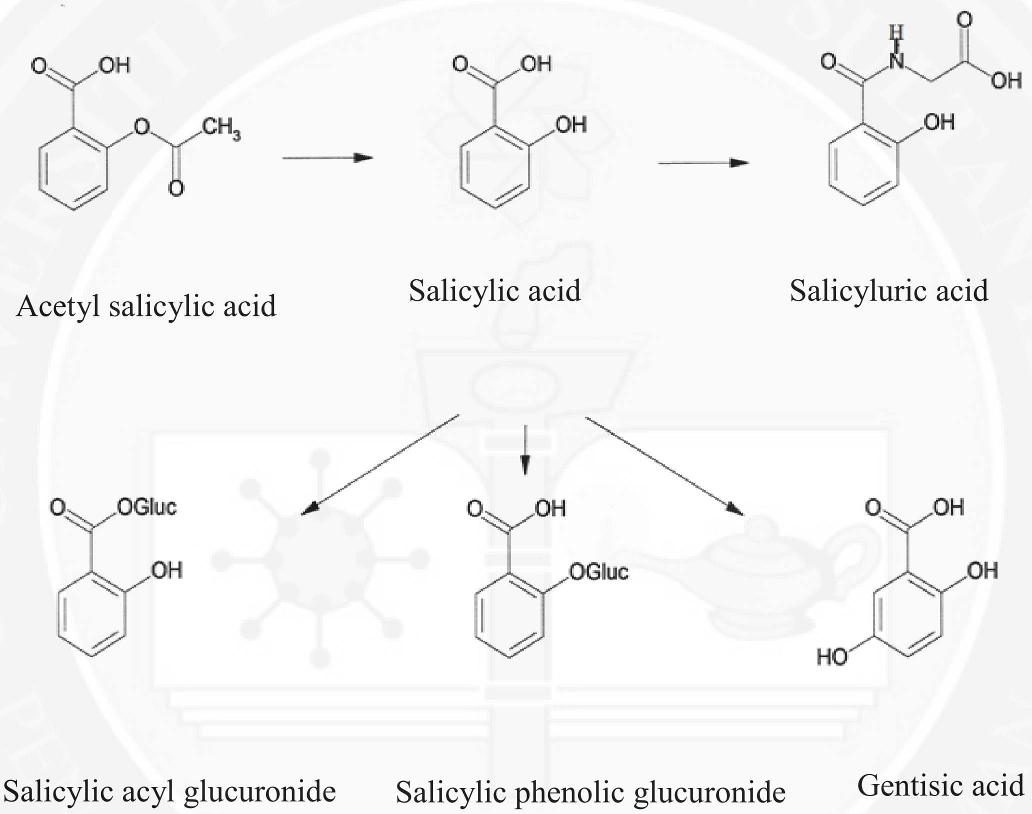

Figure 1.1. Chemical structures of acetyl salicylic acid (ASA) and its metabolites salicylic acid (SA), salicyluric acid (SU), gentisic acid (GA) and two SA glucuronides

to its versatile capability in various technological applications; pharmaceuticals (Ambrogi, Fardella, Grandolini, & Perioli, 2001), carrier for drugs (Tyner, Schiffman, & Giannelis, 2004), urea biosensor and supports (Vial, Forano, Shan, Mousty, Barbouni, Martelet et al., 2006), electrode modifiers (Wang, Zhang, Evans, & Duan, 2005) and others.

It's has received considerable attention in recent years because of the potential applications such as ion-exchangers, catalysts or catalyst supports, and antacids (Cavani, Trifiro, & Vaccari, 1991). The structure of LDH consists of positively charged mixed metal hydroxide layers separated by charge balancing anions and water molecules.

The LDHs consist of positively charged metal hydroxide sheets with anions located between the layers to compensate the positive layer charges. The compositions are generally represented as, where M^{2+} and M^{3+} are divalent and trivalent cations, respectively, x is the ratio $M^{3+}/(M^{2+} + M^{3+})$, and is an anion with a charge of n (such as NO_3^-, CO_3^{2-}, Cl^-, or SO_4^{2-}). M^{2+} and M^{3+} species represent Zn^{2+}, Ni^{2+}, Mg^{2+} or Cu^{2+} and Al^{3+}, Cr^{3+}, Fe^{3+}, or Ga^{3+} respectively. Various kinds of organic and inorganic anions have been immobilized into layers by the ion-exchange or co-precipitate method (Cavani, Trifiro, & Vaccari, 1991). In co-precipitate method, the precursors for the host as the mother liquor are mixed together with the guest species followed by the aging process to form a well ordered layered nanohydrid. Aisawa, Takahashi, Ogasawara, Umetsu, and Narita (2001) and Dupin, Martinez, Guimon, Dumitriu, and Fecther (2004) have stated the intercalation of the guest molecules into the interlayer of the host by using anion exchange method.

1.2.1 Structure and Properties of Layered Double Hydroxides

The general chemical formula of these lamellar solids can be written as $[M_{1-x}^{2+}M_x^{3+}(OH)_2](A^{n-})_{x/n}\cdot mH_2O$, where M^{2+} and M^{3+} are divalent and trivalent cations respectively, and A^{n-} is an interlayer anion. Such A^{n-} anions may be polymers, organic dyes (Orthman, Zhu, & Lu, 2003), surfactants or organic acids (You, Zhao,& Vance, 2002). The interesting properties of these materials are the result of the structural brucite-like sheets. It consists of metal cations octahedral coordinated to OH^- and interlayer region containing water and anions which compensate the positive charge of the brucite-like sheets. The synthesis of surfactant intercalated layered double hydroxides, as reported in the literature, controlled to consider this type of materials as sorbent for organic solutes and particularly the negatively charged species. The organophilic nature of surfactant in the LDH interlayer would permit the sorption of many types of organic molecules (Akçay & Yurdakoc, 2000). Water molecules also exist in the interlayer space.

Hydrotalcite like clays (HT) is promising because spatial constraints and surface chemical effects induced by these materials can lead to new patterns of reactivity and selectivity. The function of the new electrode that constructed from hydrotalcite is to attract ion species. The heterogeneous electron transfers kinetics and to the mass transport which takes place to compensate the excess of negative or positive charge, generated during the electron transfer through a hydrotalcite clay film (Therias & Mousty, 1995; Yao, Taniguchi, Nakata, Shimazu, Takahashi, & Yamagishi, 1998; Therias, Lacroix, Schollhorn, Mousty, & Palvadeau, 1998). Figure 1.2 shows the structure of LDH.

1.3 Significance of Study

Medication is essential life and health to people of the world. Therefore, this study is conducted to investigate the salicylate in pharmaceutical samples using potentiometric ion selective electrode based on (ISE). Potentiometric method is a simple method to determine salicylate. Therefore in this study, this method is chosen to determine the salicylate because it offers great advantages such as fast response, low cost, selectivity and sensitivity compared to other methods (Ganjali, Norouzi, Rezapour, Faridbod, & Pourjavid, 2006). The use of the direct potentiometric promises a good measure for performance compared to other methods (Bakker, Buhlmann, & Pretsch, 1997).

The aim of this study is to produce membrane sensor with zinc aluminium layered double hydroxide-4-(2,4-dichlorophenoxy)butyrate nanocomposite as a salicylate ion selective electrode in pharmaceutical sample.

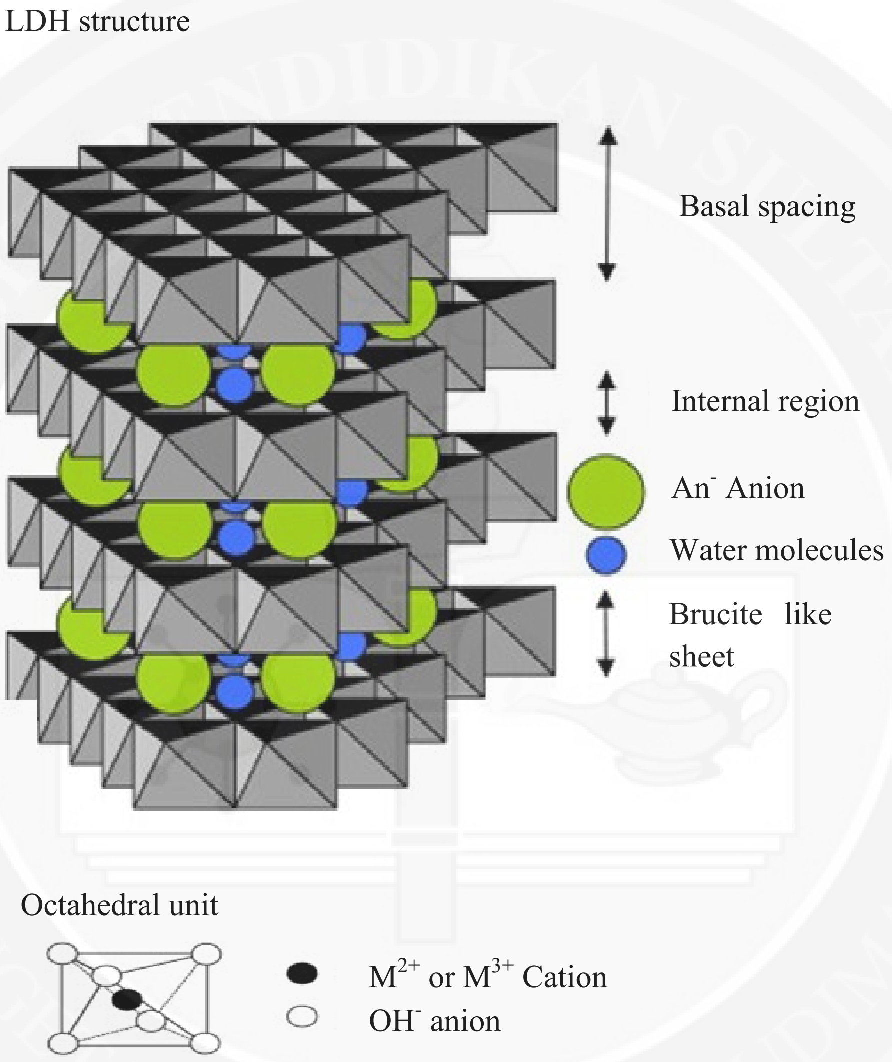

Figure 1.2. Structure of layered double hydroxides (LDHs)

1.4 Electrochemical Sensors

After the 1980s, miniaturized electrochemical sensor became available for detection of many different toxic gases, with the sensor exhibiting good sensitivity and selectivity. In fact, the appearance of the electrochemical sensor used to detect various gases may be similar, but their functions are markedly different. Consequently, one can expect varying performance from each of these sensors, in term of sensitivity, selectivity, response time and operating life.

Electrochemical sensors continue to be a mainstay of analytical chemistry as demands for increasingly selective and sensitive detection methods grow. In contrast to spectroscopy and chromatography, electrochemical sensors are inexpensive, simple, and adaptable to demanding environments where robust, miniaturized analytical method is required. This is obvious especially in the field of potentiometric sensor where recent research has focused on enhancing the ability of ion selective electrodes to operate effectively in both high concentration of background analytes (Ardakani, Jalayer, Safari, Sadeghi, & Zare, 2005).

Electrochemical approaches are widely used in the development of microbial biosensors. According to the detection principle, electrochemical techniques can be divided into amperometry (measure current), potentiometry (measure voltan), conductometry (measure conductivity), voltammetry, and microbial fuel cell (MFC). Potentiometry involves the measurement of the potential difference between the working electrode, the reference electrode and the potential signal exhibits concentration dependent behavior. The transducer employed in the potentiometric technique is usually a gas-sensing electrode or anion-selective electrode (Bobacka, Lindfors, Lewenstam, & Ivaska, 2004).

Moreover, electrochemistry is most suitable for investigating the redox properties of drugs that can give insight into its metabolic fate. The data obtained from electrochemical techniques are often correlated with molecular structures and pharmacological activities of drugs (Sattarahmady, Heli, & Faramarzi, 2010).

Electrochemical process is a change of electric energy from the electrode phase to the other phase in solid and liquid. Electricity in a chemical process produces chemical on the electrode to the sample phase. Electrode reaction processes the movement of the electrical energy, which provides the basis for the detection. There are general rules that should be used in all electrochemical sensors in which the system requires a closed electric circuit. Thus, at least two electrodes electrochemical are needed to complement tools.

Besides, the general aspects of electrochemical sensors are the transition between the electric energy detector, or a detector, and support equipment, where the entire system involves electronic circuits. In other words, the movement of electricity in the sample may consist of electronic, ionic or combination of the two.

1.5 Introduction to Potentiometric Method

Potentiometric is one of the measurements used for measuring ion in the chemistry. It monitors potential values under zero current flow, to determine the analytical concentration desired component in an analyte. In this method, the potential difference between an indicator electrode (i.e. ion-selective electrode, redox electrode, metal-metal oxide electrode) and the reference electrode is measured as the analytical potential. The potential of the electrochemical cell is due to the changes in free energy that occurs if the chemical phenomena reach an equilibrium, in which case, the difference between the cathodic and the anodic potentials is the potential of the electrochemical cell and is calculated using the so-called Nernst equation.

Another source of the potential may be physical phenomena which does not involve explicit redox reactions but having non-zero free energy initial condition. For example of such phenomena is ion concentration gradient across a semi-permeable membrane. This phenomenon is the basis of measurements that uses ion-selective electrodes. According to which the below equation is used to determine the concentration of the analyte.

$$E_{mem} = E° - \frac{RT}{nF} \ln a_i \qquad \text{.....................................} \; 1.1$$

Where E_{mem} represent are potential across membrane, E° is a standard potential, R is gas constant, T is temperature, n is number of electron transfer, F is Faraday constant and a_i is the activity of ion interest respectively.