CHAPTER 1

INTRODUCTION

1.1 Flow Injection Analysis (FIA)

The ever-increasing demand for analyses in clinical, agricultural, pharmaceutical, industrial and other types of analytical control has led to the development of a large number of different instruments for automatic analysis. The additional advantages of automation, such as increased precision, decreased cost of individual assay, and the satisfactory reliability of automated equipment have further stimulated developments in this field. The first air-segmented continuous flow analyzer was developed by Skeggs in 1957 to overcome the sample throughput problem. This type of analyzer has been commercially refined by Technicon and is marketed under the trade name AutoAnalyzer [1-3].

In the early 1970s, it was demonstrated that air segmentation in continuous-flow analysis was not essential and that a sample can be injected into a flowing stream. Perhaps the first use of an unsegmented stream as a medium in which to perform analyses appeared in 1970 when Nagy, Feher, and Pungor described a system in which samples were injected into a flowing stream and were carried through a magnetically stirred chamber and thence to a flow-through voltammetric cell. In 1975, Stewart, Beecher and Hare in the United States and Ruzicka and Hunsen in Denmark simultaneously modified this technique by dispensing with the mixing chamber and using flow-induced sample dispersion to provide contact between analyte and reagent. This technique of unsegmented continuous-flow analysis has become known as Flow Injection Analysis (FIA). The high sample throughput resulting from the elimination of the air bubble makes FIA a reliable and cost effective approach for automation of analytical methods [2-4].

1.1.1 Principle and Theory

The basis components for FIA are illustrated in Figure 1.1.

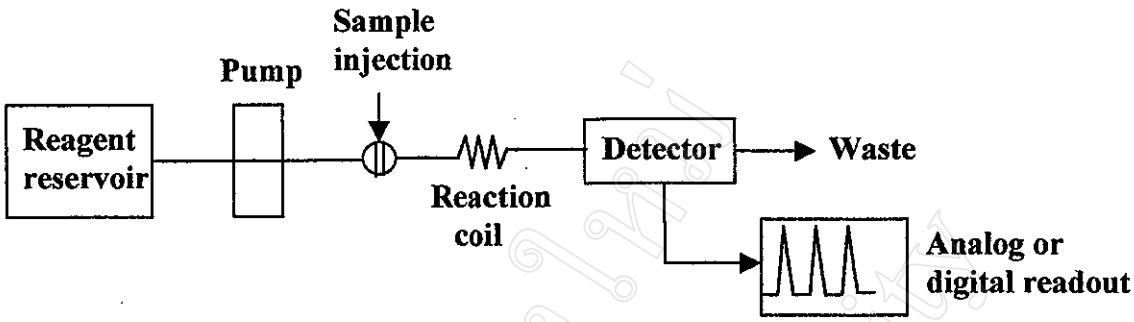


Figure 1.1 Basis components for FIA [4]

A few microliters of sample is injected as a plug into a flowing reagent stream via a syringe or valve, and after that, it passes through a reaction coil and a detector where a transient peak signal is recorded in proportion to the analyte concentration [4].

Immediately after injection with a sampling valve, the sample zone in a flow injection apparatus has the rectangular concentration profile shown in Figure 1.2 (a). As it moves through the tubing, band broadening or **dispersion** takes place. The shape of the resulting zone is determined by two phenomena. The first is convection arising from laminar flow in which the center of the fluid moves more rapidly than the liquid adjacent to the walls thus creating the parabolic-shaped front and the skewed zone profile shown in Figure 1.2 (b). Broadening also occurs as a consequence of diffusion. Two components of diffusion can, in principle, occur – radial or perpendicular to the flow direction and longitudinal or parallel to the flow. It has been shown that the latter is of no significance in narrow tubing, whereas radial is always important under this circumstance. In fact, at low flow-rates it may be the major source of dispersion. When such conditions exist, the Gaussian-shaped distribution shown in Figure 1.2 (d) is approached. In fact, flow injection analyses are usually performed under conditions in which dispersion by both convection and radial diffusion occurs; peaks like that in Figure 1.2 (c) are then obtained [3,5].

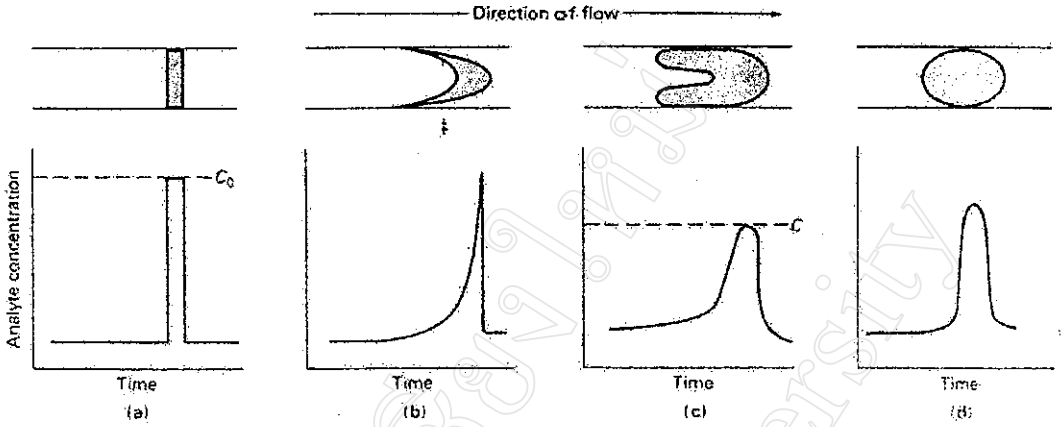


Figure 1.2 Effects of convection and diffusion on concentration profiles of analytes at the detector [3]:
(a) no dispersion;
(b) dispersion by convection;
(c) dispersion by convection and radial diffusion;
(d) dispersion by diffusion

Dispersion between sample and reagent or diluent in FIA is reproducible and controllable. Under such conditions, neither physical nor chemical equilibration is required for achieving reproducible readout at any preselected residence time [6].

The dispersion coefficient D, proposed by Ruzicka and Hansen, is used most often for such evaluation, and is simply the ratio of the concentration of the constituent of interest in a fluid element of the injected zone before and after the dispersion had taken place [6,7]. By denoting C^o as the original concentration of the injected sample solution and C^{max} as the concentration in the element of fluid corresponding to the peak maximum, the dispersion is related to the peak height H by:

$$D = C^o / C^{max} = \text{const.}\ (H^o / H)$$

where const. is a conversion factor between instrument readout and concentration obtained by calibration [8].

The actual experiment to measure D is as follows. A dye such as bromothymol blue is pumped through the entire FIA manifold, i.e., both the carrier and the reagent lines. The signal is evaluated and the

concentration, C^o, which is representative of the pure, undiluted dye solution, is measured. Then, the dye is replaced with a carrier solution, which is pumped through the system. With bromothymol blue, borax is used in order to maintain the proper pH. Finally, the bromothymol blue solution is injected into the manifold. The observed signal is recorded and C^{max} is calculated. The dispersion coefficient can then be calculated [2].

The FIA experimental parameters or factors that may influence dispersion include: sample volume, carrier flow-rate, flow-rate ratio between sample carrier and merging reagent, geometrical dimensions and configurations of manifold components, viscosity of the fluids and temperature [6]. The effects may be summarized as a collection of 'rules' concerning dispersion coefficient [9]. These are:

(a) D increases with increasing tube length
(b) D increases with increasing tube diameter
(c) D increases with increasing average flow-rate (this is a rather gross generalization as there are many reaction zones in use for which D is largely independent of the average flow-rate and there are situations in which D increases as the average flow-rate decreases)
(d) D increases with increasing detector volume
(e) D increases with increasing molecular diffusion coefficient (the effect is only observed for large differences in this parameter)
(f) D decreases with increasing volume injected (this is the single most powerful method of changing D)
(g) D decreases with the use of packed beds and bead strings
(h) D decreases with increasing tortuosity of tubing (e.g. tight coiling)
(i) D decreases with increasing temperature (again this is a rather gross simplification as the effect observed depends on the variation in diffusion coefficient and viscosity with temperature)

The dispersion coefficient is useful in that it allows comparisons of different manifolds. Further, it provides a means of verifying and monitoring the extent of sample dilution resulting from any changes made to the manifold during method development [2].

1.1.2 Basic Components

A flow injection analyzer consists of four major components. A propelling system to transport the carrier stream to the detector. An injection system to introduce the liquid sample into the carrier stream. A reaction zone to introduce reactants and achieve the appropriate mixing in the moving stream, and finally a detector to continuously monitor the following stream.

(a) Propelling systems

The liquid delivery or propulsion device is a critical component in all FIA systems. FIA is a technique based on highly reproducible timing, - a feature that demands pulseless and reproducible flow-rates in liquid delivery. FIA systems are in essence low-pressure systems, with seldom more than a few bars pressure developed in the conduits. There are three types of liquid delivery devices that are usually utilized: pressurized bottle (including constant head), peristaltic pump, and syringe pump. By far the peristaltic pump has gained the largest popularity and acceptance. If pressures larger than 10 psi are desired and HPLC pump can be used [2,6]. Aquarium air pumps in either pressure- or suction-mode have been applied to FIA as low-cost solution-propelling device [10].

(b) Injection systems

The injection system is a necessary requirement to insert a defined and reproducible volume of the sample into the carrier stream. The first injection system for FIA is a needleless syringe [1]. Rotary valve injectors and syringe injectors are commonly used. Insertion of a sample can also be accomplished through interaction of two or more pumps (hydrodynamic injection) [2]. A home-made low-cost rotary valve with two sample loops has also been reported to use as the injection system [10].

(c) Reaction zone

The reaction zone composes of tubings, connectors and mixing reactors. PTFE tubings of 0.35-1.0 mm i.d. are used most often for such purposes. Connection tubes may be connected to the different components or prolonged either by push-fitting using different diameter

tubings or by means of threaded fitting connectors [6]. Coiled tubings, mixing chambers and glass bead columns are utilized as mixing reactor.

(d) Detectors

Any detection systems, which could be adapted for flow-through detection, may be used as detectors for FIA. FIA systems so far reported include optical (spectrophotometric, fluorimetric, chemiluminescent, refractometric and atomic absorption and emission spectrometric), electrochemical (amperometric, potentiometric, coulometric and conductiometric), enthalpimetric and radiometric detection [8,11]. A few of the other notable FIA detector combinations are FIA-Fourier Transform Infrared (FIA-FTIR), FIA-Raman and FIA-Mass Spectrometry (FIA-MS) [2].

FIA monitors the response by the detection/measurement system to the changing concentration of a determinant or its chemical derivative with time. Information is therefore available as a continuum of data points, which can be:

(a) displayed as an analogue signal on a potentiometric recorder from which manual calculations can be made.
(b) fed into a microprocessor or computer system programmed to provide individual sample results in the required format.

Common practice is to compare the responses from samples with those obtained from a series of standards, which have been analyzed in the same way under identical conditions and from which an appropriate calibration can be obtained [9]. FIA peak has complex shape, the concentration of analyte can be derived in peak height, peak area and peak width.

1.1.3 Liquid-Liquid Extraction

Liquid-liquid extraction is one of the most versatile techniques for separation and concentration in the analytical laboratory. Despite its indisputable effectiveness in the removal of interfering matrices and the preconcentration of the trace analytes, its popularity has been somewhat impaired under batch operation conditions due to the tediousness of the operation. The main drawback with extraction procedures has been that they involve several consecutive steps often requiring transfers between vessels. Thus these procedures are generally rather laborious and time-consuming when done manually; transfer of solutions between vessels

may also cause contamination problems. A further nuisance created by batch extractions is the often-annoying odor and toxicity of organic solvent vapours released into the laboratory atmosphere. Other undesirable consequences in a manual extraction have been that organic solvents are expensive and there are disposal problems [6,12,13]. In order to circumvent these drawbacks, various mechanized or automatic extraction systems have been designed. Among the more successful of these are based on FIA systems.

The first reported on implementing liquid-liquid extraction with FIA systems was made by Karlberg and Thelander [14], and Bergamin et al. [15] in 1978, proved to be a powerful tool in automated analysis [6,16]. The aim to attempt to apply the flow injection principle to extraction procedures is to achieve better economy of extraction methods with respect to time and solvent consumption [14]. FI liquid-liquid extraction systems are readily automated, while the closed extraction system greatly minimizes contamination risks as well as release of solvent vapours. A further advantage of FI liquid-liquid extraction is that much higher phase transfer factors can be achieved. This may be important for achieving higher sensitivities, lower sample consumptions or/and better precisions [6].

1.1.3.1 Principle

The principle for liquid-liquid extraction based on flow injection is shown in Figure 1.3.

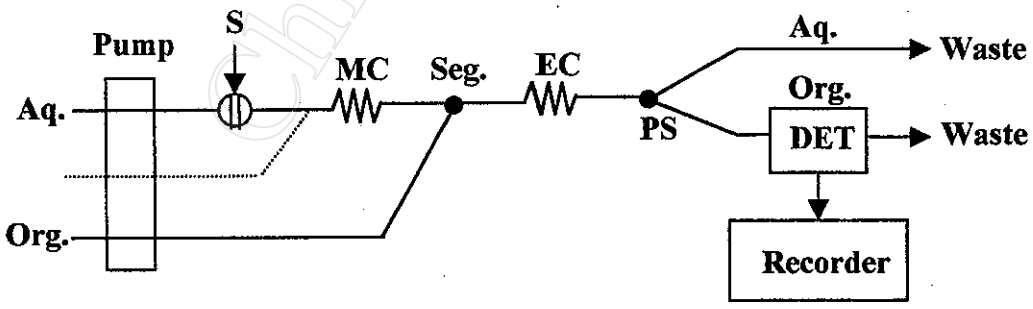


Figure 1.3 Principle for liquid-liquid extraction based on flow injection.
Aq. = aqueous phase, Org. = organic phase, S = sample,
MC = mixing coil, Seg. = segmentor, EC = extraction coil,
PS = phase separator, DET = detector
Broken line denotes addition of an optional reagent to the aqueous phase [2].

A defined volume of the sample is injected into a carrier (or reagent) stream, which is segmented with an immiscible solvent. Extraction takes place in a narrow-bore PTFE tube (i.d. typically 0.5 mm). The organic phase, now containing the extracted analyte, is separated from the aqueous phase and transported to the flow through detector [2]. The separated extracts containing the analyte are presented to the detector through different modes of delivery, depending on specific features of the detection systems. The modes may be categorized as:

(a) on-line direct delivery
(b) on-line collection-delivery
(c) off-line collection-delivery

The different modes are shown schematically in Figure 1.4 (a), (b), (c) respectively.

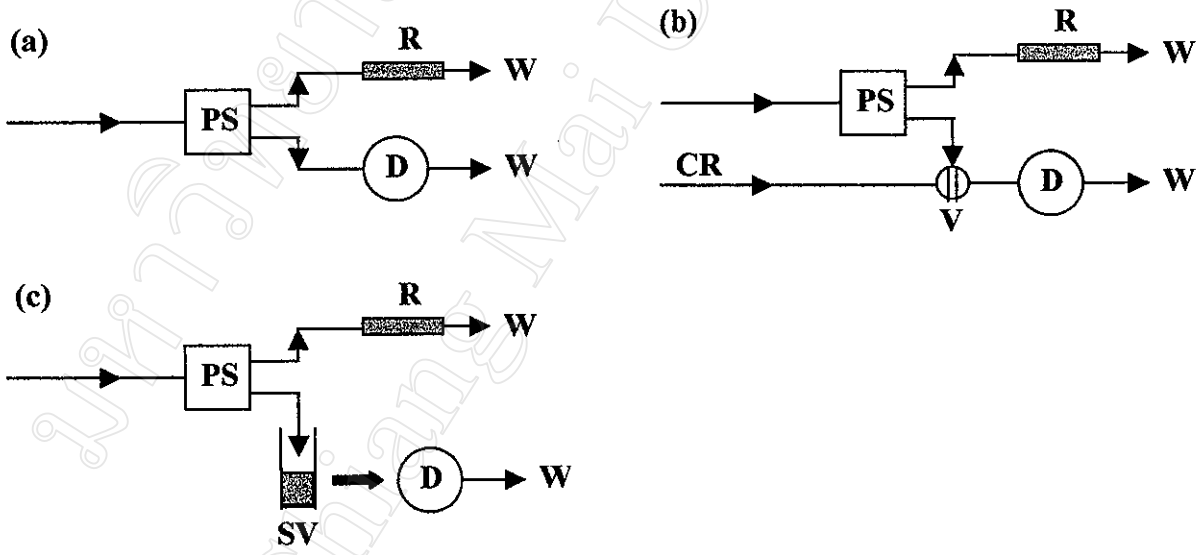


Figure 1.4 Schematic presentation of the modes of delivery of separated phase to the detector [6].
(a) on-line direct delivery
(b) on-line collection-delivery
(c) off-line collection-delivery
PS = phase separator, R = restrictor or impedance coil,
D = detector, W = waste, CR = gas or liquid carrier,
V = extract collection valve, SV = extract collection vial

Mode (a), which is characterized by continuous delivery of the separated phase to the detector immediately following separation, is used mainly for spectrophotometric, fluorimetric and chemiluminescence detectors. Mode (b) is used mainly for flame atomic absorption (AA) and inductively couple plasma (ICP) spectrometric systems, which require specific sample uptake rates for achieving optimum sensitivities. The exit flow-rates of the separated phase are normally too low to meet the demands of the detector. For this reason a supplementary interface, composed of an additional sampling valve, is used to collect a defined volume of the separated phase (concentrate) under the low flow-rates optimized for the extraction and separation. The collected concentrate is then injected into a carrier and delivered to the detector at the required flow-rates for obtaining optimum detection signals. Mode (c) is reserved for detection systems such as electrothermal AAS, which by nature are not suitable for continuous operations. The liquid-liquid separations are therefore completed off-line as a sample work-up procedure. The concentrates or extracts are collected and stored in small vessels before presenting to the detector. Therefore the extraction system can be physically separated from the detection system [6].

1.1.3.2 Theoretical Aspects

(a) Mechanism of phase transfer

The transfer of analyte from one phase to another in liquid-liquid extraction is achieved at the interface between the two immiscible phases. In most cases phase transfer factors of 0.8-0.99 can be achieved in extraction coils usually in no more than a minute. This high extraction efficiency cannot be fully explained by merely considering the mass transfer at the interface on the two ends of the segments, the area of which is indeed very limited. This induced further investigations into the mechanism of phase transfer in FI liquid-liquid extraction systems. With the aid of an ingenious photographic technique, Nord and Karlberg [17] were able to provide evidence on the formation of a thin film of 0.01-0.05 mm thick on the extraction coil tube walls by the phase which wetted the tube material. In most applications the analyte is extracted from the aqueous phase into an organic phase in order to increase the organic phase interfacial area relative to its volume, PTFE tubes wettable by the solvent are used so that organic solvent films are formed on the tube walls (Figure 1.5). Since the organic phase forms a film on the PTFE tube wall, all aqueous segments will be surrounded by organic phase. The

analyte species present in an aqueous segment may then enter either into the film region or directly into the bulk region of the organic phase. The film largely increases the phase transfer area, particularly in relatively narrow tubes, and is responsible for the high efficiency in phase transfer [2,6].

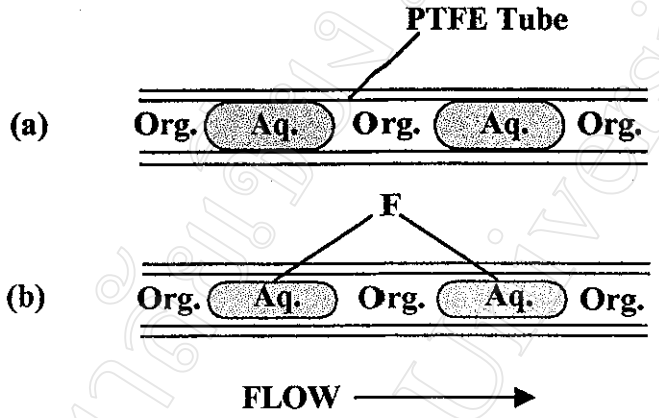


Figure 1.5 Schematic diagram showing film formation in a liquid-liquid extraction coil tubing [6].
(a) static conditions; (b) flow conditions
Aq. = aqueous phase; Org. = organic phase; F = organic film

There is no evidence that the film thickness contributes significantly to the phase transfer efficiency, however, thicker films may induce the break-up of small segments of the film forming phase to form larger segments during the extraction and cause the development of irregular segmentation. Thick films can also enhance analyte dispersion. The film thickness increases with an increase in flow-rate [6,17].

(b) Dispersion

In FI liquid-liquid extraction systems analyte dispersion may occur in four stages of operation:

(1) dispersion before phase segmentation
(2) dispersion during extraction
(3) dispersion in the phase separator
(4) dispersion after phase separation, during transport to the detector, and in the detector

In principle, analyte dispersion before segmentation and after phase separation (i.e. stages 1 and 4) may be controlled as in normal FIA since the flowing stream is composed of a single phase. When high sensitivities are required, the dispersion should be minimized by injecting sufficiently large sample volumes, using short, thin conduits or knotted reactors for transportation to the segmentor and detector. The merging of reagents into the sample before segmentation should also be carefully designed to minimize dilution effects [6].

In order to achieve high phase transfer factors, the extracion coil lengths are usually substantially longer than normal FIA reaction coils. This feature would have been a principle source of analyte dispersion in the extraction system; however, the phase segmentation hinders the mass transport between segments of the same phase, making dispersion effects less serious. On the other hand, the film formation on the extraction tube walls which is responsible for the high extraction efficiencies also provides a "bridge" in between neighbouring segments of the tube-wetting phase. This instigates mass transfer from the leading segments backward to the succeeding segments, causing dispersion of the analyte. This dispersion will lower the peak height registered by the detector. If the analytical evaluation is based on peak height the result will be interpreted as a loss in sensitivity [2,6,17,18].

The phase separator may be an important source of dispersion if the dead volume of the separator is not carefully minimized. An important benefit of membrane phase separators is that the associated chambers or cavities, particularly for outflow of the "clean" separated phase, can be made extremely small [6].

1.1.3.3 Instrumentation

(a) Phase segmentors

The phase segmentors are utilized in FI liquid-liquid extraction systems where the immiscible organic and aqueous inflows are brought into contact with regular alternate segments in a defined ratio and delivered through a single outlet channel. The merging-tube segmentors with a T-design, modified from Technicon A-4 connectors, were the first to be used for phase segmentation [14]. Later, various designs of merging segmentors have been reported. After a comparison of different designs, including the T, Y and W configurations for the merging tubes Kawase

[19] found no significant differences in the segmentation patterns. Swedish workers [20,21] have introduced phase segmentors with a coaxial design. Such coaxial segmentors are based on droplet formation of one phase in another, and are reported to produce more reproducible and controllable segmentation than the merging-tube designs. Kuban and Ingman [22] reported a dual channel dropping segmentor which allows the simultaneous mixing of aqueous solutions of sample and reagent and segmentation of the resulting homogeneous mixture by an immiscible organic solvent, also based on the principle of the coaxial segmentor [6].

(b) Extraction coils

The extraction coils in which phase transfer of the analyte occurs in the segmented stream are usually helically coiled PTFE tubing with 0.5-1.0 mm i.d.. Such coils are suitable for transfer of analyte from an aqueous sample into an organic solvent, but tubings of glass or other hydrophilic materials are required for reversed transfers [6].

(c) Phase separators

The phase separators are applied to continuously separate the segmented stream into two parts, with the one composed of a single phase used for determination. The phase separator is usually the most important component, which determines the performance of FI liquid-liquid extraction system. It is expected to function efficiently, and to achieve good separation of the two phases in the smallest feasible dead volume in order to reduce the dispersion. Phase separators may be classified according to the different mechanisms of phase separation [6]. The earlier separator designs were all based on differences in densities of the immiscible phases. These are designated here as gravitational phase separators [14,23]. An obvious advantage of gravitational phase separators is their simple construction, the separator often being transformed from standard T-connectors for flow analysis with little additional effort. However, when using such designs considerable care and experience are required to avoid contamination of the flow-cell with aqueous phase particularly at the beginning of the operation. It is also difficult to separate a segmented stream composed of two phases with similar densities or more complicated extraction systems such as water-methanol-chloroform using these separators [24]. Later, separator designs were introduced which were based on different affinities of the immiscible phases to a separation membrane, hence the name, membrane

phase separators [25,26]. The latter come closer to the requirements of an ideal phase separator, and are used almost exclusively nowadays under a variety of different designs, including sandwich-type and tubular membrane phase separators [12,24,25,27-29]. Column phase separator for liquid-liquid extraction, which is in the form of a packed column, has been also reported by Toei [30].

1.2 Anionic Surfactants

Surfactants embrace "any compound that affects (usually reduces) surface tension when dissolved in water or water solutions, or which similarly affects interfacial tension between two liquids. Soap is such a material, but the term is most frequently applied to organic derivatives such as sodium salts of high molecular weight alkyl sulfates or sulfonates [31]." Surfactants constitute the most important group of detergent components, and they are present in all types of detergents. The surfactants of both soap and synthetic detergents perform the primary cleaning and sudsing of the washing action in the same way through the reduction of surface tension. The cleaning process consists of (1) thoroughly wetting the dirt and the surface of the article being washed with the soap or detergent solution, (2) removing the dirt from the surface, and (3) maintaining the dirt in a stable solution or suspension (detergentcy). In wash water, soaps or detergents increase the wetting ability of the water so that it can more easily penetrate the fabrics and reach the soil. Then soil removal begins. Each molecule of the cleaning solution may be considered a long chain. One end of the chain is hydrophilic (water-loving); the other is hydrophobic (water-hating, or soil-loving). The soil-loving ends of some of these molecules are attracted to a soil particle and surround it. At the same time the water-loving ends pull the molecules and the soil particles away from the fabric and into the wash water. This is the action which, when combined with the mechanical agitation of the washing machine, enables a soap or detergent to remove soil, suspend it, and keep it from redepositing on clothes [31,32].

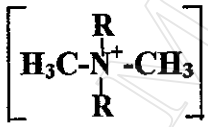
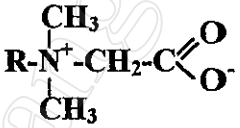
In most cases the hydrophobic portion is a hydrocarbon containing 8 to 18 carbon atoms in a straight or slightly branched chain. In certain cases, a benzene ring may replace some of the carbon atoms in the chain, for example, $C_{12}H_{25}$-, $C_9H_{19}.C_6H_4$-. The hydrophilic functional group may vary widely and may be anionic, e.g., $-OSO_4^-$ or SO_3^{2-}; cationic, e.g., $-N(CH_3)_3^+$ or $C_5H_5N^+$; or nonionic, e.g., $-(OCH_2CH_2)_nOH$ [31]. A

surfactant can be placed in one of four classes, depending on what charge is present in the chain-carrying portion of the molecule after dissociation in aqueous solution [32]:

(a) anionic surfactants
(b) nonionic surfactants
(c) cationic surfactants
(d) amphoteric surfactants

Table 1.1 provides an overview of these classes.

Table 1.1 Surfactants of various ionic nature [32]

Surfactant	Formula	Electrolytic dissociation	Ionic nature
Alkyl poly(ethylene glycol)ethers	**$RO\text{-}(CH_2\text{-}CH_2\text{-}O)_nH$**	**no**	**nonionic**
Alkylsulfonates	**$R\text{-}SO_3^-$**	**yes**	**anionic**
Dialkyldimethyl-ammonium chlorides		**yes**	**cationic**
Betaines			**amphoteric**

1.2.1 Uses

Anionic surfactants are the most common agents in detergents designed for laundry, dishwashing and general cleansing. Various types of anionic surfactants, that are either already widely in use or have favorable characteristics, are illustrated in Table 1.2.

Table 1.2 Key anionic surfactants [32]

Structure		Chemical name	Acronym
$R\text{-}CH_2\text{-}C(=O)\text{-}ONa$	$R = C_{10\text{-}16}$	soaps	
$R\text{-}C_6H_4\text{-}SO_3Na$	$R = C_{10\text{-}13}$	alkylbenzenesulfonates	LAS
$R^1\text{-}CH(SO_3Na)\text{-}R^2$	$R^1+R^2 = C_{11\text{-}17}$	alkanesulfonates	SAS
$H_3C\text{-}(CH_2)_m\text{-}CH{=}CH\text{-}(CH_2)_n\text{-}SO_3Na$ + $R\text{-}CH_2\text{-}CH(OH)\text{-}(CH_2)_x\text{-}SO_3Na$	n + m = 9-15 n = 0,1,2,... m = 1,2,3,... x = 1,2,3 $R = C_{7\text{-}13}$	α-olefinsulfonates	AOS
$R\text{-}CH(SO_3Na)\text{-}C(=O)\text{-}OCH_3$	$R = C_{14\text{-}16}$	α-sulfo fatty acid methyl esters	SES
$R\text{-}CH_2\text{-}O\text{-}SO_3Na$	$R = C_{11\text{-}17}$	fatty alcohol sulfates, alkyl sulfates	FAS
$R^2\text{-}CH(R^1)\text{-}CH_2\text{-}O\text{-}(CH_2\text{-}CH_2\text{-}O)_n\text{-}SO_3Na$	a) $R^1 = H$, $R^2 = C_{10\text{-}12}$ b) $R^1+R^2 = C_{11\text{-}13}$ $R^1 = H, C_1, C_2, \ldots$ n = 1 - 4	alkyl ether sulfates a) fatty alcohol ether sulfates b) oxo alcohol ether sulfates	FES

From ancient times onward soaps have been used as surfactants in washing and personal hygiene. Starting in 1946 with the introduction of tetrapropylenebenzene sulfonate (TPS) as a synthetic anionic surfactant in the United States, these synthetic surfactants rapidly displaced soaps as the main ingredient in detergents owing to their excellent performance and their low cost. In contrast to soap, however, which is easily biodegraded, TPS was rather resistant to biodegradation. As a consequence, concentrations of TPS in the environment increased in parallel to increasing consumption of detergents. Finally, a point was reached at which, during the drought years 1959 and 1960, visible foams were formed on major rivers in different parts of the world, making the problem of rising surfactant concentrations evident to the general public.

In reaction, detergent laws were passed in most industrialized countries requiring detergents to be biodegradable. As a consequence, TPS was phased out before 1965 in many industrialized countries and substituted by linear alkylbenzene sulfonates (LAS) as the main biodegradable anionic surfactant [33].

1.2.2 Toxicity [32]

Proteins form adsorption complexes with anionic surfactants. Complex formation is often a consequence of polar interactions between the hydrophilic residue of a surfactant and charged sites on the protein molecule, but hydrophobic interactions can also play a role. Such complex formation results in protein denaturation, which in the case of an enzyme implies a reduction or even total loss of catalytic activity, corresponding to a change in metabolic function.

The ability of surface active agents to emulsify lipids means that repeated or prolonged exposure to surfactant-containing solutions can cause damage to the lipid film layer that covers the skin surface. As a consequence, the barrier function of the lipids is impaired, leading to increased permeability and loss of moisture. This is evidenced by dryness, roughness, and flaking of the skin. Very prolonged exposure to concentrated surfactant solutions can lead to serious damage and even necrosis. Skin tolerance varies widely among the compounds making up each class of surfactants. Nevertheless, one can generalize that tolerance to surfactants tends to increase in the order cationic, anionic, nonionic materials.

The eye is much more sensitive than skin to damage by small amounts of surfactants. Anionic surfactant solutions with a concentration above ca. 1% can produce minor eye irritation, although this is normally reversible. Serious damage is likely only if the eye comes in direct contact with a concentrated surfactant solution and if immediate and intensive flushing with water does not follow this contact.

The harmful effects of anionic surfactants on aquatic organisms are well known. In addition to their foaming properties, caused by their accumulation on the water surface, they impede the mass transfer of oxygen, which reduces the autocleaning power of water. Further, anionic surfactants can inhibit the growth of microalgae by interfering with their

metabolism. Anionic surfactants comprise about 70% of all manufactured surfactants, so they are often the subject of environmental monitoring.

1.2.3 Analytical Methods

Various techniques such as spectrophotometry, electrochemical methods and chromatography have been proposed for the determination of anionic surfactants. Some examples in brief detail are given as follows:

(a) Spectrophotometry

Spectrophotometric methods are widely used for anionic surfactants and involve the formation of a solvent-extractable compound between the anionic surfactant and an intensely coloured species of the cationic charge. Among the methods used for the determination of anionic surfactants in water, the Methylene Blue (MB) ion-pair extraction method is the most common. In this method the Methylene Blue cation forms an ion association compound with an anionic surfactant which is extracted into chloroform and measurement of the blue colour in the chloroform is made spectrophotometrically at 652 nm [34]. A modified method for Methylene Blue active substances (MBAS) has been developed [35]. The use of the cobalt complex cation of 2-(2-pyridylazo)-5-diethylaminophenol as the cationic reagent and extract anionic surfactants into benzene has been also reported [36]. A spectrophotometric determination of anionic surfactants in seawater based on ion-pair extraction with bis[2-(5-trifluoromethyl-2-pyridylazo)-5-diethylaminophenolato]cobalt(III) as counter ion has been developed [37].

A simple method for spectrophotometric determination of an anionic surfactant without liquid-liquid extraction has been studied [38]. The ion associate formed between sodium dodecylsulphate (SDS) and Rhodamine 6G was adsorbed onto the wall of a PTFE vessel by vigorous shaking. After the resultant solution was dicarded, the ion associate was dissolved in methyl cellosolve and its absorbance measured at 534 nm.

(b) Atomic Absorption (AAS) and Atomic Emission (AES) Spectrometry [33]

Atomic spectrometry both AAS and AES, can be utilized as indirect methods for the determination of anionic surfactants. The

Australian Standard Procedure uses the AAS determination of Cu ions extracted from an aqueous diaquobis(ethylenediamine)copper(II) solution by anionic surfactants into chloroform as the bis(surfactant)bis (ethylenediamine)copper(II) complex. After destruction of the complex by dilute acid, Cu is determined by AAS in proportion to anionic surfactant concentration.

(c) Voltammetry

The diaquobis(ethylenediamine)copper(II) ion [$Cu(en)_2^{2+}$] is used selectively to extract anionic surfactants into chloroform. Determination of anionic surfactants is made by monitoring the copper ions either in the chloroform phase, after $Cu(en)_2(surfactant)_2$ extraction, or in the acid phase, after back extraction. Linear sweep anodic stripping voltammery (LSASV) using conventional glassy carbon (GC), a mercury thin-film or polymer-modified electrode has been applied [39].

(d) Potentiometric Titration

Ion-selective electrodes sensitive to anionic surfactants are of increasing interest for their use as end-point indicators, as there is no need for an organic solvent. The use of specially constructed electrodes for the potentiometric titration of anionic surfactants has been reported [40].

(e) High-Performance Liquid Chromatography (HPLC)

Commercial LAS are complex mixtures of homologs and isomers. Usually, the alkyl chain length varies between 10 and 14 carbon atoms, with 11, 12 and 13 carbon atoms as the dominant homologs. Chromatographic procedures can be applied to achieve separations of individual anionic surfactants. Qualitative and quantitative determination of anionic surfactants containing aromatic residues is significantly more advanced in HPLC (because of the possibility of using a UV or fluorescence detector that is very sensitive and versatile) than that of anionic surfactants containing only aliphatic residues [33].

(f) Gas Chromatography (GC)

LAS is not sufficiently volatile to permit direct analysis by GC techniques. In order to determine LAS in environmental samples by GC methods, derivatization techniques have been developed. A method for

the determination of LAS in water and sediment samples by gas chromatography/mass spectrometry (GC/MS) has been described [41]. Sulfonates are converted to their trifluoro sulfonate derivatives in a two-step derivatization procedure.

(g) Radiometry

A radiometric method involving the use of the very stable complex cation of ferroin, $[Fe(II)(1,10\text{-phenanthroline})_3]^{2+}$, labelled with iron-59 has been reported [42]. The method is based on the reaction of ferroin with anionic surfactants to form chloroform-soluble compounds of the type $[Fe(II)(1,10\text{-phenanthroline})_3][\text{anionic surfactant}]_2$. The ferroin reagent is added to an aqueous solution in stoichiometric excess of the anionic present, and the extent of the subsequent extraction of these compounds into chloroform is proportional to the amount of anionic present. The anionic surfactants content of the sample is determined by the standard addition of sodium lauryl sulfate.

A brief review of the methods for the determination of anionic surfactants is shown in Table 1.3.

Table 1.3 A brief review of the methods for the determination of anionic surfactants

Technique	Reagent	Condition	Linear range Detection limit	Ref.
Spectro-photometry	- MB reagent solution - alkaline borate solution - 0.5 M sulfuric acid - solvent = chloroform	- liquid-liquid extraction - λ_{anal} = 650 nm	- linear range = 0.1– 1.8 mg/l anionic surfactant as Manoxol OT for 100 ml sample	43
Spectro-photometry	- phosphate buffer pH 6 - reagent = 1-(4-nitro-benzyl)-4-(4-diethyl-aminophenylazo) pyridinium bromide (NDP) - solvent = chlorobenzene	- liquid-liquid extraction - λ_{anal} = 573 nm	- detection limit = µg/l level	44

Table 1.3 Continued...

Technique	Reagent	Condition	Linear range Detection limit	Ref.
Spectro-photometry	- borate buffer pH 9.0 - reagent = Brilliant Green (+ sodium sulfite) pH 9.0 and methyl violet (+ sodium sulfite) pH 9.0	- one-phase, one-reagent - λ_{anal} = 630 nm - based on conversion of the colourless leuco-bases of triphenylmethane dyes (Brilliant Green and methyl violet) to colored (quinoid) forms by the anionic surfactants	- applicable range = 0-1500 mg/l	45
Spectro-photometry	- acetate buffer pH 5 - ferroin reagent - iron(II)-bipyridyl reagent - solvent = chloroform	- liquid-liquid extraction - the absorbance of chloroform phase is measured at λ_{anal} = 512 nm	- linear range up to 125 µg of SLS - precision = ±1.4% - limit of detection = 2.5 µg of SLS	46
Spectro-photometry	- reagent = ethyl violet - acetate buffer pH 5.0 - solvent = toluene	- liquid-liquid extraction - λ_{anal} = 612 nm	- linear range = 0-9.0x10 $^{-6}$ M SDS (in toluene) - recovery = 98-107%	47
Spectro-photometry	- acetate buffer pH 5 containing sodium sulfate and EDTA - reagent = ethyl violet solution - solvent = benzene and toluene	- liquid-liquid extraction - λ_{anal} = 615 nm - absorbance of ion-pair in the organic phase is measured	- recovery = 97–107% ($D\text{-}OSO_3^-$) - standard deviation = 1.6 - 2% - linear range = 0 - $5x10^{-7}$ M of anionic surfactants in the aqueous solution	48
Spectro-photometry	- acid MB ($1x10^{-3}$ M) - solvent = chloroform	- one-time extraction - λ_{anal} = 654 nm - requires only one half of sample, one tenth of chloroform and one sixth of the analytical time compared with the official analytical method	- linear range = $5x10^{-8}$ - $1.5x10^{-6}$ M DBS - RSD = 7.5% (n=10)	49
Kinetic-photometric method	- solution A = SDS + 1,10-phenanthroline + Triton X-100 + distilled water - solution B = Fe(II) + distilled water	- solution A+ solution B - λ_{anal} = 500 nm - temp. = 50 °C - based on the accelerating effect of micelles of the surfactant on the reaction between iron(II) and 1,10-phenanthroline, which is monitored via the ferroin complex formed	- determination range = 50-400 µg SDS/ml - detection limit = 15 µg SDS/ml - RSD = 3% (200 µg SDS/ml)	50

Table 1.3 Continued...

Technique	Reagent	Condition	Linear range Detection limit	Ref.
Sorption-spectrometric method	- SG = silica gel - I = didecylamino-ethyl-β-tridecyl-ammonium iodide - MO = methyl orange - FI = fluorescein - Solid-phase reagents = SG loaded with I-MO and I-FI associates	- based on removal of the dyes from the surface of loaded SG into an aqueous solution by SDS - the amount of dyes in solution can be determined by spectrophotometric (MO) or luminescence (FI) methods	- visual test scales for SDS determination in water at one fifth of the maximum admissible concentration (MAC) level was prepared	51
Photometric titration	- indicator = tetrabromophenol-phthalein in acidic medium + Triton X-100 (non-ionic surfactant) + bulky cation - titrant = distearyl-dimethylammonium ion	- pH = 3.2 - fibre-optic sensor with a 640 nm interference filter	- linear range = $1.5x10^{-6}$ - $2x10^{-4}$ M	52
Potentiome-tric titration	- standard titrant = Hyamine 1622 (cationic surfactant)	- indicating electrode = an easily made membrane electrode - titration speed = 15 min/ 20 cm^3	-	53
Potentiome-tric titraion	- titrant = Hyamine 1622 (cationic surfactant)	- ion-pair potentiometric titration - ion-selective electrode = depositing PVC membranes containing surfactant ion pair as ion exchangers on a graphite support	- responsible range = 10^{-2}–10^{-6} M	54
Reversed-phase HPLC with UV detection	- mobile phase = acetonitrile-water (50:50, v/v) containing 0.1 M sodium perchlorate	- analytical column = A Wakosil 5C4 (butyl silica gels, particle size 5 μm, weak non-polar reversed-phase column) - precolumn = A TSK precolumn IC-Conc-A (anion-exchange precolumn) - separation: isocratic elution at ambient temperature - UV detector: λ_{anal} = 220 nm	- Linear range = 10-200 μg/l - overall recovery for total LAS = 99 %	55

Table 1.3 Continued...

Technique	Reagent	Condition	Linear range Detection limit	Ref.
Reversed-phase HPLC with Fluorescence detector	- mobile phase = water-acetone mixtures - ion-pair extraction system: solvent = chloroform, reagent = acridinium chloride solution	- reverse-phase column: Hypersil SAS and Hypersil ODS - post-column ion-pair extraction detection - chloroform phase is monitored fluorimetrically	- linear range up to 4 μg of anionic surfactant injected - detection limit range between 1 and 5 ng,	56
HPLC-ICP-AES	- mobile phase = methanol / 0.05 M aqueous ammonium acetate (4:1, v/v)	- column = 10 μm styrene-divinylbenzene, 250x4.1 mm - ICP-AES monitor the 180.7 nm sulfur line	- 2σ detection limit = 15 ng sulfur - RSD = 4 % - linear range = 23-1869 ng sulfur	57

1.2.4 FIA Methods

Flow-injection systems have been applied to the determination of anionic surfactants. Normally the described systems use liquid-liquid extraction, with spectrophotometric detection or atomic absorption spectrometry. Flow-injection systems with potentiometric detection have been described for the determination of anionic surfactants. The use of tensammetric detection has also been applied. Flow-injection systems for the determination of anionic surfactants are summarized in Table 1.4.

Table 1.4 A brief review of the FIA methods for the determination of anionic surfactants

Sample	Reagent/Condition	Measurement Technique	Linear range Detection limit RSD Sample rate	Ref.
SDS sample solution	Two-line manifold - carrier solution = cetyl-dimethylbenzylammonium chloride (CDMBA-Cl) - reagent solution = BCP-phosphate buffer pH 8.1 Three-line manifold - carrier solution = Distilled water - reagent solution 1 = CDMBA-Cl - reagent solution 2 = BCP-phosphate buffer pH 8.1	- Spectrophotometry - λ_{anal} = 588 nm - based on depression of the decrease in absorbance at 588 nm by the formation of the ion associate of the quaternary ammonium surfactant with SDS in Bromocresol Purple (BCP) solution at pH 8.1	Two-line manifold: - linear range = up to $3x10^{-5}$ M SDS - RSD = 0.4% ($2x10^{-5}$ M SDS; n=3) - sample rate = 30/h Three-line manifold: - detection limit = down to 10^{-6} M SDS - RSD = 0.7% ($6x10^{-6}$ M SDS; n=3) - sample rate = 50/h	58

Table 1.4 Continued...

Sample	Reagent/Condition	Measurement Technique	Linear range Detection limit RSD Sample rate	Ref.
Lake water and tap water	- MB reagent - on-line liquid-liquid extraction - solvent = chloroform	- Light Emitting Diode (LED) based dual-wavelength spectrophotometric system - $\lambda_{non\text{-}specific}$ = 850 nm - λ_{anal} = 660 nm	- linear range = up to 2.5 mg LAS/l - detection limit = 0.03 mg LAS/l - RSD = 1.5% (2.0 mg LAS/l)	59
Detergent and sewage water	- acetate buffer pH 5 - reagent = ethyl violet solution - off-line liquid-liquid extraction - solvent = toluene	- Spectrophotometry - toluene phase is measured at 610 nm in a FI system	- linear range = 0.01-1.0 mg SDS/l - RSD = 2% (0.5 mg SDS/l; n = 10)	60
River water	- carrier stream = distilled water - reagent stream = MB + sodiumsulphate + acetate buffer pH 5 - on-line liq./liq. extraction - extraction solvent = o-dichlorobenzene	- Spectrophotometry - λ_{anal} = 658 nm	- linear range = up to $3x10^{-5}$ M and $7x10^{-5}$ M SDS (injection volume = 300 and 100 µl respectively) - detection limit = $1.8x10^{-8}$ M SDS - RSD = 4.4 and 6.5% using peak heights and peak areas respectively ($1.4x10^{-7}$ M SDS; 300 µl; n = 10) - sample throughput = 20 samples/h	61
River water	- continuous solvent extraxtion - ion-pair extraction reaction with MB in chloroform - membrane phase separator - carrier solution = reagent solution = MB pH 2.0 ($KH_2PO_4 + K_2SO_4 + H_2SO_4$) - extraction solvent = 10% (v/v) methanol in chloroform	- Spectrophotometry - λ_{anal} = 660 nm - injection of the coloured organic phase into a chloroform stream	- linear range = 0-10 µg SDS/ml - detection limit = 4 ng SDS/ml (blank solution; n = 15; student t test) - determination limit = 0.04 µg SDS/ml (ten times the detection limit) - RSD = 1.2% (0.5 µg SDS/ml; n = 20) - sample rate = 60±5 samples/h	62

Table 1.4 Continued...

Sample	Reagent/Condition	Measurement Technique	Linear range Detection limit RSD Sample rate	Ref.
Waste water samples	- two-step solvent extraction flow injection system - phase separator = gravitational design - solvent = chloroform - carrier = demineralized water - R1 = buffered MB solution (carbonate buffer pH 10) - R2 = MB washing solution (acid MB)	- Spectrophotometry - λ_{anal} = 652 nm - based on the official MB method	- linear range = up to 6.0 mg/l of sodium dodecyl sulfonate - RSD = 4.6% (2.0 mg/l; n = 7) - recovery = 89-107% - sample rate = 10/h	63
Washing powders	- carrier = water - R1 = hexadecyltrimethyl-ammonium bromide (CTAB)/Triton X-100 solution - R2 = p-diphenylamino-azobenzene sulfonate (PDABS) solution	- Spectrophotometry - λ_{anal} = 530 nm - based on solvatochromism of PDABS (azo dye)	- sample rate of 60/h - RSD = 0.9% ($2x10^{-5}$ M dodecyl-benzenesulfonate (DBS); n = 11) - detection limit (S/N = 3) = $2x10^{-7}$ M for both DBS and sodium dodecyl sulfate (SDS) - linear range = 0-$4x10^{-5}$ M	64
Surface waters, municipal waste water and ground waters	- carrier = deionized doubly distilled water (pH 6.0, adjusted with 0.1 M acetic acid) containing 0.001% m/v potassium dichromate and 0.001% m/v thiourea - reagent = 0.002% m/v Brilliant Green in 0.04% v/v ethanol	- Spectrophotometry - λ_{anal} = 625 nm	- sample throughput 50/h - linear range up to 20.0 mg SLS/l - detection limit = 100 µg SLS/l - RSD = 0.5% (10.0 mg SLS/l; n = 6)	65
Aqueous sample	- carrier = KH_2PO_4 solution - reagent stream = MB + KH_2PO_4 + K_2SO_4 + H_2SO_4 - extraction solvent = chloroform - on-line single extraction	- Spectrophotometry - absorbance of the chloroform stream is measured at λ_{anal} = 660 nm	- sample throughput = 40 samples/h - determination range = 0.03-0.65 mg SLS/l	66
Unknown surfactant mixtures	- phase separator = PTFE porous membrane type - on-line single liq./liq. extraction - carrier = MB + NaH_2PO_4 + H_2SO_4 + methanol - extraction solvent = chloroform	- Spectrophotometry - absorbance of the chloroform phase is measured at λ_{anal} = 660 nm	- determination range = up to 1.25 mM anionic surfactant - limit of detection = 15 µM surfactant - sample throughput = 80 samples/h - good reproducibility within 1.5% coefficient of variance	67

Table 1.4 Continued...

Sample	Reagent/Condition	Measurement Technique	Linear range Detection limit RSD Sample rate	Ref.
Synthetic and real water samples	- continuous liquid/liquid extraction - reagent = MB + NaH_2PO_4 + H_2SO_4 + methanol - solvent = chloroform-carbon tetrachloride (3+1)	- Spectrophotometry - λ_{anal} = 650 nm - on-line monitoring - the ion-pair continuously formed in the aqueous phase was passed through the organic plug situated in the cuvette for the required time to obtain a suitable absorbance-time recording	- detection limit = 20 ng/ml - RSD = 6.7% - sample throughput = 20/h	68
River water	- carrier = distilled water - cationic azodye = 1-methyl -4-(4-diethylaminophenyl-azo)-pyridinium cation (MEP) - reagent solution = MEP + sodium sulfate and adjust to pH 5 with acetate buffer - phase separator with a PTFE porous membrane (0.8 μm pore size) - solvent = chloroform	- Spectrophotometry - absorbance of the organic phase separated is continuously measured at λ_{anal} = 564 nm	- sample rate = 30/h - linear range up to $2x10^{-6}$ M or $3x10^{-5}$ M of anionic surfactant (injection volume = 300 or 100 μl respectively) - RSD = 1.5% (300 μl of $1x10^{-6}$ M SDS; n = 10) - detection limit = as little as $1x10^{-8}$ M of anionic surfactant	69
-	- on-line single liq./liq. extraction - on-tube detection without phase separators using a glass capillary flow cell (i.d. = 0.8 mm) - regular-segment flow - reagent = 4-(4-dimethyl-aminophenylazo)-2-methyl-quinoline (4-MQ) - carrier = water - organic phase stream = 4-MQ chloroform solution - reagent = Rhodamine B - carrier = water - organic phase stream = Rhodamine B benzene solution	 - Spectrophotometry - λ_{anal} = 560 nm - Spectrofluorimetry - λ_{ex} = 318 nm - λ_{em} = 575 nm	 - the lowest determinable concentrations of anionic surfactants = $2x10^{-6}$ M - determination range = $2x10^{-6}$ – $1x10^{-5}$ M dodecylsulphate	70

Table 1.4 Continued...

Sample	Reagent/Condition	Measurement Technique	Linear range Detection limit RSD Sample rate	Ref.
Synthetic and real water samples	- reagent = MB in $CHCl_3$ - a continuous liq./liq. extraction - an organic plug containing the reagent is placed and retained at the detection point while a large volume of sample (aqueous phase) is passed through it	- Spectrophotometry	- determination limit = 20 ng/ml - RSD = 6.7% - sample throughput = 20/h	71
Waste waters	- automatic continuous liq./liq. extraction - formation of the detergent-[1,10-phenanthroline-copper (II)] ion pair - extraction solvent = methyl isobutyl ketone - carrier solution = 1,10-phenanthroline-copper (II) complex solution + acetate buffer pH 4.75	- measurement of copper present in the organic layer by AAS	- linear range = 0.1-5.0 μg/ml - RSD = 0.8%	72
Printing plates washing solution of the print industry	- carrier solution = dodecylbenzenesulphonate (DBS) - conditioning solution = K_2SO_4 with a 0.2 M ionic strength, and its pH adjusted to 2.5 with conc. H_2SO_4	- Potentiometry	- linear range = $1x10^{-4}$ - $1x10^{-3}$ M - sample rate = 30 samples/h	73
Known standards	- carrier stream = titrant = 10^{-6} M Hyamine 1622 - injection volume = 70 μl - flow-rate = 0.90 ml/min - reference electrode = standard Corning calomel electrode - flow-through surfactant-selective electrode has been developed	- (Potentiometric) Pseudotitration - relating peak width to the logarithm of the concentration	- a linear calibration graph may be produced - lack of precision	74
Detergents	- carrier stream = deionized water ($5x10^{-6}$ M surfactant) - supporting electrolyte = 0.1 M Na_2SO_4 - working electrode = mercury-coated gold electrode - reference electrode = silver/silver chloride electrode filled with 3M KCl - counter electrode = uncoated gold	- Tensammetry (measure the capacitance of the electrical double layer of an electrode)	- determination range = 10^{-5} - 10^{-4} M - calibration graph is not linear, approximation by a polynomial or a cubic spline function - accuracy of $\pm$ 4% - sample rate = 60/h	75

Table 1.4 Continued...

Sample	Reagent/Condition	Measurement Technique	Linear range Detection limit RSD Sample rate	Ref.
River and tap water samples	- BSA = bovine serum albumin - ANS = 8-anilino-1-naphthalenesulfonic acid - carrier solution = Tris buffer (20 mM, pH 8) + BSA (0.1% m/v) + ANS ($3x10^{-5}$ M) - based on the interactions of SDS with BSA, a surface active protein, in the presence of a fluorescent probe, ANS	- Spectrofluorimetry - xenon-pulsed light source - λ_{ex} = 384 nm - λ_{em} = 470 nm - excitation and emission slits = 15 nm (both)	- linear dynamic range extends from the limit of quantification up to $1x10^{-4}$ M SDS - RSD = 4% - detection limit = $2x10^{-6}$ M SDS	76

1.3 Hyoscine Butylbromide

Hyoscine butylbromide (or scopolamine butylbromide) is one of the antimuscarinic agents and classified as a quaternary ammonium compound. The molecular structure is shown in Figure 1.6.

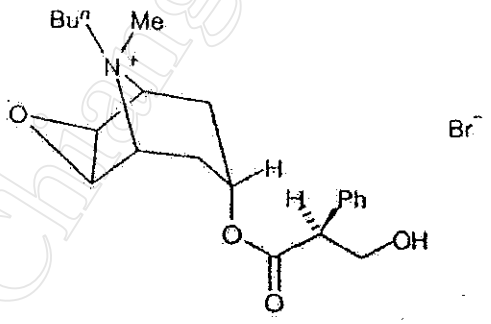


Figure 1.6 Hyoscine butylbromide (or scopolamine butylbromide) [77]

Antimuscarinic agents are competitive inhibitors of the actions of acetylcholine at the muscarinic receptors of autonomic effector sites innervated by parasymphthetic (cholinergic postganglionic) nerves, as well as being inhibitors of the action of acetylcholine on smooth muscle lacking cholinergic innervation. They are also described as

parasympatholytic agents, atropinic agents, atropine-like agents, and as anticholinergic agents, although the latter term should encompass compounds with antinicotinic actions. Antimuscarinics are classified as tertiary amine or quaternary ammonium compounds. At therapeutic doses tertiary amine antimuscarinics have little effect on the actions of acetylcholine at nicotinic receptors. However, the quaternary ammonium antimuscarinics exhibit a greater degree of antinicotinic potency, and some of their side-effects at high doses are due to ganglionic blockade; excessively high doses may even produce neuromuscular block. There are also pharmacokinetic differences between tertiary amine and quaternary ammonium antimuscarinic agents. Quaternary ammonium compounds are less lipid soluble than tertiary amines; their gastro-intestinal absorption is poor and they do not readily pass the blood-brain barrier or conjunctiva [78].

1.3.1 Uses [78]

Hyoscine butylbromide is used in gastro-intestinal disorders because of its marked inhibitory effect on gastro-intestinal motility and its antisecretory effect. Hyoscine butylbromide may relieve visceral spasms of the gastro-intestinal tract. It may thus be of use in relieving the pain due to smooth muscle spasm in diverticular disease, dyspepsia, and irritable bowel syndrome; it is no longer considered appropriate for use in infantile colic. Hyoscine butylbromide has also been tried in an attempt to relax the smooth muscle in oesophageal spasm, although result is often disappointing. It should be avoided in patients with oesophageal reflux because of a tendency to relax the oesophageal sphincter.

1.3.2 Analytical Methods

The extractive spectrophotometry is a general procedure for the quantitative analysis of quaternary ammonium compounds in antimuscarinic drugs. In practice, a buffered aqueous solution containing the quaternary ammonium compound and a suitable indicator dye is shaken with an organic solvent, and the concentration of the resulting ion-pair in the organic phase is determined spectrophotometrically. Several dyes are examined with various extraction solvents [79]. Hyoscine butylbromide formed an ion association compound with hexanitrodiphenylamine which is extracted into dichloromethane and measurement of the colour in the dichloromethane is made spectrophotometrically at 420 nm [77].

A rapid fast derivative spectrophotometric assay of hyoscine butylbromide in pure and in pharmaceutical formulation has been developed [80]. The assay depends upon extracting the picrate salt of hyoscine butylbromide into chloroform from aqueous medium and measurement of peak amplitude at 430 nm or peak-trough amplitude at 365/330 nm. A second-derivative UV spectrophotometric method for the simutaneous determination of medazepam and hyoscine butylbromide in sugar-coated tablets without prior separation has been described [81].

An HPLC method using indirect conductometric detection has been proposed for the determination of atropine and atropine-like alkaloids (including hyoscine butylbromide) in phamaceutical preparations [82].

1.4 Yttrium

The name yttrium comes from the Swedish mine Ytherby. In spite of its relatively high abundance, the technical application was rare until the 1960s, due to the difficulties in separation from the lanthanides, with which it is generally found. In the last decades new techniques of separation and purification as well as new applications of yttrium alloys and compounds, e.g., as red phosphor in colour television and fluorescent tubes have been developed [83].

1.4.1 Physical and Chemical Properties [83]

Yttrium (Y), a silver-gray metal with the atomic number 39 (atomic mass 88.9, density 4.47 g/cm^3, melting point 1523 °C, boiling point 3338 °C), contains 3 electrons more than the rare gas krypton. In water, only the trivalent state is stable, it is oxidized in moist air and inflammed at 500 °C, burning in a light red flame, whereby the white, in water colourless Y_2O_3 is formed. The Y(III) fluorides, oxalates, halides, carbonates, and hydroxides have low solubility. In solution, Y^{3+} hydrolizes slightly before precipitation of the hydroxide occurs above pH 6.

1.4.2 Occurrence and Uses [83]

In general yttrium is found together with the lanthanides and occurs in minerals such as monazite, bastnasite, xenotime, yttrialite, gadonilite, yttriocrasite, and in complex minerals such as samarskite and euxenite. Monazite sand contains 3% Y and bastnasite about 0.2%. Xenotime (from Malaysia) contains about 60% Y, 10% Yb, and 10% Dy.

The main technical application of yttrium as oxide, oxidesulfide or vanadate in combination with europium as an activator is as red phosphor in colour television and fluorescent tubes. Since 1965, this application has resulted in a remarkable growth of the yttrium industry. In the future, the application of yttrium as a supraconductor element may further raise its production. $YBa_2Cu_3O_7$ has, for instance, a critical temperature for supraconduction of about 92 K, which allows cooling with liquid nitrogen.

In metallurgy yttrium metal increases the stability of heating alloys and Cu-Ni-steel against oxidation, and Y_2O_3 increases the strength of ZrO_2. In ceramic industry Y_2O_3 is used as crucible material and imparts shock resistance and low expansion in glass and ceramics. Yttrium is used in laser instruments and is a catalyst in ethylene polymerization. Several yttrium compounds are used in electronics and in data processing as store elements and modulators. Y_2O_3 forms with ThO_2 a transparent glass with high permeability ("Yttralox") and with ZrO_2 the emission source for "Nernst"-lamps, which have been used for a long time in mining. Yttrium-aluminum garnet ($Y_3Al_5O_{12}$) is valued as a gem stone.

In nuclear industry Y-alloys increase the strength and resistance of reactor materials, yttrium hydride is applied as neutron moderator because of its temperature stability.

1.4.3 Analytical Methods

Many techniques such as spectrophotometry, electrochemical methods and chromatography have been proposed for the determination of yttrium. Examples are as follows:

(a) Voltammetry

Adsorptive stripping voltammetry (AdSV) has attracted considerable attention for the determination of trace and ultratrace metals. The basis of AdSV lies in a preconcentration mechanism because the metal complex, formed after the addition of the suitable ligand in the analyte solution, is accumulated by adsorption on the electrode surface and then is reduced by a process of cathodic stripping. The use of AdSV for the determination of trace amounts of yttrium and some rare-earths has been reported [84]. The method allows yttrium to be determined at ng/ml levels and below, by controlled adsorptive accumulation of the yttrium-solochrome violet RS (SVRS, 5-sulpho-2-hydroxybenzeneazo-2-naphthol) complexes at the hanging mercury drop electrode followed by reduction of the adsorbed complexes.

(b) Polarography

A practical method for the polarographic determination of yttrium has been described [85]. The procedure is based on the reduction of the yttrium-solochrome violet RS (SVRS) complex. Experimental conditions include the use of Triton X-100 in order to achieve good separation of the Y-SVRS and SVRS peaks. Application of the procedure to the determination of yttrium as a major component in the superconductor $YBa_2Cu_3O_y$ gave good results.

(c) Atomic Absorption (AAS) and Atomic Emission (AES) Spectrometry

Atomic absorption spectrometry (AAS) is a sensitive means for the quantitative determination of more than 60 metals or metalloid elements. AAS for the determination of yttrium has been reported [86]. Atomic emission spectrometry (AES) has been studied in order to apply for the determination of yttrium [87,88]. The atomic emission spectrum of yttrium has not been found in the air-acetylene flame because of the high dissociation energy of YO (7.0 eV). Therefore, many studies on yttrium by flame emission spectrometry have been made using the N_2O-C_2H_2 flame [89,90] and the O_2-C_2H_2 flame [91] with good results.

(d) Neutron Activation Analysis (NAA)

Activation methods are based upon the measurement of radioactivity that has been induced in samples by irradiation with neutrons or charged particles, such as hydrogen, deuterium, or helium-3 ions. The determination of yttrium by neutron activation analysis (NAA) has been proposed [92].

(e) High-Performance Liquid Chromatography (HPLC)

Dynamic ion exchangers are formed when hydrophobic ions, which are present in the mobile phase, are sorbed into the hydrophobic surface of a reversed-phase to produce a charged double layer at the surface where ion exchange can occur. These exchangers gave improved column efficiency of HPLC for metal ions, and greater flexibility with regard to choice of separation conditions. Consequently the application of these dynamic ion exchangers was studied for the determination of rare earths, Y and Th in samples from different circuits of a refining process for uranium ore [93]. Optimization of the effective capacity of the dynamic ion exchanger and the selectivity of postcolumn reaction detection permitted analysis down to 0.1 μg/ml of the rare earths and yttrium in the presence of U, Th, and a number of other metal ions.

(f) Spectrofluorimetry

A spectrofluorimetric method based on the formation of a fluorescent complex is proposed for the determination of yttrium. The reaction of salicylaldehyde carbohydrazone with yttrium in an aqueous ethanolic medium (60% v/v ethanol) has been studied [94]. With excitation at 360 nm, the yttrium(III) chelate has an emission maximum at 442 nm; the reaction is carried out at pH 6.3-6.9.

(g) X-Ray Fluorescence Spectrometry

X-ray fluorescence analysis is an appropriate method for the determination of many trace elements. The determination of the trace elements Rb, Sr, Y, Zr and Nb on small geological samples (100 mg) fused in lithium tetraborate by x-ray fluorescence spectrometry has been disscussed [95].

(h) Inductively Coupled Plasma (ICP) Spectrometry

The isolation of rare earth elements (REEs) from geological materials by ion-exchange chromatography with Dowex 50W-X8 has been described. Elution curves for Y, La, Ce, Nd, Sm, Eu, Gd and Yb are determined by ICP-AES [96]. A method for the determination of individual rare earth elements and yttrium in granites and greisens on the basis of a combination of thin-layer chromatographic separation and clean-up of the rare earth element group on a Dowex 50-X8 cation exchanger in combination with ICP-AES has been also developed [97]. A rapid method for the determination of yttrium, scandium, and other rare earth elements (REEs) in uranium-rich geological samples and in pitch blende type of samples by ICP-AES after separation of uranium by selective precipitation of the analytes as hydroxides using H_2O_2/NaOH in the presence of iron as carrier has been described [98]. Direct ICP-MS determination of trace and ultratrace amounts of yttrium, thorium, uranium and the lanthanides in geological materials after decomposition in a microwave oven has been proposed [99].

(i) Spectrophotometry

Arsenazol and III have been used for the spectrophotometric determination of yttrium(III) [100]. Other chromogenic reagents employed for the determination of yttrium(III) include 4-(2-pyridylazo) resorcinol (PAR) [101,102], 4-(2-thiazolylazo)resorcinol (TAR) [103], Alizarin S [104], 1-(5-methyl-2-pyridylazo)-2-naphthol [105], xylenol orange, quinalizarin and pyrocatechol violet [106].

A brief review of the methods for the determination of yttrium is shown in Table 1.5.

Table 1.5 A brief review of the methods for the determination of yttrium

Technique	Reagent	Condition	Linear range Detection limit	Ref.
Spectro-photometry	- reagent = naphthazarin (5,8-dihydroxy-1,4-naphthoquinone; NAZA) in ethanol	- ethanol-water medium containing 50% v/v ethanol - an ionic strength of 0.1 M ($NaClO_4$) - pH = 5.8 - λ_{anal} = 590 nm	- linear range up to 9.42 μg Y^{3+}/ml - $\varepsilon = 1.15 \times 10^4$ l/mol.cm at 590 nm - working range = 1.95-8.86 μg/ml - RSD = 0.8% (5.6 μg/ml; n=10)	107

Table 1.5 Continued...

Technique	Reagent	Condition	Linear range Detection limit	Ref.
Spectro-photometry	- reagent = 4-(2-thiazolylazo)-resorcinol (TAR) in methanol	- borate buffer pH 8.1 - λ_{anal} = 540 nm	- linear range = 0.12-1.4 µg of yttrium/ml - $\varepsilon = 6.04 \times 10^4$ l/mol.cm	108
Spectro-photometry	- reagent = 7-(2-pyridylazo)-5-chloro-8-hydroxy-quinoline (PACHQ) in ethanol	- Britton-Robinson buffer pH 6.5 - λ_{anal} = 390 nm	- linear range = 0-8.89 µg/ml - standard deviation = 0.002 A (8.89 µg Y(III)/ml; n=10) - $\varepsilon = 0.33 \times 10^4$ l/mol.cm	109
Spectro-photometry	- reagent = quinizarin green (QG; [1,4-bis(4-methylanilino)anthra-quinone]) in dimethylformamide	- in the presence of 40% dimethylformamide - 20 °C - ionic strength of 0.1 M ($NaClO_4$) - tris (hydroxymethyl) aminomethane buffer pH = 7.7 - λ_{anal} = 600 nm	- linear range = 2×10^{-5}-3×10^{-4} M of Y(III) - $\varepsilon = 4.6 \times 10^3$ l/mol.cm - standard deviation = 0.005 A (1.6×10^{-4} M Y(III); n=10)	110
Spectro-photometry	- reagent = arsenazoIII - ammonium acetate buffer solution - dilute nitric acid	- pH 2.5 - λ_{anal} = 660 nm - yttrium is separated from chromium (VI) by precipitation of yttrium hydroxide from an ammoniacal chloride solution	- can apply to the determination of 50 ppm to about 4% of yttrium in chromium	111
Spectro-photometry	- reagent = pyrocate-chol violet in water - ascorbic acid - gelatin - ammonium acetate	- pH 8.5 - λ_{anal} = 665 nm - yttrium is separated from uranium, zirconium, thorium, iron and molybdenum by solvent extraction with tri-n-octylphosphine oxide	- ε = 25,900 at λ = 665 nm - linear range up to 1.8 µg/ml	112
Spectro-photometry	- reagent = arsenazo [3-(2-arsonophenyl-azo)-4,5-dihydroxy-2,7-naphthalene-disulfonic acid] - 20% hexamethylene-tetramine	- λ_{anal} = 580 nm - yttrium is separated as fluoride from large quantities of iron by coprecipitation with thorium from a solution containing ammonium fluoride - yttrium is separated from thorium by anion exchange	- determination range = 0.01-0.1%	113

Table 1.5 Continued...

Technique	Reagent	Condition	Linear range Detection limit	Ref.
Spectro-photometry	- reagent = molybdo-phosphoric acid - 1:10 sulfuric acid - 8:1 molybdate-phosphate reagent - aqueous 25% sodium citrate dihydrate - tin(II) chloride solution	- pH 4.8 - λ_{anal} = 695 nm	- linear range = 0-8 μgY/ml - ε = 24,000	114
Spectro-photometry	- reagent = pyro-catechol violet (PV) - cationic surfactant = tetradecyldimethyl-benzylammonium (zephiramine; zeph) ion	- pH 9.0 - λ_{anal} = 660 nm	- ε = 3.3×10^4 l/mol.cm - linear range up to 1.2 μg/ml	115
Spectro-photometry	- reagent = arsenazoI	- pH 6-7 - λ_{anal} = 570 nm - extraction and separation of yttrium, neodymium and samarium from succinate solution with tri-n-octylamine (TOA)	-	116
Spectro-photometry	- reagent = arsenazoIII - acetate buffer pH 4.7	- multivariate calibration - coloured complex system Y-Ba-Cu-Arsenazo III - water-acetone solution system - calibration solutions = Y+Ba+Cu ion solution (according to the design arrangements) - absorbance is measured between 595 and 680 nm at fifteen selected wavelengths	- the stoichiometric coefficients referred to the Cu content can be estimated within the error ranges $Y_{1.00\pm0.03}Ba_{2.00\pm0.07}Cu_{3.00}O_x$	117
Gravi-metrically	- reagent = 8-hydroxy-quinoline	- 3-fold excess of 8-hydroxyquinoline dissolved in glacial acetic acid (5% solution) - temperature for the reaction = 70 °C; 3 h - adjust pH with concentrated ammonia solution - precipitation at pH 5.5 - dry at 100±5 °C for 4-8 h	- yttrium can be weighed as $Y(C_9H_6NO)_3$ or after ignition to the oxide	118

Table 1.5 Continued...

Technique	Reagent	Condition	Linear range Detection limit	Ref.
ICP-AES	- concentrated HCl, HNO_3, $HClO_4$ and HF - ammonium and sodium oxalate solutions - Dowex 1-X8 (Cl-form; 100-200 mesh) strong anionic exchanger	- determination of Ce, Y and Th in sea water, pore water, suspended matter, sediments and biota - double coprecipitation with $Mg(OH)_2$ and CaC_2O_4 to pre-concentrate Ce, Y and Th from sea and pore water - acid digestion to solubilise sediments, suspended matter and biota	- detection limit = 0.62 ng/g (0.003 ng/ml) for Y in biota and sediments (water)	119
ICP-AES	- nitric solution for ICP-AES measurement	- determination of lanthanides and yttrium in rare earth ores and concentrates - separation of these elements from the other matrix constituents - select optimum conditions of ICP-AES by a simplex method	- determination limits, accuracy and precision have been reported for each elements	120

1.4.4 FIA Methods

FIA was found to be a powerful technique, not only for performing serial analysis but also for separation and preconcentration operations. A method utilizing a dual-column on-line ion-exchange FIA system coupled with ICP-AES is investigated for the simultaneous determination of 14 rare earth elements (REEs) and yttrium in geological samples [121].

1.5 Cobalt and Manganese

1.5.1 Cobalt

Cobalt is a component of vitamin B_{12}, and in this form it is essential for all higher animals and for man. As inorganic cobalt is required for bacterial vitamin B_{12} synthesis in the rumen, adequate amounts must be present in the feed of ruminants [83]. Because of mining activities and its wide-spread industrial uses, cobalt also belongs to the metals posing potential dangers due to excessive exposures. At risk are primarily metal workers. Exposures to cobalt-containing dusts cause

damage to lungs, heart, and skin. Cobalt also belongs to the group of occupational carcinogens and is considered dangerous under conditions that may be normally encountered at the work-place [122].

1.5.1.1 Physical and Chemical Properties [83,122]

Cobalt (atomic number 27, atomic mass 58.93) belongs to the group of transition elements. Its atomic nucleus normally contains one stable isotope, ^{59}Co. However, radioactive isotopes such as ^{60}Co, ^{57}Co, ^{58}Co have been detected in atomic fallout and in marine organisms exposed to fallout. Metallic cobalt forms a lustrous, gray, strongly ferromagnetic solid with a density of 8.9 g/cm^3 (20 °C), a melting point of 1495 °C, and a boiling point of 3100 °C. It is not attacked by air or water at ambient temperature, slowly dissolved by dilute non-oxidizing acids, rapidly by concentrated nitric acid. Common oxidation states of cobalt are +II and +III. However, compounds of Co(0), Co(+I), and Co(-I) are also known.

1.5.1.2 Uses [83]

Cobalt is a component of the so-called superalloys used to make critical parts of jet engines, gas-turbines, and of other machines operating under stress at high temperatures. It is also a component of the so-called stellites. These alloys are composed of 50-60% cobalt, 30-40% chromium, and 8-20% tungsten and are valued for their extreme hardness, strength, and heat resistance. In addition, cobalt is a component of magnetic steels and aluminum alloys with superior ferromagnetic properties.

Cobalt compounds are useful chemical catalysts for the synthesis of fuels (Fischer-Tropsch process), the synthesis of alcohols and aldehydes from olefins, hydrogen and carbon monoxide at elevated temperatures and pressures ("oxo process", "hydroformylation"). They are also used in petroleum refining and the oxidation of organic compounds. In the oxo process cobalt carbonyl, $Co_2(CO)_8$, is employed or generated in situ. For the selective production of n-butanol from propylene, hydrogen and CO, an organophosphine-modified cobalt carbonyl complex is used as the catalyst. Cobalt salts are proven oxidation catalysts, e.g., for the production of terephthalic acid by the oxidation of p-xylene, and the manufacture of phenol by the oxidation of toluene.

1.5.1.3 Analytical Methods

Various techniques have been developed for the determination of cobalt. Some examples in brief detail are given as follows:

(a) Photoacoustic Spectroscopy (PAS)

Photoacoustic spectroscopy (PAS) is a useful technique for the analysis of solids. A PAS method in which the analysis is converted from solution to a solid film before it is determined by a gas-microphone PAS system has been described [123]. Sub-nanogram detection limit of Co has been achieved, together with linear dynamic range over 2-3 orders of magnitude, using a 17-mW continuous-wave He-Ne laser.

(b) Spectrofluorimetry

A new reagent, 5-(4-arsonicphenylazo)-8-(4-toluenesulfonamido) quinoline (APTSQ), has been synthesised. APTSQ was found to be a sensitive and selective reagent for the fluorimetric determination of trace amounts of cobalt. In the presence of H_2O_2, cobalt reacts with APTSQ in solutions above pH 8.7, forming a product, which shows intense fluorescence with λ_{ex} at 229, 287 and 331 nm and λ_{em} at 376 nm [124].

(c) Chemiluminescence

Many chemiluminescence reagents can be used for the determination of Co(II) [125-130], luminol being the most popular with a detection limit for Co(II) lower than 10 ng/l. 2,6,7-Trihydroxy-9-(4'-chlorophenyl)-3-fluorone (Cl-PF) is a xanthone dye. When Cl-PF was oxidized with hydrogen peroxide in alkaline solution in the presence of trace amounts of Co(II), chemiluminescence could be observed. Trace amounts of Co(II) strongly catalysed this chemiluminescence reaction, especially in the presence of the cationic surfactant cetyltrimethylammonium bromide (CTMAB), and the chemiluminescence intensity was proportional to the concentration of Co(II) [131].

(d) Atomic Absorption Spectrometry (AAS)

Trace elements present in environmental, biological and biochemical samples are usually quantified by AAS either with an air-acetylene flame or using a graphite furnace. Cobalt can be determined by AAS sequentially from a solution derived from a single acid decomposition of pyrites samples [132]. Various methods have been published for the determination of trace amounts of cobalt using AAS following complexation with various ligands such as 2-nitroso-1-naphthol [133-135], dithizone [136], acenaphthenequinone dioxime (ANDO) [137], 3-methyl-1-phenyl-4-stearoyl-5-pyrazolone [138] and 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol (5-Br-PADAP) [139]. The application of direct solid atomization AAS to determine Co in silicates by using a graphite furnace and graphite cups has been reported [140]. A slurry sampling Zeeman electrothermal atomization atomic absorption spectrometry (ETAAS) technique for the reliable determination of cobalt in soil and river sediment samples (without any addition of chemical modifiers) has been already proposed [141].

(e) Inductively Coupled Plasma – Mass Spectrometry (ICP-MS)

Reproducibility testing of a sequential extraction scheme for the determination of trace metal speciation in a marine reference sediment by ICP-MS has been studied [142]. The 12 elements determined in the extracts are scandium, chromium, cobalt, nickel, copper, zinc, cadmium, tin, cesium, lead, thorium and uranium.

(f) Voltammetry

Adsorptive stripping voltammetry (AdSV) has been established as a reliable trace analysis technique. A method for the determination of Co by adsorptive differential pulse voltammetry using 1-phenylpropane-1-pentylsulfonylhydrazone-2-oxime as a selective complexing agent has been developed [143]. A differential pulse cathodic voltammetric method for the sensitive and selective determination of Co(II) at a 1-(2-pyridylazo)-2-naphthol modified carbon paste electrode has been described [144]. A reliable procedure for the determination of cobalt has been reported [145], in which the complex of cobalt with dimethylglyoxime is analysed by cathodic stripping square wave voltammetry based on adsorptive collection at a hanging mercury drop electrode. AdSV for the determination of Co(II) has been proposed [146];

Co(II) ions were complexed with dimethylglyoxime and the complexes were adsorbed on the surface of a glassy carbon rotating disc electrode, which was pre-plated with mercury. The stripping step was carried out by using a square wave potential-time excitation signal.

(g) High-Performance Liquid Chromatography (HPLC)

The separation and simultaneous determination of mixtures of metal ions as their chelates with organic reagents by HPLC has been utilized in inorganic analysis. A wide variety of organic reagents have been used to complex metal ions prior to separation by HPLC. The complexing agents such as 4-(2-thiazolylazo)resorcinol (TAR) [147], 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol (5-Br-PADAP) [148], and picolinaldehyde 4-phenyl-3-thiosemicarbazone (PAPT) [149] have been reported for this purpose. These reagents form either neutral or ionic chelates with cobalt and a large number of metal ions, and the chelates in the eluate can be detected spectrophotometrically.

(h) Radiometry

A substoichiometric radiochemical solvent extraction method has been reported [150] for the determination of cobalt, employing β-hydroxy-naphthaldoxime and chloroform as reagent and extractant, respectively.

(i) Spectrophotometry

Various spectrophotometric methods for the determination of cobalt using 2-nitroso-1-naphthol [151], nitroso R salt (2-hydroxy-1-nitroso-3,6-naphthalenedisulfonic acid disodium salt) [152], dithizone (diphenylthiocarbazone), 4-(2-pyridylazo)resorcinol (PAR), 1-(2-pyridylazo)-2-naphthol (PAN), Chromazurol S, 1-nitroso-2-naphthol, and 8-hydroxyquinoline [153] have already been reported. The method of thin-layer spectrophotometry for the determination of trace amounts of cobalt(II) has been developed [154]. The reagent PAN is used for this purpose because the cobalt(II)-PAN complex is strongly fixed on a membrane filter. A brief review of the spectrophotometric methods for the determination of cobalt is shown in Table 1.6.

Table 1.6 A brief review of the spectrophotometric methods for the determination of cobalt

Sample	Reagent	Condition	Linear range Detection limit	Ref.
Soil and vitamin B_{12}	- reagent = 4,4'-diazo-benzenediazoaminoazo benzene (BBDAB) in N,N-dimethyl-formamide (DMF) - Triton X100 - $Na_2B_4O_7.10H_2O$ buffer - mixed masking agent = KCN+NaF+sodium tartrate	- pH 10.2 - λ_{anal} = 540 nm	- linear range = 0-7 μg per 25 cm^3 cobalt(II) - $\varepsilon = 1.72x10^5$ l/mol.cm	155
Hydrofining catalysts, alloys and salts	- reagent = biacetyl-monoxime 2-pyridyl-hydrozone (BMPH) in dimethylformamide - perchloric acid	- medium = 20% of dimethylformamide - pH 5-6 - λ_{anal} = 430 nm	- ε = 3700 l/mol.cm - linear range = 0.8-15 mg cobalt/l - RSD = 1.06% (1.89 mg/l; n=15)	156 157
Alloys	- reagent = morpholine-4-carbodithioate - acetate buffer pH 5.16 - ammonia solution - perchloric acid - KNO_3 solution - naphthalene solution in acetone - chloroform - anhydrous sodium sulphate	- 0.1 M over-all ionic concentration (potassium nitrate solution) - λ_{anal} = 365 nm - pH 5.16	- linear range = 6-60 μg of cobalt - $\varepsilon = 1.396x10^4$ l/mol.cm - standard deviation = 0.007 A (30 μg of cobalt)	158
Coal fly ashes	- reagent = 2-[2-(3,5-dibromopyridyl)azo]-5-dimethylaminobenzoic acid (3,5-diBr-PAMB) - dimethylformamide solution - acetate buffer pH 4.8 - potassium periodate solution - dichloromethane	- stable green complex was extracted into dichloromethane - λ_{anal} = 673 nm - pH 4.8	- $\varepsilon = 1.55x10^5$ l/mol.cm - linear range = 0-3.5 μg of cobalt per 10 ml of dichloromethane - RSD = 0.8% (2.35 μg of cobalt; n=20)	159
Mixtures of cobalt and nickel	- reagent = 1-hydroxy-2-carboxyanthra-quinone in absolute ethanol - ammonia solution	- medium = alkaline ethanol-water mixtures - first-derivative spectrophotometry	- range of application = 0.75-4.5 μg cobalt/ml	160

Table 1.6 Continued...

Sample	Reagent	Condition	Linear range Detection limit	Ref.
Alloy steels	- reagent = 4-(1'H-1',2',4'-triazol-3-ylazo)-2-methyl-resorcinol (TrAMR) in methanol - Tris-0.1 M $HClO_4$ buffer solution pH 8.10 - ionic strength = 0.25 M $NaClO_4$	- pH 8.10 - the second-derivative spectra were recorded against a reagent blank between 650 and 400 nm - slit width = 2 nm - scan speed = 120 nm/min - response time = 7sec	- determination range = 0.12-1.18 mg cobalt/l	161
Cobalt and nickel mixtures	- reagent = benzyl-2-pyridylketone 2-pyridylhydrazone (BPKPH) in absolute ethanol - borate buffer pH 9.0	- pH 9.0 - the method is based on the interference-free character of the isodifferential points in the derivative calibration graphs	- linear range = 0-2.25 μg cobalt/ml	162
High speed tool steels and vitamin B_{12}	- reagent = ammonium thiocyanate + benzyl-tributylammonium chloride solution - phosphate buffer pH 7 - chloroform - anhydrous sodium sulphate	- pH 7 - solvent extraction - λ_{anal} = 625 nm	- linear range = 0-120 μg of cobalt - ε = 1327 l/mol.cm - coefficient of variation = 0.93% (40 μg of cobalt; n=7) - detection limit (3σ) = 0.5 μg/ml	162
Synthetic mixtures of iron and cobalt	- reagent = pyridoxal thiosemicarbazone (PT) in N,N'-dimethylformamide - acetate buffer pH 3.85 - potassium nitrate solution	- pH 3.85 - temp. = 25±0.1 °C for 5 min - λ_{anal} = 425 nm - kinetic determination of iron and cobalt mixtures without a prior separation - based on the differential reaction rate between PT and these metallic ions	- ε (Co) = 1.15×10^4 l/mol.cm	164

1.5.1.4 FIA Methods

FIA has proved to be suitable for rapid, simple and reproducible determination with inexpensive apparatus such as a spectrophotometer. Various FI spectrophotometric methods for the determination of cobalt have been reported. The use of solution chemiluminescence in analyses for inorganic and organic species at trace levels has received attention mainly because of the simplicity of the instrumentation, the low detection limits for some species, and the wide dynamic range, despite a lack of selectivity. FIA is very suitable for the determination of cobalt based on

chemiluminescence measurements. FI on-line separation and preconcentration techniques were shown to be very effective in enhancing the sensitivity and selectivity of methods based on flame atomic absorption spectrometry (FAAS) for the determination of trace metals in samples with complex matrices. Flame atomic absorption spectrophotometric methods for the determination of cobalt using a FI system with on-line perconcentration have been described. The FI methods for the determination of cobalt are reviewed in Table 1.7.

Table 1.7 A brief review of the FIA methods for the determination of cobalt

Sample	Reagent	Measurement Technique and Condition	Linear range Detection limit RSD Sample rate	Ref.
Biological sample pepper-bush (NIES-CRM No.1)	- reagent = 2-(5-bromo-2-pyridylazo)-5-(N-propyl-N-sulphopropylamino)aniline (PsAA) solution pH 4.1 - EDTA solution pH 4.1 - acetate buffer pH 4.1	- Spectrophotometry - λ_{anal} = 602 nm - temp. = 40 °C - Cu(II) enhances the rate of the slow complex formation reaction	- detection limit = 1 ng/ml - RSD = 1.4% (50 ng/ml; n=10) - linear range = 0-120 ng/ml cobalt - sample throughput = 30/h	165
Sea-water	- N,N'-diethyl-p-phenylenediamine (DePD) - R1 = DePD + Tiron - R2 = $Na_2B_4O_7$ + NaOH + H_2O_2 - carrier = acidified sea-water depleted of cobalt	- Spectrophotometry - λ_{anal} = 554 nm - based on the catalytic effect of cobalt(II) on the oxidation of DePD by H_2O_2 in the presence of Tiron as an activator - temp. = 30 °C	- linear range = 0-300 ng cobalt(II)/l - detection limit (three times the blank signal) = 1 ng/l - sample rate = 50/h - RSD = 2-8% (10-100 ng cobalt/l)	166
-	- 2(4-sulfophenylazo)-1,8-dihydroxynaphthalene-3,6-disulfonic acid (SPADNS) - R1 = H_2O_2 - R2 = SPADNS	- Spcetrophotometry - λ_{anal} = 520 nm - based on the catalytic effect of cobalt on the oxidation of SPADNS by H_2O_2 in alkaline media - temp. = 25-30 °C	- determination range = 0.05-2 ng of cobalt in 10-20 µl (5-200 µg/l) - sample rate = 60/h - RSD = 2.0% (100 µg Co/l) by normal FI and 2.5% (50 µg Co/l) in the stopped-flow mode	167

Table 1.7 Continued...

Sample	Reagent	Measurement Technique and Condition	Linear range Detection limit RSD Sample rate	Ref.
Tool steels	- carrier stream = 10% w/v ammonium fluoride - R1 = 5% w/v ammonium thiocyanate - R2 = 0.5% w/v ethylenebis (triphenylphosphonium) bromide - solvent = chloroform	- Spectrophotometry - λ_{anal} = 625 nm - based FI extraction into chloroform of the ion associate ethylenebis(triphenyl-phosphonium)tetrathio-cyanatocobaltate(II) - segmenter = mixing chamber - membrane phase separator	- injection rate = 20/h - linear range = up to 20 μg/ml - detection limit = 0.23 μg cobalt/ml - RSD = 0.75% (10 μg/ml; n=10)	168
-	- reagent = 2-hydroxy-benzaldehyde thiosemi-carbazone (2-OH.BAT) - carrier = 2-OH.BAT + acetate buffer (pH 5.2)	- Spectrophotometry - λ_{anal} = 400 nm - simultaneous determination of cobalt and nickel based on the different formation rate of their complexes with 2-OH.BAT - three FIA configuration are presented	-	169
-	- reagent = 2-hydroxy-benzaldehyde thiosemi-carbazone (2-OH.BAT) - carrier of pH 5.2 consisting of a mixture of 2-OH.BAT solution + acetate buffer pH 5.1 + distilled water	- Spectrophotometry - two serial injection valves - inserts two zones of the same sample simultaneously into a channel, which results in a two-peak recording - the manifold was applied to individual kinetic and differential kinetic determination of cobalt and nickel based on their different complexation rates with 2-OH.BAT	- linear range = 5.0-50.0 μg/ml for both analytes - sampling frequency = 15/h	170 171
Tool steel samples	- reagent = 4-(2-pyridylazo) resorcinol (PAR) - R1 = 0.01 M sodium citrate - R2 = 0.1 M sodium tetraborate - R3 = 0.001 M PAR - R4 = 0.1 M Na_2EDTA + 0.01 M sodium pyrophosphate	- Spectrophotometry - λ_{anal} = 520 nm - the method exploits differences in reaction rates between cobalt and nickel citrate complexes and PAR	- determination range = up to 5.00 mg/l - sampling frequency = 40/h	172

Table 1.7 Continued...

Sample	Reagent	Measurement Technique and Condition	Linear range Detection limit RSD Sample rate	Ref.
-	- reagent = ethylene glycol-bis(2-aminoethyl ether)-N,N,N',N'-tetraacetic acid (EGTA) and 4-(2-pyridyl-azo)-resorcinol (PAR) - R1 = EGTA + TRIS buffer pH 8.05 - R2 = double distilled water - R3 = PAR	- Spectrophotometry - exchange reactions between the EGTA complexes of Fe(III), Co(II), and Zn(II) and PAR were used - stopped-flow injection analysis - temp. = 25±1 °C - diode array detector - using partial least-squares regression	-	173
-	- reagent = 2-carboxyl-2-hydroxy-5-sulfoformazyl-benzene (Zincon) - carrier = water - R = borate buffer pH 9.0 + Zincon	- Spectrophotometry - simultaneous spectrophotometric resolution of binary and ternary mixtures with the aid of a multivariate calibration method - using partial least squares program - wavelength range = 400-770 nm	- application range = 0.397-1.590 μg Co(II)/ml	174
Several steel samples	- reagent = pyridoxal-4-phenyl-3-thiosemicarbazone (PPT) - R1 = PPT in N,N-dimethylformamide (DMF)-water (3+7 v/v) - R2 = 3 M $HClO_4$ - C_{18} packed in the flow cell - eluent = 30% $HClO_4$ in DMF-water (3+7 v/v)	- Spectrophotometry - simultaneous determination of cobalt and copper in binary mixtures by use of a diode-array detector accommodated in a flow-through sensor and first-derivative spectrometry - using preconcentration step - first-derivative spectrum was recorded over the range 200-500 nm	- detection limit = 0.03 μg/ml for both - RSD = 2.0% (P=0.05; n=11) - sampling rate = 36/h	175

Table 1.7 Continued...

Sample	Reagent	Measurement Technique and Condition	Linear range Detection limit RSD Sample rate	Ref.
Sea water	- 1 M HCl/ 0.1 M HNO_3 - 0.05 M HCl - 0.02 M gallic acid/ 0.4 M H_2O_2 - 0.15 M NaOH/ 4% methanol - immobilized 8-hydroxy-quinoline column	-Chemiluminescence - Co-enhanced chemiluminescent oxidation of gallic acid in alkaline hydrogen peroxide - a preconcentration/ separation step in the FIA manifold with an in-line column of immobilized 8-hydroxyquinoline was included to separate the Co from alkaline-earth ions	- one sample analysis = 8 min - detection limit = 8 pM - average SD = $\pm$5%	176 177 178
Water and vitamin B_{12}	- carrier = water - R1 = 0.001 M Luminol + KOH + Na_2CO_3 - R2 = $3x10^{-4}$ M KIO_4	- Chemiluminescence - based on the measurement of metal-catalysed light emission from luminol oxidation by potassium periodate - a flow cell formed by a spiral of transparent tubing suitable for chemiluminescence measurement - pH = 12.9	- detection limit = 0.01 ng Co(II)/ml - linear range = up to 12 ng Co(II)/ml	179
Biological materials	- R1 = 2% sodium citrate in 1 M pH 9.2 ammonia-acetic acid buffer - R2 = 0.5% nitroso-R salt/ 0.01 M tetrabutylammonium bromide (TBABr) solution - C_{18} micro-column - eluent = ethanol - masking agent for iron = sodium citrate solution	- FAAS - using a FI system with on-line preconcentration and separation by ion-pair adsorption of the cobalt-nitroso-R salt complex in the presence of tetrabutyl-ammonium bromide as a counter ion reagent - collecting time = 60 s	- sampling frequency = 45/h - detection limit (3σ) = 3 µg/l - RSD = 2.4% (50 µg/l)	180
Commer-cially available soda-lime-magnesia silica glasses	- carrier 1 = 0.1 M NH_4Oac buffer (pH = 2.7) - carrier 2 = 1 M NH_3-NH_4Cl buffer (pH = 8.5) - Chelex-100 minicolumn - eluent = 200 µl plug of 5 M nitric acid	- FAAS - FI ion-exchange preconcentration, using a minicolumn loaded with Chelex-100 - sample (adjusted to a pH of 7.0$\pm$0.1)	- detection limit = 20 ng Co/ml - precision = $\pm$1.5% (0.5 µg/ml) - linear range = up to 1.2 µg/ml	181

Table 1.7 Continued...

Sample	Reagent	Measurement Technique and Condition	Linear range Detection limit RSD Sample rate	Ref.
Oriental tobacco leaves certified standard material	- carrier stream = deionized water - R = 5 mM NRS solution (NRS = 1-nitroso-2-naphthol-3,6-disulphonate) - alumina microcolumn - eluent = sodium hydroxide	- FAAS - using alumina loaded with NRS for the on-line preconcentration of cobalt(II) - volume-based system and time-based system	- detection limit = 0.44 µg/l - RSD = 2.3% (10 µg/l) - recovery = 97%	182

1.5.2 Manganese

Manganese (Mn) is in its inorganic species a ubiquitous, essential element in nature and in its occurring concentrations hardly toxic. Relatively large doses can be tolerated without injury. The manganese cycle plays a role in surface waters (interactions with the aquatic biota). Interactions with other metal compounds are also known. Environmental damage caused by this metal is not known so far. It is available in plants and animal cells in relative high concentrations in the mitochondria, where it acts as a cofactor for the activation of some enzymes [83].

1.5.2.1 Physical and Chemical Properties [83]

Manganese, atomic mass 54.94 and atomic number 25, is a very brittle, hard heavy metal of white-gray colour; density, 7.2 up to 7.4 g/cm^3; melting point, 1244 °C; boiling point about 2000 °C. It belongs to the 7^{th} Subgroup of the Periodic Table and is adjacent to iron. Manganese shares many mutual physico-chemical properties with iron. Manganese ores are very often found together with iron ores.

Manganese exists mostly in the oxidation state +2 in natural salts; and in stable native black manganese oxide, MnO_2, its valence is +4. Synthetic compounds are known in nearly all valence stages between –3 and +7. Permanganate as a strong oxidant has the valence +7. Manganese dioxide and the salts manganese carbonate, manganese sulfide, and manganese metasilicate are poorly water-soluble compounds. Important water-soluble compounds are manganese sulfate, manganese chloride, manganese nitrate, and the permanganate ion (MnO_4^-).

1.5.2.2 Uses [83]

The predominant portion (approximately 90%) of manganese is processed into ferro-manganese in blast furnaces and is used for alloying. This metal is necessary for binding oxygen and sulfur during the steel process to a large extent. Furthermore, it is used for the production of alloys together with aluminum, magnesium (electron), and copper (e.g., manganese bronze).

Black manganese oxide (MnO_2) is used as a depolarizer in dry-cell batteries. For various chemical reactions manganese(IV) oxide, manganese chloride, and manganese stearate are used as catalysts (for instance, manganese additives are suggested to improve the regeneration of Diesel exhaust filters, but 85% of the used manganese derivatives will be emitted. Manganese compounds, furthermore, are used as feed additives, fertilizers, pigments, dryers, wood preservatives, and for coating welding-rods. With reference to the organic compounds the fungicide manganese ethylene-bis(dithiocarbamate) (Maneb) and the antiknock agent methylcyclopentadienyl-manganese-tricarbonyl (MMT) are of importance.

1.5.2.3 Analytical Methods

Many techniques have been proposed for the determination of manganese. Examples are as follows:

(a) Spectrofluorimetry

Spectrofluorimetry is essentially a trace analysis technique and is one of the most powerful tools in chemical analysis. 2-(α-Pyridyl) thioquinaldinamide (PTQA) has been reported as a metallofluorescent reagent for the determination of trace amounts of manganese [183].

(b) Candoluminescence Spectrophotometry

The intense yellow candoluminescence given by manganese in a calcium oxide - calcium sulphate matrix when placed in a hydrogen-nitrogen-air flame has been used to investigate the determination of manganese in commercial samples of precipitated calcium carbonate [184].

(c) Atomic Absorption (AAS) and Atomic Emission (AES) Spectrometry

Atomic absorption spectrometry (AAS) is regarded as a useful technique for the determination of metals. The methods for extraction of manganese dithiocarbamate complexes for AAS have been described [185,186]. Direct methods have been developed for the determination of manganese by flame AAS [187] and electrothermal AAS [188,189]. Flame AES has been reported for the determination of manganese [190].

(d) Inductively Coupled Plasma (ICP) Spectrometry

ICP-AES appears to offer advantages of simultaneous multi-element analysis, low detection limits and wide linear dynamic range. The method evaluating function (MEF) is defined as the expected value of the analysis as a function of the "true" content of the analyte in the samples. MEFs for the multi-element determination of Fe, Mn and Ti by ICP-AES have been established [191]. Separation of metalloporphyrins (vitamin B12, cobalt protoporphyrin, manganese protoporphyrin, and zinc protoporphyrin) by capillary electrophoresis with inductively coupled plasma mass spectrometric detection has been developed [192].

(e) Polarography

The polarographic reduction of manganese at a dropping mercury electrode has been studied in the presence of complexing agents such as δ-valerolactam [193] and 2-amino-3-hydroxypyridine (AHP) [194]. The catalytic method for the determination of trace amounts of manganese employing catalytic oxidation of fuchsin with oscillopolarographic detection has been reported [195].

(f) Voltammetry

A method to determine manganese by square-wave adsorptive stripping voltammetry after controlled adsorptive accumulation of the manganese-ammoniumacetate at the glassy carbon electrode has been reported [196].

(g) Potentiometry

A kinetic method for the micro-determination of manganese(II) based on its catalytic action on the chloranilate-dithionite reaction has been described. A chloranilate liquid membrane ion-selective electrode was used to monitor the reaction [197].

(h) High-Performance Liquid Chromatography (HPLC)

Reverse-phase HPLC has been used to determine simultaneously trace levels of Al, Fe, and Mn after direct injection of their 8-quinolinol complexes onto a Bondasphere ODS column [198].

(i) X-Ray Fluorescence Spectrometry (XRF)

XRF spectrometry is a routinely applied technique for both qualitative and quantitative multi-element analysis, particularly for solid samples which often require minimal pretreatment prior to analysis. The quantitative X-ray fluorescence analysis of geological materials using partial least-squares regression has been reported [199].

(j) Radiometry

The use of radiotracers in the study of the distribution of manganese and zinc in the ultrafiltrate fractions of fresh waters has been described [200].

(k) Spectrophotometry

Spectrophotometric determinations of trace concentration of metal ions are usually simple, quick, accurate, and precise. Several spectrophotometric methods have been used to determine manganese. The peroxydisulphate and periodate methods are the most commonly used routine procedures [34]. A number of spectrophotometric procedures have been described for the analysis of manganese(II) using 4-(2-pyridylazo)resorcinol (PAR) [201], 1-(2-pyridylazo)-2-naphthol (PAN) [105], formaldoxime [202,203], sodium diethyldithiocarbamate [204], triethanolamine [205], 2-theonyltrifluoroacetone [206], calcichrome, biacetyl oxime thiosemicarbazone, and dipicolinic acid [153]. A brief review of the spectrophotometric methods for the determination of manganese is summarized in Table 1.8.

Table 1.8 A brief review of the spectrophotometric methods for the determination of manganese

Sample	Reagent	Condition	Linear range Detection limit	Ref.
Gasoline	- bromine in carbon tetrachloride - nitric acid - phosphoric acid - potassium periodate	- the manganese compound is decomposed using a solution of bromine in carbon tetrachloride - the manganese is extracted with phosphoric acid, and a mixture of nitric and phosphoric acids is added to oxidize the organic material in the extract - the extracted manganese is determined by a periodate oxidation - λ_{anal} = 525 nm	- accuracy = within 2% of the true value	207
Water	- reagent = o-tolidine in dilute phosphoric acid (1+3) - dilute ammonia solution (1+1) - ammonium iron(III) sulphate solution - magnesium chloride solution	- oxidation products of manganese react with o-tolidine to produce a yellow colour - oxidation with atmospheric oxygen in alkaline solution in the presence of magnesium and iron(III) salts - λ_{anal} = 440 nm - measuring cells, 2 cm	- linear range = up to 1.6 mg/l	208
-	- reagent = 4-(2-pyridylazo) resorcinol (PAR) - borate buffer pH 10	- allowing the solution to equilibrate for about 15 minutes to ensure complete colour development - λ_{anal} = 500 nm - pH 10	- linear range = 2-20 μM (0.1-1.1 μg Mn(II)/ml - ε (Mn(II)-PAR) = 78000 l/mol.cm	209
Nonferrous alloys	- antimony trichloride solution - phosphate buffer 0.5 M, pH 6.70 - 0.015 M sodium periodate solution	- based on its catalytic effect on the periodate-antimony(III) reaction - temp. = 20 °C	- determination level = 10^{-8}-10^{-6} M - average error about 2%	210
Foodstuffs	- 3-(2-hydroxyphenyl-azo)pyridine-2,6-diol (HPAPD) in ethanol - buffer pH 9.3 (NH_4OH/HCl) - 0.08 M H_2O_2 - 3 M NaCl	- based on its catalytic effect on the oxidation of HPAPD - λ_{anal} = 472 nm - pH 9.3 - temp. = 25±0.1 °C	- linear range = 0.5-9.1 ng Mn(II)/ml - RSD = 3.7% (2.23 ng/ml; n=11)	211

Table 1.8 Continued...

Sample	Reagent	Condition	Linear range Detection limit	Ref.
Alloys	- ascorbic acid - chelating agent = 2-(5-bromo-2-pyridyl-azo)-5-diethylamino-phenol (5-Br-PADAP) + poly(oxyethylene)$_n$ 4-nonylphenyl ether (n=10) (PONPE-10) solution - 0.01 M dimercapto-succinic acid (DMSA) - 0.1 M diethylene-triamine (Dien) - 0.1 M citrate solution - ammonium buffer solution pH 10	- using efficient masking method - DMSA and Dien were an excellent combination for the specific determination of manganese(II) - λ_{anal} = 567 nm	- linear range = 0-8.08 µg of Mn(II) per 25 ml - $\varepsilon = 1.2 \times 10^5$ l/mol.cm - RSD = 0.39% (6.06 µg of manganese(II); n=9)	212
Agricultural samples such as soils and wines	- 0.75%m/v 3-hydroxy-benzaldehyde azine (3-OHBAA) in ethanol - copper(II) solution in 1% v/v nitric acid - 0.1 M potassium peroxydisulphate solution - conc. ammonia - ethanol	- indirect kinetic determination - based on its inhibitory effect on the copper(II)-catalysed oxidation of 3-OHBAA by potassium peroxydisulphate in an ethanol-ammonia medium - λ_{anal} = 465 nm - temp. = 30±0.1 °C	- linear range = 0.5-5.0 ng/ml - RSD = 1.5% (5 ng/ml; n=11) - detection limit = 0.13 ng/ml	213
Decoction of a traditional Chinese medicines	- Malachite Green solution - potassium periodate solution - sodium fluoride solution - ethanoic acid/ ammonium acetate buffer pH 3.8	- kinetic spectrophotometry - based on the catalytic effect of manganese(II) on the oxidation of Malachite Green by potassium periodate - λ_{anal} = 615 nm - temp. = 40 °C; 30 min.	- determination range = 0.2-2 ng manganese(II) - detection limit = 0.1 ng	214
Tap and river water	- chelating sorbent was synthesized by chemical attachment of aminocarboxylic (diethylenetriamine-tetraacetate, DETATA) groups to cellulose filter-paper (2.5 cm in diameter) - borate buffer pH 6.8 - 3,3',5,5'-tetramethyl-benzidine (TMB) in ethanol - periodate (KIO_4) solution	- sorption-catalytic technique - a hybrid technique based on a catalytic reaction carried out on the surface of a paper-based sorbent - Mn(II) exhibits its catalytic action in the oxidation of TMB with periodate on filter-paper with or without attached DETATA groups - λ_{anal} = 650 nm	- limit of determination = down to 5×10^{-6} mg/l - linear range = 5×10^{-6}-2.5×10^{-3} mg/l - RSD ≤ 5% for ≥ 6×10^{-4} µg Mn	215

Table 1.8 Continued...

Sample	Reagent	Condition	Linear range Detection limit	Ref.
Water samples	- digestion acid = HCl + hydroxylamine hydrochloride - acid-wash = HCl (4% by volume) - reagent = formal-doxime solution = hydroxylamine hydrochloride + 37% formaldehyde - ascorbic acid solution - buffer solution = NH_4Cl/NH_4OH pH 10.0 - masking agent = hydroxylamine hydrochloride + EDTA	- using batch digestion by autoclaving in acid medium followed by automated colourimetry - based upon the formation of the manganese-formaldoxime complex - cation interference is suppressed by complexing agent - colour interference is eliminated by using a blanking stream which is synchronized with the colour stream - λ_{anal} = 480 nm - pH = 10.0±0.2	- $\varepsilon = 1.1 \times 10^4$ - linear range = 0-0.200 mg Mn/l - detection limit = 0.006 mg Mn/l	216 217

1.5.2.4 FIA Methods

Usually batch procedures are time consuming. The applications of FIA to kinetic-catalytic methods leads to reproducible results with strict control of the mixing of the reagents and reaction time and thus overcomes the problems in batch methods. Some oxidation processes of organic compounds catalysed by manganese(II) have been applied to FIA for the determination of traces of this ion. Various FIA methods for the determination of manganese are summarized in Table 1.9.

Table 1.9 A brief review of the FIA methods for the determination of manganese

Sample	Reagent	Measurement Technique and Condition	Linear range Detection limit RSD Sample rate	Ref.
Natural waters	- carrier (R1) = $1x10^{-3}$ or 0.1 M HCl - R2 = 0.50 M H_2O_2 - R3 = N,N-dimethyl-p-phenylenediamine (DPD) + 1,2-dihydroxybenzene-3,5-disulfonate (tiron) + L-cysteine - R4 = m-phenylenediamine (PDA) + triethylene-tetramine (trien) + 0.4 M NH_3	- Spectrophotometry - λ_{anal} = 650 nm - based on its catalytic effect on the oxidative coupling of DPD with PDA in a presence of hydrogen peroxide - the catalytic activity was greatly enhanced by the presence of trien and tiron - temp. = 35±0.1 °C - pH = 9.7-9.9	- linear range = 0.05-1.0 ng Mn(II)/ml - RSD = 1.5% (0.3 ng/ml; n=10) - detection limit (S/N=2) = 10 pg/ml - throughput rate = 25/h	218
Natural water	- 0.1 M Tiron (1,2-dihydroxybenzene-3,5-disulphonic acid) - $2x10^{-2}$ M 1,10-phenanthro-line (used as an activator) - 0.5 M hydrogen peroxide - borate buffer pH 9.5 - 0.002% bromothymol blue (BTB)	- Spectrophotometry - λ_{anal} = 620 and 440 nm - catalytic kinetic spectrophotometry - based on the principle of Mn(II) catalysis of the Tiron-hydrogen peroxide reaction - combination with a microcomputer, by using gradient dilution and the stopped-flow method, only a single standard solution was needed for calibration	- sampling rate = 40/h - RSD ≤ 5.5% (n=6)	219
High-purity titanium and silicon, high-purity HF, HCl and HNO_3	Ion-exchange separation system - cation exchange resin (Amberlite CG-120, H^+-form) - R1, R4 = 1.5 M HF/ 0.2 M HCl - R2 = water - R3 = 6 M HCl FI system - carrier = acetate buffer pH 4.4 - R1 = malachite green solution - R2 = potassium periodate solution	- Spectrophotometry - λ_{anal} = 615 nm - preliminary microscale ion-exchange separation - catalytic effect of manganese on the malachite green/ periodate reaction is utilized - main reaction coil was immersed in a thermostated water bath at 50±0.1 °C - cell chamber was maintained at 20±0.1 °C	- linear range = up to 7 ng of manganese - RSD = 2% (3 ng of manganese; n=5)	220

Table 1.9 Continued...

Sample	Reagent	Measurement Technique and Condition	Linear range Detection limit RSD Sample rate	Ref.
Some analytical-reagent grade reagents and food products such as coffee and rice	- carrier = H_2O - R1 = succinimide dioxime (SIDO) - R2 = 1.5 M NaOH	- Spectrophotometry - λ_{anal} = 695 nm - catalytic effect of Mn(II) on the oxidation of succinimide dioxime in alkaline medium - variation of the reaction temperature between 25 and 45 °C allows the determination range to be extended from 0.2 to 1300 ng/ml	- sampling frequency = 45/h - RSD = 1.3-1.0%	221
Deep sea water	- eluent = 0.5 M HNO_3 - reagent = N,N-diethyl-aniline - oxidant = potassium periodate	- Spectrophotometry - λ_{anal} = 475 nm - based on the catalytic properties of manganese in the oxidation of N,N-diethylaniline with potassium periodate - associated with an in-valve separation/ preconcentration using a microcolumn filled with fibrous diethylenetriaminetetra acetic acid as an ion exchanger - temp. = 30 °C	- measurement range = 0.0002-0.4 µmol/l - RSD = 5-8% - Sample throughput = 4-12/h	222
Seawater	- eluent = HCl - reagent = leucomalachite green (LMG) in HCl - oxidant = potassium periodate - Tris buffer pH 7.8	- Spectrophotometry - on-line concentration of Mn(II) onto 8-hydroxyquinoline immobilized onto a vinyl polymer gel - detection of the malachite green formed from the reaction of leucomalachite green and potassium periodate with Mn(II) acting as a catalyst - seawater at pH = 7.8±0.2	- limit of detection = 36 pM (concentrating 15 ml of seawater) - precision = 5% (= 400 pM) - analysis time = 5.5 min per sample	223

Table 1.9 Continued...

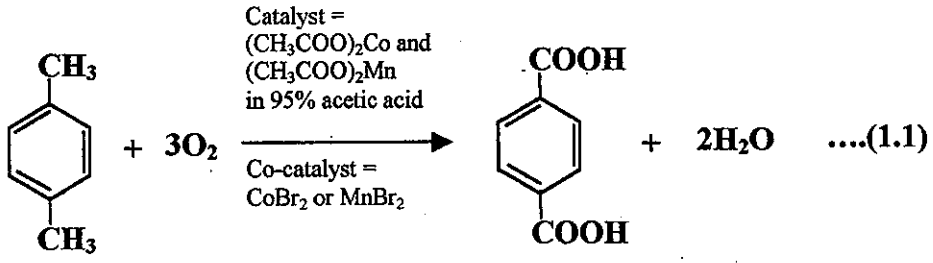
Sample	Reagent	Measurement Technique and Condition	Linear range Detection limit RSD Sample rate	Ref.
Natural water and effluent streams	- carrier = 0.1 M HNO_3 - solid-phase reactor packing consisted of PbO_2 suspended on silica gel beads	- Spectrophotometry - using a solid-phase reactor incorporated into a FI system - Mn^{2+}-ions in sample injected into a carrier stream, were oxidized by solid lead(IV) dioxide suspended on silica gel beads to form MnO_4^--ions which were detected spectrophotometrically at 526 nm - temp. = 60 °C	- linear range = 1-5 mg/l - detection limit = 0.56 mg/l - RSD ≤ 1.8% - recovery = 94.7-103.1%	224
Natural waters and plant digests	- reagent = formaldoxime solution = hydroxyl-ammonium chloride + 37% m/v formaldehyde - carrier = water - reduction stream = 5% m/v ascorbic acid - neutralisation stream = 6 M NaOH	- Spectrophotometry - formation of Mn(II)-formaldoxime complex - λ_{anal} = 455 nm	- sample throughput = 135/h - standard deviation = better than 1% - linear range = 0.2-2 mg manganese/l	225
-	- carrier = salicylaldehyde thiosemicarbazone (SAT) + ethanol + ammonia + hydrogen peroxide	- Fluorimetry - determination of manganese and iron - based on their catalytic action on the oxidation of SAT by hydrogen peroxide - λex = 357 nm - λem = 437 nm	Sequential method - linear range = 48-200 ng/ml - RSD = 1% - sample rate = 30/h Differential method - linear range = 40-600 ng/ml - RSD = 1.2-2.5% - sample rate = 23/h	226
-	- sorbent = C_{18} bonded silica gel - eluent = methanol or ethanol - chelating agent = dialkyldithiophosphates (DDP)	- AAS - FI sorbent extraction - pH = 3 for extraction	-	227
Stainless steels	- electrolyte solution = 0.5-2.0 M nitric or hydrochloric acid and equimolar mixtures of these acids from 0.25 to 1.0 M	- ICP-AES - on-line electrolytic dissolution in FIA	- sample throughput = 60 solid samples/h	228

Table 1.9 Continued...

Sample	Reagent	Measurement Technique and Condition	Linear range Detection limit RSD Sample rate	Ref.
Water samples	- carrier electrolyte = 0.1 M sodium sulfate supporting electrolyte, adjusted to pH 4.0-4.3 with 1.0 M nitric acid	- Galvanostatic Stripping Chronopotentiometry - a flow-through electrochemical cell, with a porous working electrode made of crushed glassy carbon - deposition at +1.2 V versus an Ag-AgCl reference electrode - the deposit was dissolved galvano-statically by applying a current of between –50 and –1000 μA - monitoring the potential of the working electrode	- working range = from $1x10^{-4}$ M down to $1x10^{-7}$ M - RSD = 2-4% ($5x10^{-6}$ M)	229

1.5.3 Oxidation of Xylenes to Terephthalic Acid [230,231]

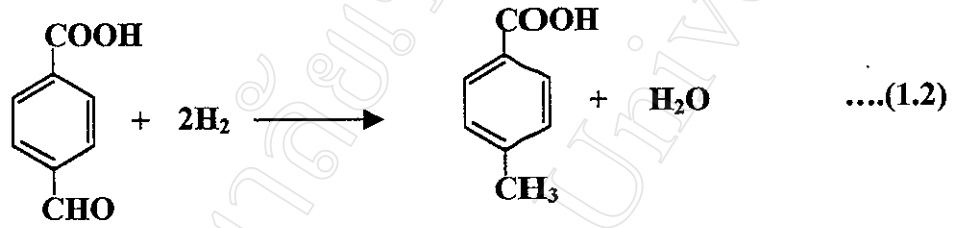
Commercial methods for preparing terephthalic acid which are widely accepted involve the liquid-phase oxidation of alkylbenzene such as para-xylene with a gas containing molecular oxygen in a lower aliphatic monocarboxylic acid as a solvent in the presence of a catalyst containing a heavy metal such as cobalt, manganese, or a bromine compound. The Amoco process is the most widely used process. In the commercial operation, a catalyst combination of Co and Mn acetate in 95% acetic acid is employed. A mixture of NH_4Br and tetrabromoethane serves as co-catalyst. However, variants of the Amoco process involve the addition of a co-catalyst in the form of $CoBr_2$ or $MnBr_2$ whereby bromine functions as a regenerative source of free radicals. p-Xylene is oxidized with air in autoclaves, fitted with stirrers, at 190-205 °C and 15-30 bar. The reaction is



....(1.1)

The equipment must be lined with titanium or Hastelloy C on account of the corrosive catalyst solution. The oxidation product is cooled and the terephthalic acid, which has crystallized out, is separated.

In the purification section of the plant, the crude acid is dissolved (under pressure) in water at 225-275 °C and then subjected to hydrogenation in the presence of, for example, a Pd catalyst. By this means, 4-carboxybenzaldehyde (which has been formed as a by-product) is hydrogenated to p-toluic acid with a Pd/charcoal catalyst, thereby removing a source of difficulty in the polycondensation process. The reaction is



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The aqueous solution is cooled, causing the pure terephthalic acid to crystallize out with 99.9 percent purity.

1.6 Research Aims

The aims of this research work are as follows:

1. To develop a FIA system involving on-line solvent extraction for the determination of anionic surfactants.
2. To develop a FIA system involving on-line solvent extraction for the determination of hyoscine butylbromide in antimuscarinic drugs.
3. To adapt a batch arsenazoIII method to a FIA procedure for the determination of yttrium in ore leachates of reference materials and samples.
4. To develop a FIA system for the spectrophotometric determination of cobalt and manganese in samples from a petrochemical process.