ELSEVIER

MICROCHEMICAL JOURNAL

Microchemical Journal 65 (2000) 87–95

www.elsevier.com/locate/microc

On-line flow injection solid sample introduction digestion and analysis: spectrophotometric and atomic absorption determination of iron, copper and zinc in multi-vitamin tablets ☆

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Received 4 March 2000; received in revised form 19 April 2000; accepted 23 April 2000

Abstract

An on-line flow injection system with solid sample introduction, digestion, treatment and analysis was proposed. The solid sample powder is inserted into a special chamber and carried by the digestion solution to a thermally heated PVC coil (1.4 mm i.d.). The analyte metal as the chloro-complex was retained on a coarse-particle (> 0.5 mm) anion exchange resin mini column. The resin beads are held between two plastic screens which allow insoluble residue to pass through to waste. After a brief column wash, the analyte is eluted with diluted HNO_3 and determined spectrophotometrically or by atomic absorption. The proposed novel configuration of the multi-channel pinch valve allows handling slurries without tube blockage or valve damage. The system performance was tested by the determination of Fe, Zn and Cu in multi-vitamin tablets. Fe was determined spectrophotometrically as the thiocyanate complex while Zn and Cu were determined by atomic absorption. Compared with conventional digestion and analysis procedures the flow system yields a reasonably accurate relative error (RE) < 2% and precise results with relative standard deviation (R.S.D.) in the range of 2.5–4.2%.

Keywords: On-line digestion; Flow injection; Solid sample insertion; Anion exchange; Spectrophotometry; Atomic absorption; Vitamin tablets; Iron; Copper; Zinc

☆ Dedicated to Professor P.K. Dasgupta.

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0026-265X/00/$ - see front matter
PII: S0026-265X(00)00035-7

1. Introduction

With the advent of instrumental analysis, sample preparation is becoming the largest single contributor to variance in analytical results and accounts for most of the analysis time and cost. Since most analytical instruments handle liquid samples, attention is being directed towards improving sample dissolution.

Several strategies have been devised to achieve faster, easier and more automated sample preparation; which include test-tube heating block digestion [1], fusion with suitable fluxes [2–5], sequential closed vessel microwave assisted digestion [6–13], selective leaching of the analyte of interest [14] and direct aspiration of a sufficiently small particle size slurry [15]. Only few attempts were made to couple a solid sample digestion step to a flow injection analysis system [8–11]. This is mainly due to the fairly long digestion time which results in a low analytical throughput. A second reason for the difficulty with a combined solid-sample digestion flow analysis system is the need for a filtration step of the insoluble residue encountered in many sample preparation procedures.

Fixed volume solid sample injection into the system requires a homogeneous suspension. This is achieved by aspiration of a finely pulverized sample suspension in a suitable liquid in the presence of anti-settling agents with efficient stirring [6,13]. This is a must for volumetric sampling and necessary for complete transfer of the slurry to the digestion unit. Particle size distribution and settling are still major drawbacks in such systems. Slurry injections with conventional valves could cause frequent system blockages and could scratch the soft valve's movable parts with subsequent leaks and eventual failure. Aspiration by peristaltic pumps also suffers from incomplete sample transfer, potential loss on pump tube walls and connectors, and inter-sample contamination.

Still another problem with on-line sample digestion is gas bubble formation and pressure build-up during the dissolution step [6,12]. A debubbling unit is necessary prior to a continuous flow spectrophotometric or potentiometric detection step. Obviously, total dissolution is ideal for elimination of tube blockage by insoluble residue. However, total dissolution may require a lengthy multi-step digestion and harsh conditions [6,12] which do not lend themselves to automation. In many cases, total dissolution is unnecessary and could reduce matrix interference and save time and reagents [14].

In this work a filterless on-line solid sample introduction and digestion module is coupled to a spectrophotometric or atomic absorption spectroscopic detector. The solid powdered sample is inserted manually into the carrier digestion solution and heated thermally to accelerate the digestion step. The residue and air bubbles are passed to waste through a coarse screen while the analyte (as the chloro-complex) is ion exchanged in a mini column of coarse-particle anion exchange resin. Finally, a carrier solution is aspirated to strip the analyte from the resin and direct it to the detector.

2. Experimental

2.1. Reagents and standards

All solutions were prepared with distilled deionized water. Hydrochloric acid (4 M) was passed twice through an anion exchange resin in the chloride form to remove impurities of analyte ions. The following solutions were prepared from reagent grade chemicals or better; 0.1 M potassium thiocyanate, 0.1 M nitric acid, 10^{-3} M iron(III) nitrate, 10^{-4} M zinc(II) chloride, 10^{-3} M Cu(II) nitrate and 5% (w/v) hydrogen peroxide.

2.2. Samples

Multi-vitamin tablets were purchased from a local pharmacy. The tablets (Supradyn Effervescent tablets, F. Hoffmann-La Roche Ltd. Basel, Switzerland) were pulverized in an agate mortar to a fine powder and homogenized. Each tablet (≈ 1.00 g) contains 1.25 mg of iron as iron(II) carbonate or sulfate and 0.5 mg of zinc as the sulfate, 0.1 mg of Cu as the sulfate. The powder was kept in a clean glass vial in the dark prior to use.

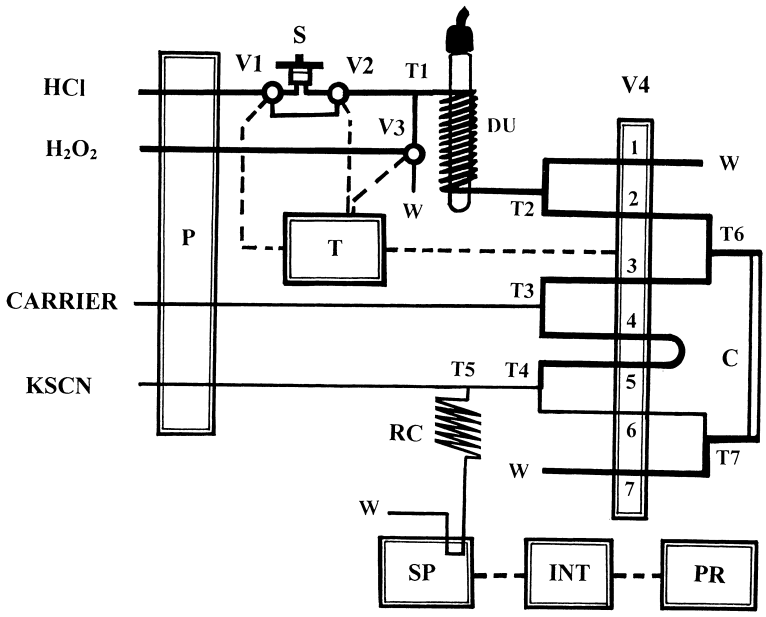

Fig. 1. A schematic diagram for on-line solid sample digestion and flow injection analysis with spectrophotometric detection. P, peristaltic pump; HCl, carrier digestion solution; H_2O_2, oxidant; CARRIER, eluent carrier, 0.10 M HNO_3 solution; V1, V2, V3 are three-way solenoid valves; S, solid sample insertion device; DU, thermal digestion unit; V4, Multi-channel pinch solenoid valve; T, programmable timer; C, anion exchange mini-column; RC, reaction coil; SP, spectrophotometer; INT, integrator; PR, printer; W, waste; line thicknesses indicate relative internal diameter size, and dashed lines are electrical connections.

Comparative determination of iron copper and zinc was carried out by digesting 1.000 ± 0.001 g of the tablet powder in 15 ml of aqua regia (HCl/HNO_3, 3:1 v/v) in a 250-ml conical flask to near dryness. The resulting salts were dissolved in 2.5 ml of conc. HNO_3, diluted to 50 ml, filtered into a clean 250-ml volumetric flask using a Whatman #42 cellulose filter paper, diluted to the mark with water and shaken well. The solution was analyzed for Fe, Cu and Zn by atomic absorption in the manual mode. The tubes used for the flow system were either PVC or Teflon as required. The edges of the polypropylene connectors and tees were sharpened with a pencil sharpener to eliminate internal tube corners which may trap solid particles. Large pore size tubing (1.0–1.4 mm i.d.) were used for slurry flow and narrow pore (0.5 mm i.d.) tubes for aqueous solution streams. Materials of unknown chemical resistance were tested for suitability by soaking in 6 M HCl for 48 h.

2.3. Apparatus

Fig. 1 is a schematic diagram of the proposed system for combination solid sample digestion and spectrophotometric determination of iron in multi-vitamin tablets. Flow streams are propelled by a four-channel constant speed peristaltic pump (Ismatec, model mini-S820) in 1.2-mm i.d. PVC tubes or 0.5-mm i.d. Teflon tubes as indicated below. Valves V1 through V3 are electrically triggered, pinch type solenoid valves (P.N. 075P3WMP12-32, Biochem Valve Corp., Boonton, NJ). V4 is a multiple pinch type solenoid valve (P.N. 0136/-99) which was purchased from Cole-Parmer Co. Vernon Hills, IL). This allows pinching up to 10 channels simultaneously. In order to pinch smaller diameter tubes, the steel pinching pin was lined with a 1-mm-thick PVC sleeve. This narrows the clearance between the pinching pin and the retaining metal base.

The sample digestion section of the apparatus

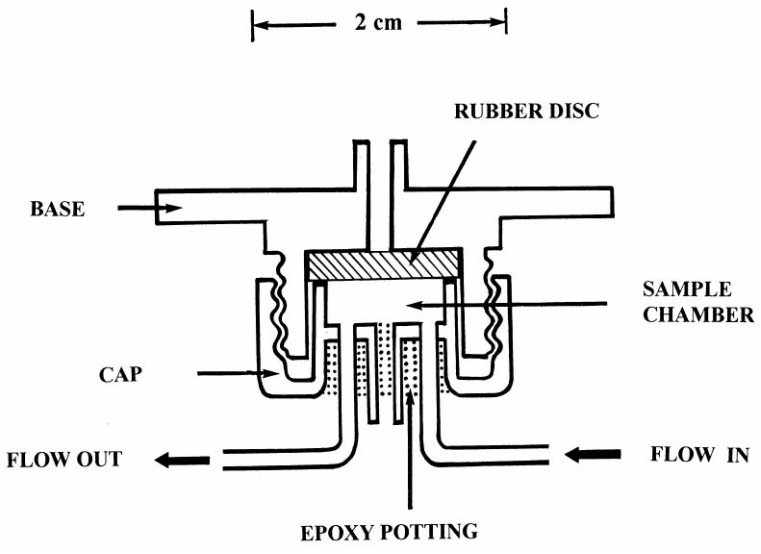

Fig. 2. A cross-section of the solid sample insertion chamber. The material of construction is PVC and Teflon, and the nominal chamber volume is 0.25 cm^3.

used 1.0–1.4-mm i.d. PVC tubing with small barbed tees (Nalgene) for branching. All valves were powered by a 12-V DC power supply and their operation was controlled by a sequential process programmable timer model FXo-14MR-ES through a handheld programming unit model FX-10P-E (Mitsubishi Electric Corp., Tokyo, Japan).

The sample insertion chamber, S, is shown in Fig. 2. It is a modified PVC unit originally used to control the flow rate in drip irrigation systems. A second hole (1.2 mm diam.) was drilled adjacent to the central hole in the cap and two pieces of Teflon tubes (1.0 mm i.d., 1.4 mm o.d.) were snugly inserted to serve as inlet and outlet ports. Epoxy potting was applied around the tubes for extra strength. The barbed inlet in the base section was rendered closed by placing a rubber disc ($\sim$ 1 mm thick and 11 mm diam.) inside the unit. When the two pieces are screwed together the inside edge of the cap presses against the soft rubber disc creating a sealed chamber ($\sim$ 0.25 ml).

The thermal digestion unit (DU), is made from a 450-cm PVC coil (1.2 mm i.d., 0.4 mm wall thickness) wound around the 30-mm o.d. cylindrical glass envelope of a 100-W tungsten lamp (Philips). The 220-V AC circuit for the lamp is equipped with a light dimmer to control illumination and thus the amount of heat generated.

The mini anion exchange column, C, is a 12-cm-long 1.8-mm i.d. silicone tube which comes with multiple pinch valves (Biochem Valve Corp.). The column is filled with 0.66 g of strong anion exchange resin beads (Amberlite IRA-400, $>$ 0.5 mm diam.). The resin beads are retained by a pair of plastic screens, and a pair of 2-mm i.d. polypropylene tees. The ends of the column are crimped to the right angle arms of the tees by fine nickel–chrome wires. The plastic screens which were cut from a bandage are resistant to attack by 6 M HCl and are probably made of PVC or Teflon. Fig. 3 depicts the screen as seen under the optical microscope. The screen allows insoluble residue ($<$ 0.5 mm size) to pass through but retains resin beads ($>$ 0.5 mm diam.).

The spectrophotometric detection of iron is achieved by an 80-μl internal volume flow-through cell (Hellma compact, P.N. 0100-1224, Germany) which was fitted inside the sample compartment of a visible spectrophotometer (model 6100, Jenway, France). Data acquisition and display was performed by a single channel integrator equipped

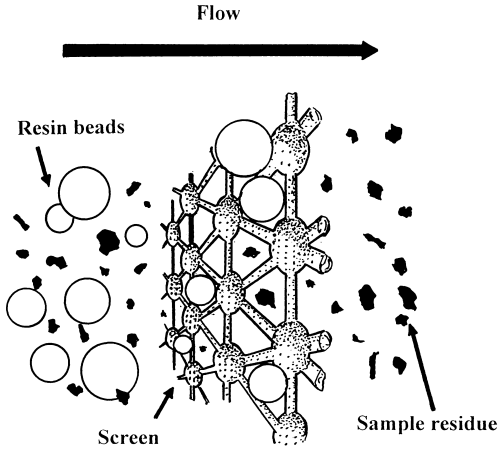

Fig. 3. Depiction of the screen at the end of the mini-column for retention of analyte on anion exchange resin beads and passage of the insoluble sample residue to waste.

with a video screen for real time signal display (PE Nelson) and a Hewlett-Packard printer (Model 690C).

2.4. Procedure

In a typical run the digestion lamp is turned on and adjusted to the proper heating setting. Next, V1, V2 and V3 are switched on for 30 s thus diverting oxidant flow to waste and by-passing the digestion solution flow stream (6 M HCl) around the sample insertion unit. The weighed sample is placed in the chamber and the unit screwed tight. Then, V4 is activated for 3.5 min and V1, V2 and V3 are deactivated. Both the oxidant stream and digestion solution stream drive the solid sample into the digestion coil. During this cycle, the digested material and the residue are pumped through the anion exchange resin column, C, via V4 (channels 2 and 7). In the mean time, the carrier (0.1 M HNO_3) passes through channels 4 and 5 towards the detection unit establishing a baseline signal. Channels 3 and 6 are pinched close at this stage. Next, V3 is activated for 2 min to divert oxidant flow to waste. Bubble-free HCl digestion solution flushes the digestion-ion exchange system to drive-off air bubbles. Then, V4 is activated for 0.7 min which allows the carrier solution to elute the iron(III) chloro-complex by converting it to the free cation iron(III) through channels 3 and 6. At this stage, channels 2, 4, 5 and 7 are closed while channel 1 is diverting the digestion solution to waste. The acidified iron(III) slug is then merged with 0.5 M potassium thiocyanate stream at T5. The combined stream is then pumped through the reaction coil, RC, and the flow cell of the spectrophotometer (SP) yielding a peak shaped response function. At this stage the system is ready for the next sample. Table 1 lists the timing program steps as described above.

For flame atomic absorption detection, the presence of some air bubbles in the flow system is less critical. Therefore step three was eliminated and a 30-cm-long 0.5-mm-i.d. Teflon tubing connected T4 to the nebulizer of the Unicam 929 flame atomic absorption spectrometer. The instrument was run at a starved flow of 4.0 ml min^{-1} which is lower than the 'natural' aspiration rate of the nebulizer (6.2 ml min^{-1}). Data acquisition was achieved using the Solaar® software in the flow injection mode.

Table 1
Time programming sequence and valve status in the on-line sample digestion and spectrophotometric determination of iron in multi-vitamin tablets

Step	Time duration (min.)	Valve status									
		V1	V2	V3	V4 (channel no.)						
					1	2	3	4	5	6	7
1	0.5	On	On	On	Off	On	Off	On	On	Off	On
2	3.5	Off	Off	Off	Off	On	Off	On	On	Off	On
3	2.0	Off	Off	On	Off	On	Off	On	On	Off	On
4	0.7	Off	Off	Off	On	Off	On	Off	Off	On	Off

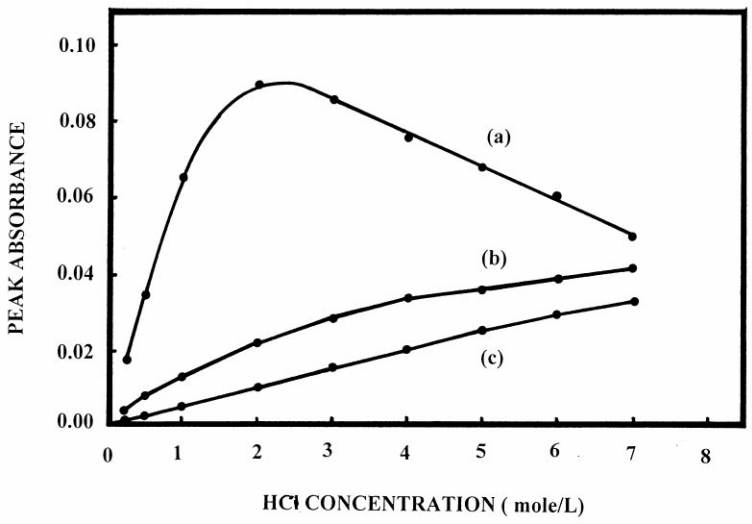

Fig. 4. The effect of HCl concentration on the retention of the chloro-complexes of Zn^{2+} (a), Cu^{2+} (b) and Fe^{3+} (c) as detected by atomic absorption spectrometry after elution with 0.1 M HNO_3 solution.

3. Results and discussion

3.1. Solid sample insertion

Initial tests were carried out using a standard iron(III) solution in a suspension of starch in 6 M HCl. Slurry pumping using a dedicated channel resulted in incomplete sample transfer into the flow system. Furthermore, some of the solid adhered to the pump tubing with subsequent inter-sample contamination and loss of analytical precision.

However, solid sample insertion into the chamber shown in Fig. 2 is quick (less than 20 s), quantitative and fairly precise when corrected for exact solid sample mass. Both powdered samples and homogeneous chunks of the tablet could be used as long as the particle size of the tablet constituents was less than 0.5 mm. Reproducibility ($n = 6$) of chunk sample insertion (3.5% relative standard deviation, R.S.D.) is better than powdered sample insertion (4.2% R.S.D.). The slower dissolution of the sample allows better opportunity for oxidation of iron(II) to iron(III) and more reproducible ion exchange partitioning. A single valve (V1) upstream of the sample insertion chamber is not adequate because back-pressure from the digestion coil drives the acid solution in the reverse direction during sample insertion.

3.2. Optimization of digestion conditions

The effect of digestion coil length on efficiency of digestion was tested using a mixture of iron(II) solution (1×10^{-5} M) in a starch suspension (5%, w/v). The iron signal increases with coil length up to 390 cm where the signal levels off. The effect of HCl concentration on the resin's retention of metal chloro-complexes was optimized by aspirating (through the HCl channel) 10 ml of the metal ions (2×10^{-5} M) in various matrix concentrations of HCl ranging from 0.1 to 8 mol l^{-1}. After washing the column with 5 ml of the proper concentration of HCl solution the retained metal was eluted with 10 ml of 0.1 M HNO_3 and analyzed by atomic absorption spectroscopy using the system in Fig. 1. The aspiration rate for both loading and elution cycles was fixed at 2.00 ml min^{-1}. Fig. 4 is a plot of peak absorbance for various elements of different HCl matrix concentration. For zinc, a 2 M HCl matrix gave maximum retention. However, the fraction of Cu and Fe retained as the chloro-complexes increase with increasing HCl concentration. The obtained peaks are slightly tailing; however, plotting peak area vs.

concentration of HCl gave a graph of similar appearance. Although as low as 2 M HCl solution is sufficient for complete dissolution of iron in pharmaceutical tablets (Supradyn), the fraction of iron(III) (as $FeCl_4^-$) exchanged is affected by acid strength; increasing HCl concentration from 1 to 8 M resulted in a sixfold increase in iron signal. Finally, 4 M HCl was chosen to represent the point where a 0.1-g sample could be used to produce an iron signal that lies within the linear range of the spectrophotometer response curve.

At maximum power (100 W) the digestion solution flowing at a rate of 2 ml min^{-1} reached a temperature of 55°C as measured at the downstream end of the coil. Attenuation of the lamp (10 steps) resulted in a progressively lower digestion temperature. When actual sample digestion was performed with the light at maximum power the iron signal was 65% higher compared with similar digestion at room temperature. Digestion time could be cut down by 30% at full lamp power. However, analytical precision is slightly poorer (4.2 vs. 3.1 R.S.D.). This is probably due to the variable ion exchange distribution constant with variable temperature. Another reason for the poorer precision is the irregular pressure build-up due to gas expansion with occasional fluctuation in flow rate which affects the ion exchange process. Precision can be preserved by thermostatting the column. However, no attempt was made to do so in order to keep the apparatus as simple as possible.

Incorporation of the multi-channel pinch valve, V4, in the unique configuration shown in Fig. 1 allows slurry flow in wide channels with less chance for blockage. This arrangement is a substitute for placing the column in the loop section of the conventional six-port rotary injection valve. It is simpler and less expensive alternative to the five three-way solenoid valves assembly used earlier [16,17]. The plastic screens hold the resin beads (and analyte) but allows fine (< 0.5 mm) solid residue to pass unimpeded. Furthermore, column back pressure is low because glass frits or fine filters are not used. This arrangement is only limited to cases where the analyte can be retained by an ion exchanger. The system described here was used for isolation of few anionic complexes but could be extended to cations by incorporation of a cation-exchange resin column and neutralization of the acidic digest with base.

3.3. The detection systems

Initially, a spectrophotometric detector tuned at 480 nm [18] was used for the determination of iron as detailed in Section 2. Upon elution with 0.1 M HNO_3 a double peak was obtained as shown in Fig. 5a. The first peak is almost always of constant height irrespective of the iron concentration while the height of the second peak is directly proportional to the iron concentration. This artifact is due to the difference in refractive index of the eluted solution (4 M HCl) compared with that of the eluant 0.1 M HNO_3. The same peak shape was produced when an iron(III) solution in 4 M HCl was injected in a 0.1 M HNO_3 carrier using a rotary sample injection valve. This artifact peak could be eliminated by matching the refractive index of both the sample and the fluent; Injecting an iron(III) solution in (6 M HCl) using a 5 M $NaNO_3$ carrier solution gave no split peaks, however, the baseline is too noisy to be useful for the spectrophotometric determination of iron.

Coupling the apparatus to an atomic absorption spectrometer with starved flow gave no double peaks (Fig. 5b). Atomic absorption detectors are not affected by the presence of bubbles between the resin beads, therefore, step three in Table 1 could be eliminated without loss of precision or accuracy, and with increased sampling frequency from 9 to 15 samples h^{-1}.

3.4. Application to multi-vitamin tablets

Triplicate analysis of Fe, Cu and Zn in multivitamin tablets was carried out using the proposed flow system at 45 ± 2°C and compared with the manual method detailed in Section 2. Powdered samples containing no more that 0.35 mg Fe, 0.35 mg Cu and 0.20 mg Zn were analyzed in triplicate. Iron was assayed by spectrophotometric detection while Zn and Cu were assayed by atomic absorption detection. The upper limits of sample size were dictated by the limit of linear-

ity of the calibration curves (Fe and Zn) or by the reproducibility of retention (Cu). Calibration standards (pure chemicals in 5%, w/v starch suspension) were dispensed into the sample insertion chamber by a micro-pipette. Calibration curves were linear within the specified mass range with slopes of 0.83 ± 0.08, 0.32 ± 0.03 and 3.87 ± 0.12 A μg^{-1} for Fe, Cu and Zn, respectively.

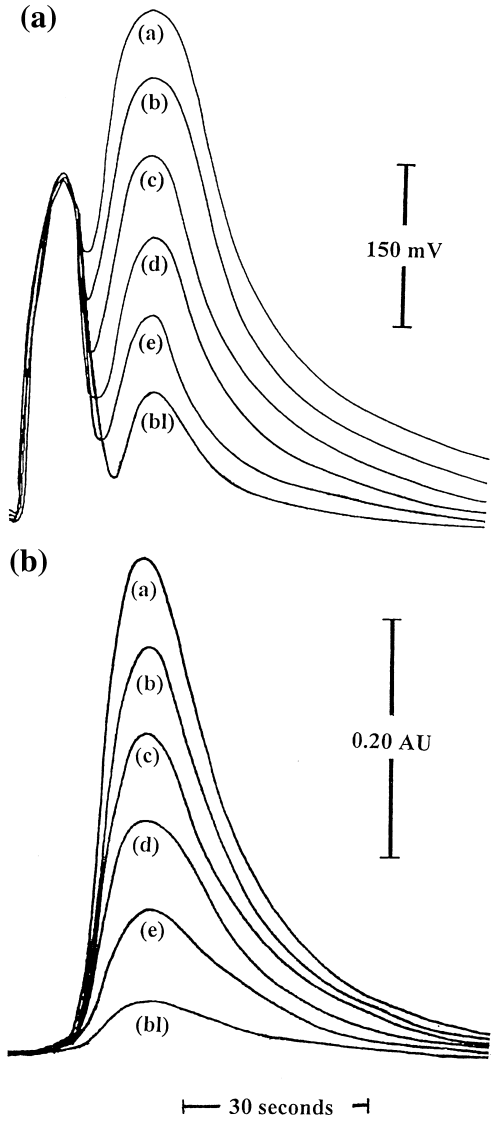

Fig. 5. Calibration signal profiles for the determination of iron in multi-vitamin tablets by on line solid sample digestion and flow injection analysis with spectrophotometric (a) and atomic absorption (b) detection. (a) 500 μg; (b) 400 μg; (c) 300 μg; (d) 200 μg; (e) 100 μg; (bl) blank.

Table 2
Comparative determination of Fe, Cu and Zn in multi-vitamin tablets by the proposed automated system and by the manual method ($n = 3$)

Elements	Concentration (mg per tablet)		
	Assay	Automated method[a]	Manual method[b]
Fe	1.25	1.18 ± 0.05	1.21 ± 0.03
Cu	0.1	0.08 ± 0.005	0.09 ± 0.004
Zn	0.5	0.49 ± 0.02	0.47 ± 0.02

[a] On-line digestion, ion-exchange separation and spectrophotometric or atomic absorption detection as developed in this work.

[b] Manual digestion with aqua regia and atomic absorption determination as detailed in Section 2 under the sub-title samples.

For all three elements the intercepts are essentially zero within statistical error. Fig. 5 depicts a typical calibration profile for iron, while Table 2 lists the analytical data for the analysis of multivitamin tablets by the automated system and by the manual method. The data indicate the feasibility of using the proposed system for automated solid sample insertion, digestion and analysis of the indicated elements in vitamin tablets. The analytical precision is slightly poorer than with the manual method, but is satisfactory for many applications.

4. Conclusions

The proposed solid sample injection, digestion and analysis apparatus is relatively simple and requires no filtration module. It offers full sample transfer to the digestion system without contamination and loss typical of slurry aspiration with a peristaltic pump.

The novel configuration of the multiple pinch-valve eliminates the need for the conventional narrow port rotary or slider type valves. The large pore size tubes and tees allow handling slurries without the risk of blockage. Furthermore, the slurry comes in touch with the transmission tubing only which eliminates the risk of valve damage. The incorporation of a coarse-bead an-

ion exchange resin and coarse screens (~20 mesh) lower back pressure, obviates the need for solid residue filtration and could be used for in-line pre-concentration where necessary. The feasibility of the system was demonstrated by analyzing Fe, Cu and Zn in multi-vitamin tablets. However, it could be applied for the determination of other transition elements that form chloro-complexes such as Cd, Co, Cr and Ag. Extending the method to cation exchange retention is also possible after proper neutralization of the digesting acid. Further applications are in progress.

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