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Short Research Article

A facile synthesis of [^{35}S]homocysteine and its derivatives from methionine [^{35}S] sulphoxide – a by-product in [^{35}S]methionine synthesis†

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Introduction

Homocysteine is a normal metabolite of the essential amino acid methionine. It is generated in a cycle through S-adenosylmethionine (SAM) and S-adenosyl homocysteine (SAH).[1] Homocysteine is remethylated back to methionine by vitamine B_{12} dependent methionine synthase and betaine-homocysteine methyltransferase. It is also converted to cysteine through the transsulfuration pathway, initiated by vitamine B_6-dependent cystathionine synthase. Elevated level of homocysteine in human blood plasma has achieved the status of an important factor in vascular disease, diseases of aging and other fundamental processes in biology and medicine.[2,3] ^{35}S-Labelled homocysteine and its thiolactone are important radiotracers being

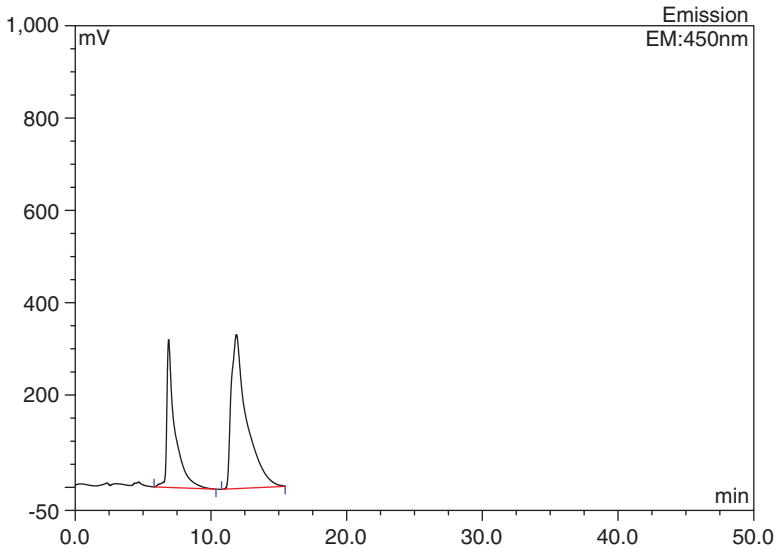

Figure 1 HPLC analysis profile of carboxymethylated homocysteine (RT 6.88 min) and methionine sulphoxide (RT 11.88 min). Figure available in colour online at www.interscience.wiley.com

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used to study the role of homocysteine in biological systems. In the method reported herein, the reaction scheme reported in the literature for the assay of methionine sulphoxide in protein by the conventional method using acetic anhydride, is made use of for the preparation of [^{35}S]homocysteine. We carried out the reaction both by a conventional heating method and by microwave irradiation. The homocysteine formed during the reaction was purified, analysed and assayed by chromatographic methods.[4]

Results and discussion

The method of preparation of [^{35}S]homocysteine is found to be very simple when compared to other methods like reduction of methionine using sodium-liquid ammonia. Addition of very low concentration of hydrogen peroxide after initial heating of methionine sulphoxide with acetic anhydride reduced the formation of the formaldehyde-homocysteine adduct, thereby increasing the yield of homocysteine. In the literature reported for the assay of methionine sulphoxide by this method, the careful quantitative transfer for the assay of formaldehyde was achieved by steam distillation. In the HPLC assay by the pre-column OPA derivatization method, fast and efficient base line separation of methionine sulphoxide, methionine and carboxymethylated homocysteine, as shown by separate individual peaks, was achieved by the modified analysis conditions employed (Figure 1). Carboxymethylation of homocysteine was carried out by reacting with iodoacetic acid.

(Analysis conditions: column : ODS, 25 cm × 0.45 cm, 5 μm particle size, mobile phase: methanol-0.1 M sodium dihydrogen phosphate pH 6.0 (30:70, v/v), flow rate—1.0 ml/min, Detection method: fluorescence detection after pre-column OPA derivatization of methionine sulphoxide and carboxymethylated homocysteine.)

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