Chapter 7

Enantioselective, potentiometric membrane electrodes based on maltodextrins

7.1 Maltodextrins as chiral selectors in the EPMEs design

Maltodextrins represent a class of very powerful chiral selectors among the chiral selective substances, e.g., cyclodextrins, crown ethers, macrocyclic antibiotics, proteins. Maltodextrins (Fig. 7.1) are complex malto-, oligo-, and polysaccharide mixtures formed by hydrolysis of starch, with DE lower than 20 [1-3].

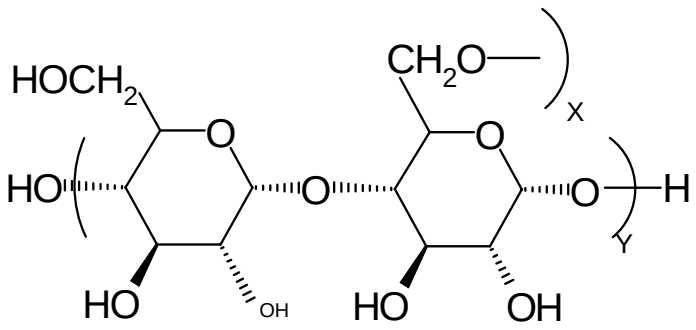

Figure 7.1 Maltodextrins

Possible types of maltodextrins have different DE values [I (4.0-7.0), II (13.0-17.0), and III (16.5-19.5)]. Variations in DE values result in maltodextrins with varying physico-chemical properties: solubility, hydroscopicity, osmolality and their effectiveness to reduce the freezing point increase with increasing DE, while viscosity, cohesiveness and coarse-crystal prevention increase as DE decreases [4,5]. Maltodextrins were intensively investigated as chiral selectors for enantiomeric separations by capillary zone electrophoresis, the maltodextrins with the highest DE values being the best chiral selectors [2,3,6-10], and they were also used in the design of enantioselective, potentiometric membrane electrode for the enantioanalysis of several drugs.

7.2 Enantioanalysis of R-deprenyl using enantioselective, potentiometric membrane electrodes based on maltodextrins

One enantioselective, potentiometric membrane electrode based on a maltodextrin is proposed for the enantioselective assay of R-deprenyl [11].

7.2.1 Reagents and materials

Graphite powder (1-2 μm), maltodextrin (DE 16.5-19.5) was purchased from Aldrich (Milwaukee, WI, USA). Paraffin oil was purchased from Fluka (Buchs, Switzerland). R-deprenyl was purchased from Sigma-Aldrich. Phosphate buffer (pH 5.8) was obtained from Merck (Darmstadt, Germany). Deionized water from a Modulab system (Continental Water System, Sand Antonio, TX, USA) was used for all solutions preparations. Lentogesic tablets (65 mg deprenyl per tablet) were obtained from Adcoc Ingram Limited (Johannesburg, South Africa).

The solution of maltodextrin (10^{-3} mol.l^{-1}) was prepared using deionized water. All standard and diluted solutions were buffered with phosphate buffer pH 5.8 using the ratio buffer:distilled water 1:1 (v/v).

7.2.2 Apparatus

A 663 VA Stand (Metrohm, Herisau, Switzerland) in combination with a μAutolab and Ecochemie (Utrech, The Nertherlands) Software version 4.9 were used for all potentiometric measurements. An Ag/AgCl (0.1 mol l^{-1} KCl) electrode served as reference electrode in the cell.

7.2.3 Electrode design

Paraffin oil and graphite powder in a ratio of 1:4 (w/w), were first thoroughly mixed, followed by the addition of an aqueous solution of maltodextrin with DE 16.5-19.5 (solution 10^{-3} mol l^{-1}). A quantity of carbon paste, free of maltodextrin, was also prepared and placed in a plastic pipette peak, leaving 3-4mm empty in the top to be filled with carbon paste containing the chiral selector. The diameter of the EPME was 3mm. Electric contact was obtained by inserting a Ag/AgCl wire into the carbon paste. The internal solution was 0.1 mol l^{-1} KCl. Prior to use, the surface of the electrode was wetted with deionised water and polished with alumina paper (polishing strips 30144-001, Orion).

7.2.4 Recommended procedure

7.2.4.1. Direct potentiometry

The potentiometric technique was used for potential determination of each standard solutions 10^{-10}-10^{-3} mol l^{-1}. The electrode was placed into stirred standard solutions and graphs of E(mV) versus pR-deprenyl were plotted. The unknown concentrations were determined from the calibration graphs.

7.2.4.2. Content uniform assay of deprenyl tablets

Each of the ten tablets were placed into 100 ml calibrated flask, dissolved and diluted to the mark using a phosphate buffer (pH 5.85):deionized water 1:1. The unknown concentration of deprenyl was determined using the direct potentiometric method.

7.2.5 Results and discussion

7.2.5.1 Electrode response

The response characteristics of the proposed electrode are as follows: slope 53.1 mV/decade of concentration, intercept, Eº 554.3 mV, linear concentration range 10^{-10} – 10^{-3} mol/L, and detection limit 3.6 x 10^{-11} mol/L, when all measurements were performed at room temperature. All values are average of ten determinations. For the calibration equation, the correlation coefficient was 0.9999. The electrode showed a non-Nernstian response for S-deprenyl proving that it can be used only for the assay of R-deprenyl.

7.2.5.2 Effect of pH on the response of the electrode

The influence of the pH values on the response of the proposed electrode was investigated by recording the emf of the cell for solutions containing 10^{-5} mol.l^{-1} R-deprenyl at pH values between 1 and 12. The plot of *E* (mV) versus pH (Fig. 7.2) indicates, that the response of the electrode does not depend on the pH changes in the pH ranges 2.0-7.0.

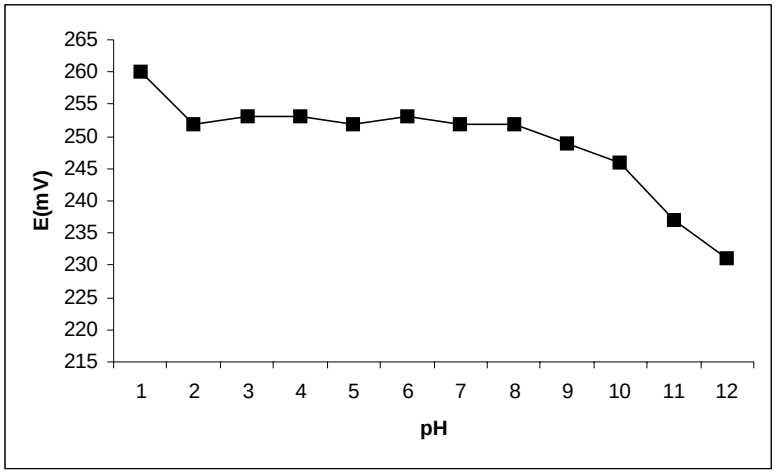

Figure 7.2 Effect of pH on the response of the enantioselective, potentiometric membrane electrode used for the assay of R-deprenyl (10^{-5} mol l^{-1} R-deprenyl solution).

7.2.5.3 Selectivity of the electrode

The selectivity of the potentiometric membrane electrode was investigated using the mixed solution method. The concentrations of interfering ions and R-deprenyl were 10^{-4} mol l^{-1} and 10^{-5} mol l^{-1}, respectively. The values of the potentiometric selectivity coefficients (Table 7.1) indicate that the electrode can be reliably used for enantioanalysis of R-deprenyl due to its good selectivity and enantioselectivity.

Table 7.1 Selectivity coefficient for the EPME based on maltodextrin used for the assay of R-deprenyl.

Interfering species (J)	K_{sel}^{pot}
S-Deprenyl	4.4×10^{-3}
PVP	3.5×10^{-3}
Creatine	4.0×10^{-3}
Creatinine	3.8×10^{-3}
Paracetamol	3.0×10^{-3}
L-glutamine	1.4×10^{-3}

All measurements were made at room temperature; all values are average of 10 determinations

7.2.5.4 Analytical applications

The assay of R-deprenyl in the presence of S-deprenyl was carried out using different ratios between R- and S-deprenyl. The results obtained (Table 7.2) confirmed once more the suitability of the proposed potentiometric membrane electrode for the enantioanalysis of R-deprenyl. No significant difference in the recovery values were recorded for the different ratios between the enantiomers.

Table 7.2 Determination of R-deprenyl in the presence of S-deprenyl.

R : S (mol/mol)	% R-deprenyl, Recovery
2 : 1	99.14 ± 0.02
1 : 1	99.78 ± 0.01
1 : 2	99.25 ± 0.02
1 : 4	99.78 ± 0.02
1 : 9	99.80 ± 0.01

All measurements were made at room temperature; all values are average of 10 determinations

The results obtained for content uniformity test of Lentogesic tablets using the proposed electrode showed, that the tested pharmaceutical formulations contain 1.36 % R-deprenyl (RSD = 0.11%, (n = 10)). The average recovery value determined was in agreement with that obtained using a HPLC method: 1.49 ± 0.17%.

7.3 Enantioanalysis of S-ibuprofen using enantioselective, potentiometric membrane electrodes based on maltodextrins

Three enantioselective, potentiometric membrane electrodes (EPMEs) based on maltodextrin with different values of dextrose equivalence(DE) (maltodextrin I: DE 4.0-7.0; maltodextrin II: DE 13.0-17.0; maltodextrin III: DE 16.5-19.5) were proposed for the assay of S-ibuprofen [12].

7.3.1 Reagents and materials

Graphite powder (1-2 μm), maltodextrins (DE 4.0-7.0 (I), 13.0-17.0 (II) and 16.5-19.5 (III)) were purchased from Aldrich (Milwaukee, WI, USA). Paraffin oil was purchased from Fluka (Buchs, Switzerland). S-ibuprofen was purchased from Sigma-Aldrich. Phosphate buffer (pH 4.00) was obtained from Merck (Darmstadt, Germany). Deionized water from a Modulab system (Continental Water System, Sand Antonio, TX, USA) was used for all solutions preparations. Myprodol capsules (200 mg ibuprofen/capsule) and Nurofen tablets (200 mg ibuprofen/tablet) were obtained from Nutrent (Sandton, South Africa).

The solutions of maltodextrins (10^{-3} mol l^{-1}) were prepared using deionized water. All standard and diluted solutions were buffered with phosphate buffer pH 4.00 using the ratio buffer:distilled water 1:1 (v/v).

7.3.2 Apparatus

A 663 VA Stand (Metrohm, Herisau, Switzerland) in combination with a μAutolab and Ecochemie (Utrech, The Nertherlands) Software version 4.9 were used for all potentiometric measurements. An Ag/AgCl (0.1 mol l^{-1} KCl) electrode served as reference electrode in the cell.

7.3.3 Electrode design

Paraffin oil and graphite powder in a ratio of 1:4 (w/w), were first thoroughly mixed, followed by the addition of an aqueous solution of maltodextrin (DE 4.0-7.0 (I), 13.0-17.0 (II) and 16.5-19.5 (III)) from 10^{-3} mol l^{-1} maltodextrin solution. A quantity of carbon paste, without maltodextrin, was also prepared and placed in a plastic pipette peak, leaving 3-4mm empty in the top to be filled with carbon paste containing the chiral selector. The diameter of the EPMEs was 3mm. Electric contact was obtained by inserting a Ag/AgCl wire into the carbon paste. The internal solution was 0.1 mol l^{-1} KCl. Prior to use, the surface of the electrode was wetted with deionised water and polished with alumina paper (polishing strips 30144-001, Orion).

7.3.4 Recommended procedures

7.3.4.1 Direct potentiometry

The potentiometric method was used for potential determination of each standard solution 10^{-10} - 10^{-3} mol l^{-1}. The electrodes were placed into stirred standard solutions and graphs of E(mV) versus pS-ibuprofen were plotted. The unknown concentrations were determined from the calibration graphs.

7.3.4.2 Content uniform assay of ibuprofen capsules and tablets

Each of the five capsules and five tablets were placed into 100 ml calibrated flask, dissolved and diluted to the mark using a phosphate buffer (pH 5.34):deionized water 1:1 (v/v) solution. The unknown concentration of ibuprofen was determined using the direct potentiometric method.

7.3.5 Results and Discussion

7.3.5.1 Electrodes response

The response characteristis exhibited by the proposed EPMEs for the assay of S-ibuprofen are summarized in Table 7.3.

Table 7.3 Response characteristics of enantioselective, potentiometric membrane electrodes based on maltodextrins I, II and III for the assay of S-ibuprofen.

Maltodextrin	Slope (mV/decade of conc.)	Intercept, E^0 (mV)	Linear concentration range (mol l^{-1})	Detection limit (mol l^{-1})
I	59.0	593.4	10^{-10} - 10^{-3}	5.5 x 10^{-11}
II	58.4	473.2	10^{-8} - 10^{-3}	8.0 x 10^{-9}
III	55.6	632.5	10^{-10} - 10^{-3}	4.1 x 10^{-12}

All measurements were made at room temperature; all values are average of ten determinations.

All the proposed membrane electrodes exhibited linear and near Nernestian responses (55-59 mV per decade of concentration) for S-ibuprofen while a non-Nernstian response was recorded for R-ibuprofen. The correlation coefficients for all the calibration graphs was 0.9999. The limits of detection were very low. The low working concentration

ranges and limits of detection may be explained by the structural conformation of the maltodextrin that can change from flexible coil at higher DE values to helix at lower DE values. The stability of the complexes formed between the chiral selector and analytes is increasing with the value of DE, because increasing the DE value will result in an increase in the diameter of the helix leading to less steric hindrance of the approach of an interacting molecule, hence more inclusion.

7.3.5.2 Effect of pH on the response of the electrodes

The effect of the pH variation on the response of the EPMEs based on maltodextrin I, II and III has been tested by recording the emf of the cell.

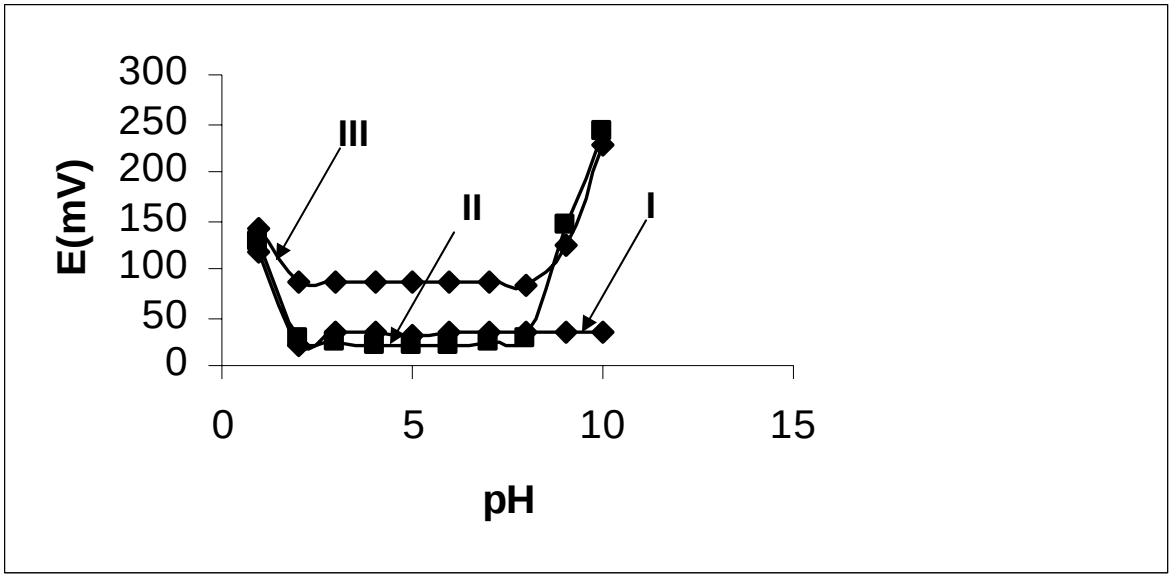

Figure 7.3 Effect of pH on the response of the enantioselective, potentiometric membrane electrodes based on maltodextrin I (I), II (II) and III (III), respectively, for the assay of S-ibuprofen (10^{-7} mol.l^{-1} S-ibuprofen solution).

All measurements were performed for a concentration of 10^{-7} mol l^{-1} of S-ibuprofen, at different pH values selected between 1 and 10. The E (mV) versus pH plots presented in fig. 7.3 shows that the response of the EPMEs are pH-independent in the pH ranges of 3.0-9.0 (maltodextrin I based EPME) and 2.0-8.0 (maltodextrin II and III based EPMEs).

7.3.5.3 Selectivity of the electrodes

The selectivity of the potentiometric membrane electrode was checked using the mixed solutions method. The concentrations of interfering ions and S-ibuprofen were 10^{-5} mol/L and 10^{-6} mol/L, respectively. The values obtained for the potentiometric selectivity coefficients show that the EPMEs are selective over paracetamol, PVP, creatine and creatinine (Table 7.4). They are also enantioselective, since the values recorded for potentiometric selectivity coefficients over R-ibuprofen are lower than 10^{-4}.

Table 7.4 Potentiometric selectivity coefficients for the enantioselective, potentiometric membrane electrodes used for the assay of S-ibuprofen.

Iterference species (J)	K^{pot}		
	EPME based on maltodextrin		
	I	II	III
Paracetamol	4.2×10^{-3}	1.5×10^{-3}	8.6×10^{-3}
PVP	1.2×10^{-3}	4.0×10^{-4}	$<<10^{-4}$
Creatine	1.1×10^{-3}	$<<10^{-4}$	$<<10^{-4}$
Creatinine	1.1×10^{-3}	$<<10^{-4}$	8.6×10^{-4}

All measurements were made at room temperature; all values are average of ten determinations.

7.3.5.4 Analytical applications

The proposed enantioselective, potentiometric membrane electrodes based on maltodextrin are useful for the determination of the enantiopurity of S-ibuprofen raw

material and for testing the content uniformity of Myprodol capsules and Nurofen tablets, by direct potentiometry. The results obtained for the uniformity content test shown that S-ibuprofen can be reliably assayed in pharmaceutical formulations, with average recoveries of 99.35 ± 0.23%, 99.32 ± 0.17% and 99.34 ± 0.19% from Myprodol capsules and average recoveries of 98.55 ± 0.31%, 98.43 ± 0.17% and 98.53 ± 0.09 % from Nurofen tablets, when EPMEs based on maltodextrins I, II and III, respectively. These results are in good agreement with those obtained using a chromatographic method: 99.30% and 98.40% S-ibuprofen in Myprodol capsules and Nurofen tablets, respectively. The results showed that tested pharmaceutical formulations contain S-ibuprofen as a main component.

7.4 Conclusion

The potentiometric, enantioselective membrane electrodes proved to be good for enantioselective analyses of R-deprenyl and S-ibuprofen. The reliability of the analytical information is evident from the RSD values obtained from recovery and content uniformity tests. The electrodes enantioselectivity made it suitable for enantiopurity assay of R-deprenyl and S-ibuprofen as both raw material and pharmaceutical tablet formulations. The construction of the electrodes is simple, fast and reproducible. Due to their good selectivity over creatine and creatinine, the proposed electrodes can also be used for the determination of R-deprenyl and S-ibuprofen in biological fluids.

7.5 References

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