

Using Nuclear Magnetic Resonance to Troubleshoot a Stability Issue in a Real-World Formulation Chassis—Application to Consumer Oral Healthcare

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Supporting Information

Table S1. Batch numbers and conditions for all samples analysed listed below in table.

Batch Number	Temperature/Pressure	Analysis Timeframe	Packaging	pH
<u>HALEON</u> <u>PLC1688B53</u>	15 °C/35psf	2 months	Glass	5.5
<u>HALEON</u> <u>PLC1688B53</u>	25 °C/60psf	4 months	PET	5.5
<u>HALEON</u> <u>PLC1688B53</u>	40 °C/75psf	4 months	PET	5.5
<u>HALEON</u> <u>PLC1688B53</u>	40 °C/75psf	4 months	HDPE white	5.5
<u>HALEON</u> <u>PLC1688B53</u>	25 °C/60psf	4 months	HDPE white	5.5
<u>HALEON</u> <u>PLC1688B54</u>	25 °C/60psf	3 months	Glass	5.5
<u>HALEON</u> <u>PLC1688B55</u>	40 °C/75psf	4 months	Glass	5.5
<u>HALEON</u> <u>PLC1688B56</u>	50 °C/150psf	5 months	Glass	5.5
<u>HALEON</u> <u>PLC1688B58</u>	40 °C/75psf	3 months	HDPE white + Refill Cap	5.5
<u>HALEON</u> <u>PLC1688B58</u>	40 °C/75psf	1 month	PET + Refill Cap	5.5
HALEONPLC 10317/76 no salicylic acid	40 °C/75psf	1 month	HDPE White	3

HALEONPLC 10317/87	40°C/75psf	0.5 months	Glass	3
HALEONPLC 10317/80-3	40°C/75psf	3 months	PET	3
HALEONPLC 10317/80	40°C/75psf	1 month	Glass	3
HALEONPLC 10317/80	40°C/75psf	1 month	HDPE natural	3
HALEONPLC 10317/80	40°C/75psf	1 month	HDPE white	3
HALEONPLC 10317/80	40°C/75psf	1.5 months	PET	3
HALEONPLC 10317/128	40°C/75psf	1 month	Glass	3
HALEONPLC 10317/128	40°C/75psf	2 months	Glass	3
HALEONPLC 10317/144 2x concentration	40°C/75psf	1.5 month	Glass	3
New Cap extract i-ProOH, evaporated to residue	15 °C/35psf	N/A	HDPE white	5.5
HDPE Bottle extract i-ProOH, evaporated to residue	15 °C/35psf	N/A	HDPE white	5.5
Polypropylene i-ProOH, evaporated to residue	15 °C/35psf	N/A	Polypropylene	5.5
PET Bottle extract i-ProOH, evaporated to residue	15 °C/35psf	N/A	PET	5.5
KU_MM1_a HDPE white token	40°C/75psf	1 month	Glass	5.5
KU_MM1_b	40°C/75psf	1 month	Glass	5.5
KU_MM2_a HDPE white token/no sal. acid	40°C/75psf	1 month	Glass	5.5
KU_MM2_b	40°C/75psf	1 month	Glass	5.5

no sal. acid				
KU_MM3_a HDPE white token/no sls	40°C/75psf	1 month	Glass	5.5
KU_MM3_b no sls	40°C/75psf	1 month	Glass	5.5
KU_MM4_a HDPE white token/no flavouring	40°C/75psf	1 month	Glass	5.5
KU_MM4_b No flavouring	40°C/75psf	1 month	Glass	5.5

Table S2. Table of qNMR integral values over 24 h time range of for a representative PEF sample to show negligible change in component concentration whilst refrigerated

GSKHALEON PLC1688B55	qNMR Absolute Integral values		
Fridge time (hours)	Sal acid	Formic acid	DHBA
0	481338213	15804234	1634711.3
2	481021952	15745255	1638120.6
24	481191099	15645537	1635186.6
RSD	0.03	0.51	0.11

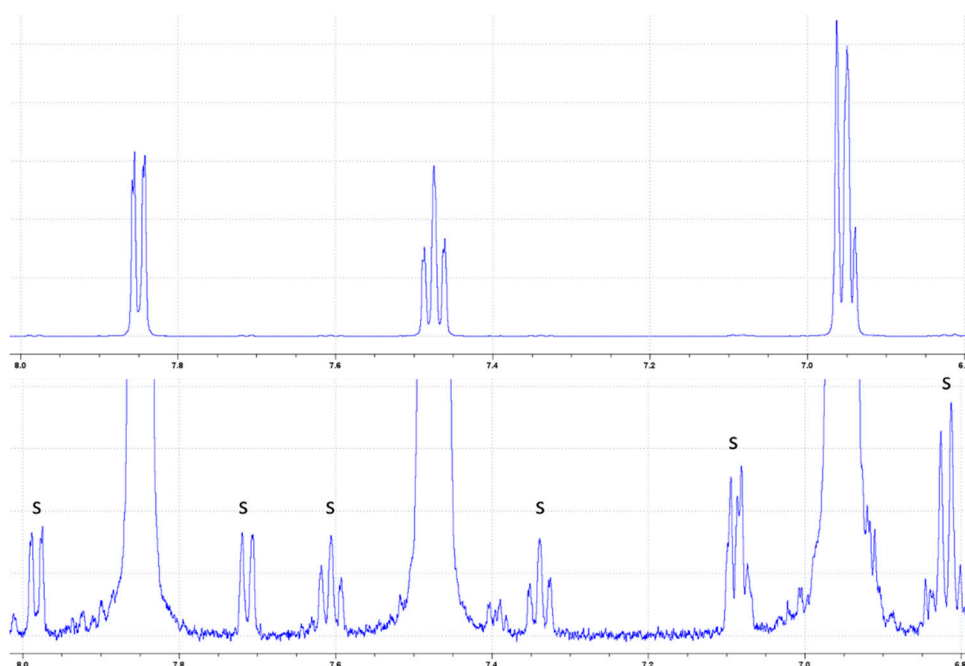


Figure S1. NMR spectra 1D ¹H of salicylic acid in H₂O/D₂O: (Top) aromatic peaks; (Bottom) Zoomed in with satellite peaks of aromatic peaks assigned.

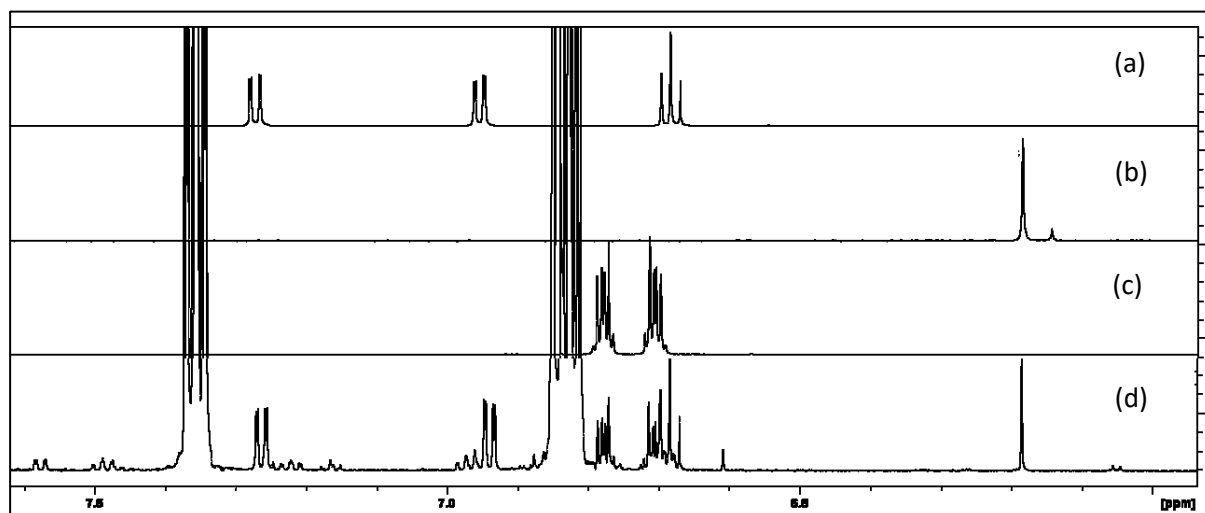


Figure S2. ^1H NMR spectrum (zoomed) of (a) 2,3-dihydroxybenzoic acid (b) maleic acid (c) o-catechol and (d) the proprietary formulation in glass container 7 weeks at 40°C .

Table S3. ICP-MS data acquired for different packaging type PEFs at stored at 40°C over 6 weeks.

Packaging	Ti conc. (ppb)	RSD
HDPE White	60.13	21.3
HDPE natural	59.09	15.9
Glass	0.09	8.7

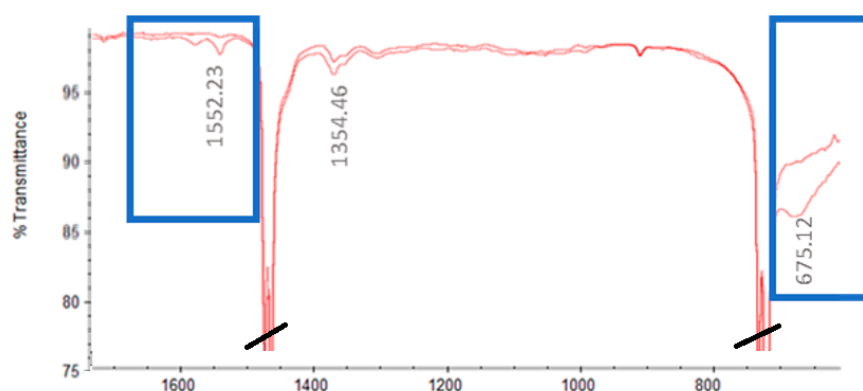


Figure S3. HDPE White (no discolouration) versus yellow surface analysis comparison with ATR-IR. Peaks that present for yellowed surface but are absent in non-discoloured surface are highlighted [12,13].



Figure S4. To visually demonstrate the rapid formation of colored compounds, hydrogen peroxide and SA were added to $\text{Ti}(\text{OMe})_4$, closely resembling the TiO_2 system in HDPE White. This phenomenon was also observed with the oxidized derivative maleic acid, which exhibited a strong orange color when exposed to Titanium methoxide and hydrogen peroxide, indicating a similar coloration interaction with oxidized derivatives of salicylic acid. (Left to right) $\text{Ti}(\text{OMe})_4$ and H_2O_2 ; $\text{Ti}(\text{OMe})_4$ and H_2O_2 and SA; $\text{Ti}(\text{OMe})_4$ and SA within 1 minute of combination.