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Correction: Chemical analysis in saliva and the search for salivary biomarkers – a tutorial review

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Correction for 'Chemical analysis in saliva and the search for salivary biomarkers – a tutorial review' by Kamonwad Ngamchuea, *et al.*, *Analyst*, 2018, **143**, 81–99.

In the published article some errors were present in Tables 1, 2 and 4.

The concentrations of blood glucose were misplaced into the 'Saliva' column. They are now moved to the correct 'Other biological fluids' column. A full, corrected Table 1 is reproduced here.



Table 1 Components of authentic human saliva and a comparison of the normal range of the concentrations between saliva and other biological fluids

| Real saliva composition | | Normal range | | Ref. | | | |
|----------------------------------|--|--|--|-------------------------------------|--|-------|-----------|
| | | Saliva | Other biological fluids | | | | |
| 1. Inorganic compounds | Na ⁺ | 20–80 mmol L ⁻¹ | Plasma 145 mmol L ⁻¹ | 11 | | | |
| | K ⁺ | 20 mmol L ⁻¹ | 4 mmol L ⁻¹ | | | | |
| | Ca ²⁺ | 1–4 mmol L ⁻¹ | 2.2 mmol L ⁻¹ | | | | |
| | Cl ⁻ | 30–100 mmol L ⁻¹ | 120 mmol L ⁻¹ | | | | |
| | HCO ₃ ⁻ | 15–80 mmol L ⁻¹ | 25 mmol L ⁻¹ | | | | |
| | Phosphate | 4 mmol L ⁻¹ | 1.2 mmol L ⁻¹ | | | | |
| | Mg ²⁺ | 0.2 mmol L ⁻¹ | 1.2 mmol L ⁻¹ | | | | |
| | SCN ⁻ | 2 mmol L ⁻¹ | <0.2 mmol L ⁻¹ | | | | |
| | NH ₃ | 3 mmol L ⁻¹ | 0.05 mmol L ⁻¹ | | | | |
| | 2. Organic compounds (non-protein and lipids) | Uric acid | 3.38 ± 0.21 mg dL ⁻¹ 217.2 ± 110.3 mol L ⁻¹ 0.1–7.5 mg dL ⁻¹ | | Serum 6.31 ± 0.24 mg dL ⁻¹ | 21–23 | |
| Bilirubin | | 0.5–5.0 μmol L ⁻¹ | Serum 0.2–1.2 mg dL ⁻¹ | | | | |
| Creatinine | | 0.12 ± 0.06 mg dL ⁻¹ 0.05–0.2 mg dL ⁻¹ | Serum 0.89 ± 0.17 mg dL ⁻¹ Serum 0.6–1.5 mg dL ⁻¹ | | | | |
| Glucose | | 4–13 mg dL ⁻¹ | Blood 80–120 mg dL ⁻¹ Blood 88.6 ± 8.0 mg dL ⁻¹ | 22 and 26 | | | |
| Cholesterol | | 0.02–5.46 μmol L ⁻¹ | Serum <5 mmol L ⁻¹ | | | | |
| Lactate | | 0.3–1.8 mM 0.1 to 2.5 mmol L ⁻¹ | Serum 0.5–1.0 mM | 28 and 29 | | | |
| 3. Protein/polypeptide compounds | | α-Amylase | 19–308 U mL ⁻¹ ^a 93 ± 62 U L ⁻¹ ^a 2.64 ± 1.8 mg mL ⁻¹ | | Serum 0.05–0.125 U mL ⁻¹ ^a | | 23 and 30 |
| | | Albumin | 0.2 ± 0.1 mg mL ⁻¹ | Serum 3.5–5.5 g dL ⁻¹ | | | |
| | | Secretory-IgA | 80–717 mg dL ⁻¹ 124.3–333.5 μg mL ⁻¹ | Serum 70–400 mg dL ⁻¹ | 23 and 32 | | |
| | | Mucin group | MUC5B: 2.4 ± 1.7 U mL ⁻¹ 1.19 ± 0.17 mg mL ⁻¹ | Serum 9.9 ± 0.8 ng mL ⁻¹ | | | |
| | Lysozyme | 3–50 μg mL ⁻¹ 59.7 to 1062.3 μg mL ⁻¹ | Serum 7.4 ± 1.8 mg mL ⁻¹ Serum 4–9 μg mL ⁻¹ | 23, 32 and 34 | | | |
| | Total proteins | 7.1–223.2 mg dL ⁻¹ 0.9 ± 0.2 mg mL ⁻¹ | Serum 6–8 g dL ⁻¹ | | | | |
| 4. Hormones | Cortisol | 3.5–27.0 mg dL ⁻¹ | Serum 2–25 mg dL ⁻¹ | 35 | | | |
| | Testosterone | 32–55 pg mL ⁻¹ | Serum 320–600 ng dL ⁻¹ | | | | |
| | Progesterone | Luteal phase 436 ± 34 pmol L ⁻¹ Follicular phase 22.1 ± 2.7 pmol L ⁻¹ | Serum male: <1 ng mL ⁻¹ Serum female: 0.1–20 ng mL ⁻¹ | | 37 | | |
| | Estrogen (Estradiol) | Luteal phase 20.6 ± 0.4 pmol L ⁻¹ | Serum male: 15–60 pg mL ⁻¹ Serum female: 15–370 pg mL ⁻¹ | | | | |

^a U mL⁻¹: enzymatic activity per unit (mL) of saliva.

The concentration of CaCl₂·2H₂O (ref. Fusayama-Meyer¹⁶) was given incorrectly. The concentration of NH₄Cl (ref. SAGF^{17,18}) was missing. A full, corrected Table 2 is reproduced here.



Table 2 Compositions of different artificial saliva recipes

| Artificial saliva compositions | | Concentration (g L ⁻¹) | | | | |
|--------------------------------|---|------------------------------------|------------------------------|-----------------------|----------------------|---|
| | | AFNOR ^{14,15} | Fusayama-Meyer ¹⁶ | SAGF ^{17,18} | Klimek ¹⁹ | Shellis ¹² |
| 1. Inorganic compounds | NaCl | 6.70 | 0.40 | 0.13 | 0.58 | — |
| | KCl | 1.20 | 0.40 | 0.96 | 1.27 | 1.16 |
| | Na ₂ HPO ₄ | 0.26 | — | — | 0.34 | 0.375 |
| | KH ₂ PO ₄ | 0.20 | — | 0.66 | 0.33 | 0.35 |
| | NaHCO ₃ | 1.50 | 0.10 | 0.63 | — | 0.54 |
| | KSCN | 0.33 | — | 0.19 | 0.16 | 0.22 |
| | | | | | (NaSCN) | |
| | CaCl ₂ ·2H ₂ O | — | 0.795 | 0.23 | 0.17 | 0.21 |
| | Na ₂ S·9H ₂ O | — | 0.005 | — | — | — |
| | Urea | — | 1.00 | 0.20 | 0.20 | 0.17 |
| | NaH ₂ PO ₄ ·H ₂ O | — | 0.69 | — | — | — |
| | NH ₄ Cl | — | — | 0.18 | 0.16 | 0.233 |
| | Na ₂ SO ₄ ·10H ₂ O | — | — | 0.76 | — | — |
| | MgCl ₂ ·6H ₂ O | — | — | — | — | 0.043 |
| | Sodium citrate | — | — | — | — | 0.013 |
| 2. Organic compounds | Ascorbic acid | — | — | — | 0.002 | — |
| | Glucose | — | — | — | 0.03 | — |
| | Uric acid | — | — | — | — | 0.0105 |
| | Creatinine | — | — | — | — | 0.0001 |
| | Choline | — | — | — | — | 0.013 |
| | Mixture of vitamins | — | — | — | — | 0.0008 |
| | 3. Protein/polypeptide compounds | Mucin | — | — | — | 2.70 ^a |
| Glycoprotein | | — | — | — | — | 2.5 |
| Alpha amylase | | — | — | — | — | 3 × 10 ⁵ Somogyi's unit L ⁻¹ ^b |
| Albumin | | — | — | — | — | 0.025 |
| Mixture of amino acids | | — | — | — | — | 0.041 |

^a Bacto-Mucin bacteriological. ^b Somogyi's unit/L is a measure of the level of activity of amylase in blood serum. One Somogyi unit is defined as the amount of amylase required to produce the equivalent of 1 mg of glucose when acting on a standard starch solution under a defined condition.³⁸

Incorrect values were given for linear ranges, LOD and the pH of the buffers for some of the detection methods in Table 4. The specific changes relate to Phosphate (linear range and buffer pH), caffeine (LOD for the molecularly imprinted electrode and linear range for the SWNCT/CC electrode), glutathione (medium for the Prussian blue/SPE electrode and linear range for the caffeic acid/GC electrode) and uric acid (LOD). A full, corrected Table 4 is reproduced here.



Table 4 Examples of methods of electroanalytical detection available for possible salivary biomarkers (listed in Table 3)

| Biomarkers | Methods | Electrodes | Linear range | LOD | Medium | Ref. |
|---|----------|---|--------------------------------|-------------------------|--|------|
| Chemicals | | | | | | |
| Calcium | ISE | Calcium-specific electrode | 2.2–8 mg per 100 mL | — | Aqueous, serum | 179 |
| Potassium | ISE | Potassium electrode with polymer membrane | 115 mM–180 mM ^a | — | Whole blood, serum | 180 |
| Phosphate | AMP, CV | Molybdate anions in chitosan/GC | 0.79 μM–3.96 μM 19 μM–95 μM | — | Deaerated Tris buffer (pH 7.2) | 187 |
| Cotinine | MPA | BDD | 0.5 μM–100 μM | 0.06 μM | PBS (pH 7.0), saliva | 188 |
| Nicotine | SWV | Anti-cotinine antibody/C-SPE | 1–100 ng mL ⁻¹ | 1.0 ng mL ⁻¹ | Serum | 189 |
| | AMP, CV | MWCNT/alumina-coated silica nanocomposite | — | 1.42 μM | PBS (pH 8) | 190 |
| | AMP | TiO ₂ /GC | 0 μM–5000 μM | 4.9 μM | PBS (pH 7.4) | 191 |
| | CV | MWCNT/BPPG | up to 1 mM | 1.5 μM | BR (pH 8) | 192 |
| | CV | CNT/SPE | 10 μM–1000 μM | 2 μM | Buffer (pH 7), artificial saliva | 193 |
| Nitrate (NO ₃ ⁻) | DPV | BDD | 0.5 μM–200 μM | 0.3 μM | BR (pH 8) | 194 |
| | EIS | Polydopamine imprinted film | 1 μM–25 μM | 0.5 μM | PBS (pH 7.4), serum | 195 |
| Nitrite (NO ₂ ⁻) | LSV | Cu plated-/BDD microelectrode array | 1.2 μM–124 μM | 0.76 μM | 0.1 M Na ₂ SO ₄ (pH 3) | 196 |
| Nitrite (NO ₂ ⁻) | AMP | Cellulose acetate membrane/Pt | 1 μM–100 μM | 0.5 μM | Acetate buffer (pH 4.0) | 197 |
| | AMP | Poly(1,8-diaminonaphthalene) film/Pt | 0.5 μM–100 μM | 0.1 μM | | |
| | AMP, DPV | Carbon black paste electrode | 0.01 μM–4 μM | 0.005 μM | Acetate buffer (pH 4.6) | 198 |
| Caffeine | DPV, LSV | Carbon black SPE | 0.1 μM–8.8 μM | 0.097 μM | | |
| | DPV, LSV | GC | 4 mM–80 mM | 6 μM | Saliva, urine | 199 |
| | CV | Nafion/GC | up to 7.0 mM | 0.04 μM | PBS (pH 7.0) | 200 |
| | CV, SWV | Pseudo CP | 1 μM–1 mM | 0.348 μM | PBS (pH 7.0) | 201 |
| | DPV | Molecularly imprinted polymer | 0.5 nM–0.16 μM | 90 pM | PBS (pH 6.5) | 202 |
| | DPV | SWCNT/CC | 0.25 μM–0.1 mM | 0.12 μM | 0.01 M H ₂ SO ₄ (pH 1.7) | 203 |
| | SWV | EPPG | 0.02 μM–100 μM | 0.008 μM | PBS (pH 7.2), urine | 204 |
| Thiocyanate (SCN ⁻) | CV, DPV | Ag-MWCNT/GC | 2.5 nM–50 nM 50 nM–1.0 μM | 1.0 nM | PBS (pH 6.0), saliva, urine | 205 |
| | CV, AMP | Ag@Cu nanorods/GC | 1 mM–10 mM | 10 nM | PBS (pH 6.0) | 206 |
| Anti-oxidants | | | | | | |
| Glutathione (GSH) ^b | CV | Copper hydroxide/CILE | 1 μM–50 μM 0.1 mM–1.8 mM | 30 nM | PBS (pH 7.0) | 207 |
| | CV, AMP | Ordered mesoporous carbon | 0 mM–2.5 mM ^a | 0.09 μM | PBS (pH 7.16) | 208 |
| | CV, AMP | Carbon microfiber | 5 μM–65 μM ^a | 0.5 μM | PBS (pH 7.5) | 158 |
| | CV | Poly(caffeic acid) nanocarbon composite/GC | 0.5 μM–5.0 mM | 0.5 μM | PBS (pH 7.0) | 209 |
| | CV | GC | 6 μM–59 μM | 1 μM | Tissue media (pH 7) | 210 |
| | CV | Prussian blue/SPE | 2 μM–0.5 mM | 2.0 μM | PBS (pH 7.4), blood | 211 |
| | CV | Nanocarbon paste | 2 μM–120 μM ^a | 2.0 μM | PBS (pH 7.5) | 212 |
| | CV | Caffeic acid/GC | >1.0 mM | 2.2 μM | PBS (pH 7.0) | 213 |
| Glutathione disulfide (GSSG) | CV, SWV | CNT-SPE | 10 μM–60 μM ^a | 3.0 μM | PBS (pH 7.0), saliva | 156 |
| | CV | Copper hydroxide/CIL | 0.4 μM–120 μM | 15 nM | PBS (pH 7.0) | 207 |
| | CV, DPV | Graphene-Pt/GC | 0.15 μM–34 μM | 0.15 μM | PBS (pH 7.0) | 214 |
| | DPV | Nitrogen doped graphene | 5.0 μM–1.3 mM | 2.2 μM | PBS (pH 6.0) | 215 |
| | CV, LSV | SWCNH/GC | 30 μM–400 μM | 5 μM | PBS (pH 7.0) | 216 |
| Ascorbic acid | CV, DPV | Poly(acid chrome blue K)/GC | 50.0–1000.0 μM | 10.0 μM | PBS (pH 4.0), urine | 217 |
| | CV, DPV | | | | | |
| Uric acid | CV, DPV | Graphene-Pt/GCE | 0.05 μM–12 μM | 0.05 μM | PBS (pH 7.0) | 214 |
| | CE/AMP | Poly(dimethylsiloxane) (PDMS)/glass microchip | 15 μM–110 μM | 1 μM | MES (pH 5.5), urine | 218 |
| | DPV | Nitrogen doped graphene | 0.1 μM–20 μM | 45 nM | PBS (pH 6.0) | 215 |
| | SWV | Clay colloids/GC | 0.5 μM–10 μM 10 μM–100 μM | 0.2 μM | Citrate buffer (pH 1.0) | 219 |
| | DPV | CIL | 2.0 μM–0.2 mM | 1.0 μM | PBS (pH 6.8), urine | 220 |
| | CV, DPV | Poly(acid chrome blue K)/GC | 1.0 μM–120 μM | 0.5 μM | PBS (pH 4.0), | 217 |



Table 4 (Contd.)

| Biomarkers | Methods | Electrodes | Linear range | LOD | Medium | Ref. |
|--------------------------------|-------------|--|--|--|--|------|
| | CV, LSV | SWCNH/GC | 0.06 μM –10 μM | 20 nM | PBS (pH 7.0) | 216 |
| | SWV | Electrochemically activated GC | 0.04 μM –2.0 μM | 9 nM | 0.5 M H_2SO_4 , urine | 221 |
| Therapeutic drugs | | | | | | |
| Theophylline | CV | MWCNT/GC | 0.3 μM –10.0 μM | 50 nM | PBS (pH 5.8) | 222 |
| | DPV | Graphene/Nafion/GC | 10 nM –1.0 μM | 6.0 nM | 0.1 M H_2SO_4 | 223 |
| Acetaminophen (paracetamol) | DPV | Cobalt phthalocyanine NP/CP | 0.4 μM –0.1 mM | 0.14 μM | PBS (pH 7.4) | 224 |
| | DPV | Urchin-like CdSe microparticles/ GC | μM –40 μM | 0.4 μM | PBS (pH 6.0) | 225 |
| | SWV | Nafion/lead–ruthenium oxide pyrochlore | 40 μM –700 μM up to 100 μM | 0.1 μM | PBS (pH 3) | 226 |
| | CV | Nafion/ TiO_2 -graphene/GC | 1 μM –100 μM | 0.21 μM | PBS (pH 7.0) | 227 |
| | DPV | Pd/graphite oxide/GC | 5 nM–0.5 μM | 2.2 nM | PBS (pH 6.8) | 228 |
| | DPV | BiO/graphite SPE | 0.5 μM –1.250 μM | 30 nM | BR buffer (pH 2.0), saliva | 229 |
| | DPV | SWCNT–graphene/GC | 0.05 μM –65 μM | 38 nM | PBS (pH 7.0), serum | 230 |
| | DPV | Functionalized MWCNT | 0.45 μM –90.0 μM | 0.35 μM | PBS (pH 7.0), saliva | 231 |
| | SWV | CoNP/MWCNT | 5.2 nM–0.45 μM | 1.0 nM | PBS (pH 7.0) | 232 |
| | SWV | MWCNT/BPPG | μM –2 μM | 10 nM | PBS (pH 7.5) | 233 |
| SWV | Graphene/GC | 2 μM –20 μM 0.1 μM –20 μM | 32 nM | $\text{NH}_3 \cdot \text{H}_2\text{O}$ – NH_4Cl (pH 9.3) | 234 | |
| pH | | | | | | |
| pH | CV | Carbon fibre microelectrode | pH 2.5–8 (buffer), pH 4–8.5 (artificial saliva) | Sensitivity: –61 mV/pH (buffer) –73 mV/pH (artificial saliva) | Buffer, artificial saliva, saliva | 235 |
| | EIS | Iridium oxide | pH 4–8 | Sensitivity: –47 mV/pH (artificial saliva) | Artificial saliva | 236 |
| | ISE | Poly(3-octylthiophene-2,5-diyl) regiorandom/SPCE | pH 4–8 | Sensitivity: –53.4 mV/pH (buffer) | Buffer, saliva | 237 |
| | ISE | Poly(terthiophene benzoic acid)/ AuZnO_x /SPCE | pH 2–13 | Sensitivity: 59.2 \pm 0.5 mV/pH (buffer) | Buffer, saliva, urine | 238 |

The methods highlighted in grey and blue have been validated in artificial saliva and real saliva, respectively. **Methods:** AMP: amperometry, CA: chronoamperometry, CE: capillary electrophoresis, CV: cyclic voltammetry, DPV: differential pulse voltammetry, EIS: electrochemical impedance spectroscopy, ISE: ion-selective electrode, LSV: linear sweep voltammetry, MPA: multiple-pulse amperometry, SWV: square wave voltammetry. **Electrodes:** BDD: boron-doped diamond, BPPG: basal plane pyrolytic graphite, CC: carbon ceramic, CIL: carbon ionic liquid, CNF: carbon nanofiber, CP: carbon paste, EPPG: edge plane pyrolytic graphite, GC: glassy carbon electrode, MWCNT: multi-walled carbon nanotube, NP: nanoparticle, SPE: screen-printed electrode, SWCNT: single-walled carbon nanotube, SWCNH: single-walled carbon nanohorn.^a Not stated in the text – values are taken from calibration curves present in the papers.



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