

Exploration of the medical periodic table: towards new targets

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Supporting Information

Table S1. Some examples of uses of the elements in therapy and diagnosis. These entries have guided our colour-coding in Fig.1, which is illustrative only and not comprehensive.

Z	Symbol	Element	Some medically-relevant uses
1	H	Hydrogen	Essential element; pH tightly controlled but variable: blood ~7.4, lysosomes 4–5, tumour tissue 6–7, endosomes (transferrin) 5.5; duodenum 6–6.5, large intestine 5.5–7, stomach 1–3; ^2H for kinetic control of organic drugs; ^3H as radiotracer.
2	He	Helium	He-O ₂ ; for treatment of chronic obstructive pulmonary disease; hyperpolarised ^3He for MRI.
3	Li	Lithium	Li ₂ CO ₃ : drug for treatment of bipolar disorders.
4	Be	Beryllium	Compounds can provoke severe immune response (chronic beryllium disease).
5	B	Boron	Boromycin: bacteriocidal polyether-macrolide antibiotic. Boronophenylalanine-based Boron Neutron Capture Therapy in combination with Cetuximab in clinical Phase I trials for head and neck cancer treatments.
6	C	Carbon	Essential element; body produces 3-6 mL CO per day- suppresses organ rejection, ‘neurotransmitter’; ^{11}C , ^{14}C used in radiopharmaceuticals.
7	N	Nitrogen	Essential element; NO is a muscle relaxant, vasodilator, hypotensive, ‘neurotransmitter’; ^{13}N used in radiopharmaceuticals.
8	O	Oxygen	Essential element; Reactive oxygen species (ROS), e.g. $^1\text{O}_2$, O_2^- , H_2O_2 , O_3 , ONO_2^- .
9	F	Fluorine	Essential element; Toughens tooth enamel as component of (fluoro)apatite; ^{18}F labelling, positron emission, radioimaging, PET scans.
10	Ne	Neon	
11	Na	Sodium	Essential element; ca. 0.14 M in blood; excessive NaCl intake increases arterial hypertension.
12	Mg	Magnesium	Essential element; Mg ^{II} is a laxative (sulphate, Epsom Salts); Mg(OH) ₂ (milk of magnesia) antacid; Mg ^{II} (aspartate) ₂ dietary supplement.
13	Al	Aluminium	Added to some vaccines as an adjuvant; Al(OH) ₃ antacid.
14	Si	Silicon	Essential element; Role in connective tissue?

			Silicates essential to prevent Al toxicity? Silicon phthalocyanine 4 photosensitizer for photodynamic therapy.
15	P	Phosphorus	Essential element; Polyphosphate abundant in all cells; oral sodium phosphate for bowel cleansing; phytate (inositol hexaphosphate) in plants can modulate metal uptake (<i>e.g.</i> Zn ²⁺).
16	S	Sulfur	Essential element; H ₂ S as signalling molecule (vasodilator and regulator of blood pressure).
17	Cl	Chlorine	Essential element; Defect in membrane Cl ⁻ transport in cystic fibrosis (CFTR gene); HOCl/OCl ⁻ , generated by myeloperoxidase in neutrophils.
18	Ar	Argon	Ionized argon gas (plasma) - coagulation to control bleeding from lesions in gastrointestinal tract.
19	K	Potassium	Essential element; natural radioisotope ⁴⁰ K 0.012% β emitter, t _{1/2} 1.3 × 10 ⁹ y.
20	Ca	Calcium	Essential element; CaCO ₃ antacid; Ca oxalate/phosphate/carbonate kidney stones.
21	Sc	Scandium	⁴⁴ Sc, positron emitter, potential for PET imaging.
22	Ti	Titanium	Budotitane and Cp ₂ TiCl ₂ clinical anticancer trials abandoned; new Cp derivatives in development; Utilisation as inert material for implants.
23	V	Vanadium	Essential element; Insulin-enhancing drugs, V ^{IV} <i>bis</i> (2-ethyl-3-hydroxy-4-pyronato) in clinical trials for type-2 diabetes.
24	Cr	Chromium	Cr ^{III} <i>tris</i> (picolinate) sold as nutritional supplement; essentiality of Cr unclear.
25	Mn	Manganese	Essential element; SOD mimetics (<i>e.g.</i> Mn ^{III} salen chloride), Mn ^{II} macrocycles for treatment of pain, neuroprotection; Mn ^{II} dipyrrodoxyl diphosphate (MnDPDP) clinical MRI contrast agent.
26	Fe	Iron	Essential element; Fe ^{II} compounds for Fe deficiency (succinate, fumarate), also Fe ^{III} with E ^o < -324 mV at pH 7 (dextran, dextrin); ferroquine in clinical Phase II trials as antimalarial agent; superparamagnetic iron oxide MRI contrast agent; Na ₂ [Fe ^{II} (CN) ₅ NO] hypotensive.
27	Co	Cobalt	Essential element; Coenzyme Vitamin B ₁₂ essential (2-3 μg/day); treatment of pernicious anaemia; CTC-96 Co ^{III} <i>bis</i> (2-methylimidazole) acacen derivative (Doxovir) has completed clinical Phase I trials for ophthalmic herpetic keratitis and adenoviral conjunctivitis and clinical Phase II trials for herpes labialis.
28	Ni	Nickel	Essential element; Potential allergen (ear rings); used in trace mineral supplements; role in body poorly understood.
29	Cu	Copper	Essential element; Cu ^{II} <i>bis</i> (histidine) for Menke's disease; ⁶⁴ Cu PET/CT scans in clinical Phase II trials

			for cervical cancer imaging; Cu-Algesic approved as anti-inflammatory agent for horses and dogs.
30	Zn	Zinc	Essential element; Zn ^{II} (gluconate) ₂ dietary supplement; ZnO skin ointment; Zn ^{II} citrate antiplaque (toothpastes).
31	Ga	Gallium	⁶⁷ Ga γ-ray radioimaging; ^{66/68} Ga PET; [Ga ^{III} (malolate) ₃] and [Ga(hydroxyquinolate) ₃] NKP-2235 in Phase I clinical trials; ⁶⁸ Ga-DOTATATE PET/CT scans in clinical development (NCT01524016) for imaging in mesenchymal tumours, and oncogenic osteomalacia, and in clinical Phase I trials for neuroendocrine cancer imaging.
32	Ge	Germanium	Possible use of Ge nanoparticles as radiosensitizers.
33	As	Arsenic	As ₂ O ₃ approved drug for treatment of leukaemia and in clinical Phase II trials for lung cancers; arsenobetaine in marine organisms; Roxarsone (3-nitro-4-hydroxyphenyl arsenic acid) growth promoter in poultry. Darinaparsin approved drug for peripheral T-cell lymphoma treatment, and in clinical Phase I clinical trials for solid tumours treatments. GSAO in clinical Phase I trials for advanced solid tumours that have not responded to therapy.
34	Se	Selenium	Essential element; Human selenoproteome consists of 25 selenoproteins; selenocysteine tRNA; Se ^{IV} sulfide active ingredient in some anti-dandruff shampoos (antifungal).
35	Br	Bromine	Daily dietary intake of bromide <i>ca</i> 2 - 8 mg (fish, grains and nuts). Concentration in blood 10 – 100 μM; substrate for eosinophil peroxidase Br/H ₂ O ₂ → HOBr.
36	Kr	Krypton	Potential for hyperpolarised ⁸³ Kr in MR imaging of airways
37	Rb	Rubidium	⁸² Rb, positron emitter, PET <i>e.g.</i> in cardiac sarcoidosis.
38	Sr	Strontium	SrCl ₂ in toothpastes (for sensitive teeth); ⁸⁹ Sr, β emitter, therapeutic radionuclide.
39	Y	Yttrium	⁹⁰ Y, β emitter, therapeutic radionuclide; ⁸⁶ Y, positron emitter, PET.
40	Zr	Zirconium	⁸⁹ Zr, positron emitter, PET imaging; ‘Aluminium zirconium tetrachlorohydrate gly’ (Zr ⁴⁺ /Al ³⁺ OH/Cl/glycine complexes) used in antiperspirants; zirconia (ZrO ₂) ceramics for orthopaedic surgery
41	Nb	Niobium	Heteropolyniobates [SiNb ₁₂ O ₄₀] ¹⁶⁻ can immobilise viruses.
42	Mo	Molybdenum	Essential element; MoO ₄ ²⁻ transport pathways; Tetrathiomolybdate [MoS ₄] ²⁻ : copper chelator for overload (<i>e.g.</i> Wilson’s) diseases and in clinical Phase II trials for both breast cancer and esophageal

			carcinoma treatments.
43	Tc	Technetium	^{99m} Tc γ -ray radioimaging-ATSM in clinical Phase II trials for cervical cancer treatment; Cardiolite (^{99m} Tc-sestamibi) and Neurite (^{99m} Tc-disicte) approved for folate-receptor positive tumours imaging; Etarfolatide (EC20- ^{99m} Tc) in clinical Phase III trials for folate-receptor positive tumours imaging; ^{99m} Tc-MIP-1404 in clinical Phase II trials for prostate cancer imaging. Trials of ^{94m} Tc (positron emitter) for PET.
44	Ru	Ruthenium	Two tetrachloride bis(N-heterocycle) Ru ^{III} complexes in clinical trials as anticancer and antimetastatic agents.
45	Rh	Rhodium	¹⁰⁵ Rh, β emitter, therapeutic radionuclide; dinuclear Rh ^{II} anticancer; photochemotherapeutic complexes.
46	Pd	Palladium	¹⁰³ Pd, electron capture, radiotherapy; Palladium bacteriophosphoribide photosensitizer TOOKAD in Phase III clinical trials for localised prostate cancer treatment, and in Phase I/II for predetermined small renal tumour targets treatment.
47	Ag	Silver	Antimicrobial; treatment of burnwounds; sulfadiazine, carbene complexes, nanoparticles; Acticoat absorbant TM silver eluting dressing in clinical Phase IV trials for prevention of lower extremity revascularization wound complications.
48	Cd	Cadmium	Induces metallothionein synthesis (detoxification); cadmium carbonic anhydrase active in marine diatoms.
49	In	Indium	¹¹¹ In γ -ray radioimaging.
50	Sn	Tin	Essential element; Little known about biochemistry as essential element; Sn ^{IV} ethyl etiopurpurin (Purlytin) photosensitizer for photodynamic therapy of psoriasis and restenosis (Phase II).
51	Sb	Antimony	Antileishmanial Sb ^V drugs: meglumine antimoniate (<i>Glucantime</i>) and sodium stibogluconate (<i>Pentostam</i>).
52	Te	Tellurium	Ammonium trichloro (dioxoethylene-O,O') tellurate is an immunomodulator
53	I	Iodine	Essential element; Thyroid hormones; iodo-organics as X-ray contrast agents; ¹²³ I, ¹²⁵ I radioimaging; ¹³¹ I radiotherapy.
54	Xe	Xenon	Anaesthetic; hyperpolarised ¹²⁹ Xe as MRI contrast agent.
55	Cs	Cesium	¹³¹ Cs, electron capture, prostate brachytherapy.
56	Ba	Barium	BaSO ₄ (barium sulphate meal) for radiographs of oesophagus, stomach and duodenum.
57	La	Lanthanum	La ₂ CO ₃ approved drug Oct 2004 (Fosrenol) for hyperphosphatemia.
58	Ce	Cerium	Flammacerium (cerium(III) nitrate-silver

			sulphadiazine) for treatment of burn wounds; Ce ^{IV} sulfate antiseptic.
59	Pr	Praseodymium	
60	Nd	Neodymium	
61	Pm	Promethium	
62	Sm	Samarium	¹⁵³ Sm, β emitter, therapeutic radionuclide; Samarium-153- lexidronam pentasodium in clinical Phase II trials for prostate cancer treatment.
63	Eu	Europium	Potential for PARACEST MRI contrast agents.
64	Gd	Gadolinium	Chelated Gd ^{III} complexes as contrast agents for MRI (e.g. DTPA, DOTA); ¹⁵⁷ Gd for neutron capture therapy; Gd ^{III} texaphyrin clinical trials as radiation and chemotherapy sensitiser.
65	Tb	Terbium	
66	Dy	Dysprosium	
67	Ho	Holmium	¹⁶⁶ Ho, β emitter, therapeutic radiopharmaceutical; Holmium-166 polylactic microspheres in clinical Phase II trials for liver neoplasms treatment.
68	Er	Erbium	
69	Tm	Thulium	¹⁶⁷ Tm for bone scanning (density).
70	Yb	Ytterbium	⁹⁰ Y therapeutic radionuclide (β emitter).
71	Lu	Lutetium	¹⁷⁷ Lu, β emitter, therapeutic radionuclide; Lu ^{III} texaphyrin photosensitizer terminated Phase II trials for breast cancer, malignant melanomas atherosclerotic plaque in coronary heart disease; IMP-288-lutetium in clinical Phase II trials for small cell lung cancer treatment.
72	Hf	Hafnium	
73	Ta	Tantalum	Utilisation as inert material for implants.
74	W	Tungsten	Tungstate, [WO ₄] ²⁻ : antidiabetic; antiviral polyoxotungstates.
75	Re	Rhenium	β-emitters ¹⁸⁶ Re, ¹⁸⁸ Re for radiotherapy.
76	Os	Osmium	OsO ₄ injection into knee joints for synovectomy (Scandinavia).
77	Ir	Iridium	¹⁹² Ir γ emitter used clinically for vascular brachytherapy.
78	Pt	Platinum	Clinically established anticancer drugs: cisplatin, carboplatin, oxaliplatin, nedaplatin, lobaplatin and heptaplatin. Lipoplatin in clinical phase II trials. Dicycloplatin in Chinese clinical phase I trials. Pt complexes including in nanoparticles and dinuclear-platinum complex CT-47463 in pre-clinical development.
79	Au	Gold	Aurothiomalate (injectable) and auranofin (oral) antirheumatoid arthritic drugs; Auranofin in clinical Phase II trials for chronic lymphocytic leukemia, small lymphocytic lymphoma, and prolymphocytic leukemia. Clinical trials planned for auranofin as treatment of amebiasis and parasite <i>Giardia</i>

			<i>intestinalis.</i>
80	Hg	Mercury	Declining use in diuretics (thiomersal), vaccines ; antimicrobial (preservative).
81	Tl	Thallium	Tl ^I often toxic, can substitute for K ^I ; ²⁰¹ Tl, electron capture, radiodiagnostic imaging (SPECT).
82	Pb	Lead	²¹² Pb, α emitter promising for radiotherapy; Can inhibit heme synthesis and cause anaemia, neurotoxicity.
83	Bi	Bismuth	Bi ^{III} subsalicylate, subgallate, subcitrate used for gastrointestinal disorders; Ranitidine bismuth citrate for antibacterial applications ²¹² Bi for radiotherapy, α and β ⁻ emitter (generated <i>in vivo</i> from ²¹² Pb by β ⁻ decay, t _{1/2} = 10.6 h); Combination of bismuth subcitrate potassium, metronidazole, tetracycline hydrochloride and omeprazole in clinical Phase IV trials for anti- <i>Helicobacter Pylori</i> infection; Lintuzumab-Bi213 in clinical Phase II trials for acute myeloid leukemia treatment.
84	Po	Polonium	
85	At	Astatine	²¹¹ At (t _{1/2} = 7.2 h, α-particle emitter) used in labelled agents for targeted radiotherapy.
86	Rn	Radon	Radioactive, environmental hazard, may accumulate in basements of dwellings; Most stable isotope ²²² Rn (t _{1/2} 3.8 d, α-particle emitter, decay product of ²³⁸ U); Thought to be a major cause of lung cancer.
87	Fr	Francium	
88	Ra	Radium	²²³ Ra (t _{1/2} = 11.4 d , α-particle emitter), is a bone-seeking radionuclide used for the treatment of skeletal metastases; Alpharadin (²²³ Ra chloride) in clinical Phase I/II trials for bone metastasis from castration-resistant prostate cancer treatment.
89	Ac	Actinium	²²⁵ Ac(t _{1/2} = 10.0 d, α-particle emitter) used for tagging antibodies in radioimmunotherapy; Actinium-225-labeled humanized anti-CD33 monoclonal antibody HuM195 in clinical Phase I trials for leukemia myelodysplastic syndrome treatment; Lintuzumab-Ac225 in clinical Phase I/II trials for acute myeloid leukemia treatment.