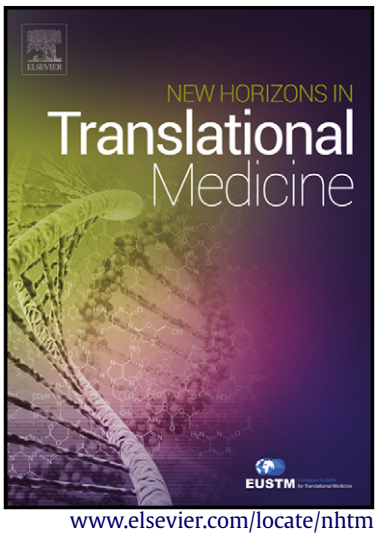

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Angelo M. Facchiano, Francesco Facchiano, Antonio Facchiano

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The role of chemical elements in melanoma

Angelo M. Facchiano[a], Francesco Facchiano[b*], Antonio Facchiano[c*]

[a]National Research Council, Institute of Food Science, Avellino, Italy

[b]Department of Hematology, Oncology and Molecular Medicine, Istituto Superiore di Sanità, Rome, Italy

[c]Istituto Dermopatico dell'Immacolata, IDI-IRCCS, 00167 Rome, Italy

[*]Corresponding authors

Dr. Antonio Facchiano

Istituto Dermopatico dell'Immacolata, IDI-IRCCS, via Monti di Creta 104, 00167 Rome, Italy a.facchiano@idi.it; tel. 39-06-66462431; 39-06-89996620

Dr. Francesco Facchiano

Department of Hematology, Oncology and Molecular Medicine, Istituto Superiore di Sanità, Rome, Italy francesco.facchiano@iss.it; tel 39-06-49902059

Abstract

Publication of several studies attest the growing interest to investigate the real impact chemical elements and industrial pollution may play have on the human health.

In the current study we present novel data referring to the occurrence of the name of all chemical elements taken from the Mendeleev table, in the title of PubMed indexed melanoma articles. Nine hundred fifty four manuscripts were found to have in the title field the "melanoma" word and at least one of the 117 chemical elements.

The occurrence of each chemical element in melanoma articles was then compared to the occurrence in epithelioma articles and squamous cell carcinoma articles, unrevealing substantial quantitative differences. Manuscripts having "skin" in the title were used as control manuscripts. The 10 elements most studied in melanoma manuscripts were found to be iodine, oxygen, ruthenium, boron, calcium, carbon, sodium, zinc, iron and technetium, accounting for more than 50% of the 954 identified manuscripts. In all such cases, the occurrence in melanoma manuscripts was found to be largely different as compared to epithelioma articles, as well as squamous cell carcinoma articles.

The role of each of these elements in melanoma is discussed.

Keywords

Human health, industrial pollution, melanoma, epithelioma, squamous cell carcinoma, chemical elements, iodine, oxygen, ruthenium, boron, calcium, carbon

Focal Points

Bedside

The ten most common elements identified to play key roles in melanoma are shown here to be different form the ten most common found in other control conditions, such as epithelioma or other skin cancers.

Benchside

New ways are necessary to organize the immense literature data currently available and to collect it in an ordered, systematic manner, easy to read and to interpret.

Industry

Systematic searches in PubMed –indexed literature leading to ordered outputs may facilitate the interpretation of published data. In the present study the role each chemical element plays in melanoma has been investigated by exhaustive searches in PubMed –indexed literature.

Governments

There is an increasing interest to investigate the impact chemical elements and industrial pollution have on the human health.

Introduction

The role metals and other chemical elements play in human medicine, animal medicine and biology is deeply investigated (Yoshihisa, 2012; Guy, 2005; Hostynek, 2003; Hostynek, 1993) given the increasing interest towards the effects chemical elements released from agricultural and industrial activities exert on human health and on the whole ecosystem. Such studies are of specific relevance in the investigation of skin diseases such as contact dermatitis, which are often related to direct allergens and chemical elements exposure, leading to metal-specific immune reactions, as recently pointed out (Shigematsu, 2014; Kobayash, 2013; Lansdown, 201; Strupp, 2011).

Several studies address the role of chemical elements as carcinogenic agents (Sun, 2014; Poirier, 2012; Caciari, 2010; Olszewski, 2006). We recently published the first study reporting a bibliometric analysis of melanoma manuscripts (D'Arcangelo, 2013); in the present study we use a

novel systematic approach to investigate the role chemical elements play in melanoma, based on a linguistic approach.

Material and Methods

In order to systematically address the role each chemical element plays in melanoma and other skin cancers, we collected a complete set of PubMed references by identifying articles indexed until may 15th 2014, containing in the "title" field the name of each of the 117 chemical elements (taken from the Mendeleev table) along with "melanoma" or "epithelioma" or "squamous cell carcinoma" or "skin" word. According to this procedure 954 melanoma manuscripts were identified, 74 epithelioma-manuscripts, 286 squamous cell carcinoma-manuscripts and 4395 skin-manuscripts, as reported in Table 1.

The occurrence of each chemical element in melanoma-, or epithelioma-, or squamous cell carcinoma- or skin- manuscripts was then calculated in absolute and percent terms, and reported in Table 1 and 2, respectively.

Results

The 5 chemical elements most present in the title of melanoma manuscripts were found to be the iodine (91 manuscripts), followed by oxygen (61 manuscripts), ruthenium (49 manuscripts), boron (46 manuscripts) and calcium (45 manuscripts). Carbon, sodium, zinc, iron and technetium are from the sixth to the tenth most present elements in melanoma manuscripts. The occurrence of each element in manuscripts having "epithelioma" or "squamous cell carcinoma" or "skin" in the title was also investigated. Table 1 reports side by side the number of manuscripts found in each category, for each chemical element in alphabetic order.

Such numbers were then expressed as percent of total manuscripts of each vertical category. Table 2 reports percent values in occurrence order, and shows that the chemical element mostly reported in melanoma field (i.e., iodine) is different from the element most studied in "epithelioma" field (i.e, radium) or in squamous cell carcinoma field (i.e, platinum) or in the skin field (i.e., sodium), highlighting biological differences in such categories.

Table 1 and 2 can be useful references to compare the role of chemical elements in different skin cancers and to highlight, at least to some extent, their relevant biological features. For instance, Table 2 shows that more than 50% of epithelioma articles contain the "radium" word in the title, while this element is absent in melanoma manuscripts.

Discussion

In the following discussion sections the attention is focused on the 10 chemical elements mostly studied in melanoma manuscripts (according to the rank reported in Table 2), accounting for more than 50% of all melanoma manuscripts (according to Table 1).

"Iodine" : first in the rank.

The word "iodine " occurs in 11% of melanoma-manuscripts (see Table 2), while Table 1 shows that only one epithelioma manuscript has "iodine" in the title.

According to the most recent literature, iodine is investigated in melanoma field mostly for its promising therapeutic effects as radioactive Iodine-125 in brachytherapy applications in uveal melanoma (McCannel, 2014; Perez, 2014; Badiyan, 2014; Mashayekhi, 2014; Quinlan-Davidson, 2013; Caminal, 2013; Collaborative Ocular Melanoma Study Group 2006; Caminal Mitjana, 2002), showing significantly better outcome as compared to uveal-melanoma patients treated with enucleation (Melia, 2006). However, in some cases local radiation-related toxic effects have been reported, such as retinopathy (Krema, 2011; Krema, 2013; Ahuja, 2012) macular oedema (Horgan, 2008), strabism (Kïratlï, 2007) or cataract (Collaborative Ocular Melanoma Study Group, 2007).

Two recent studies report iodine usage for imaging purposes in melanoma metastases (Uhrig, 2013; Cascini, 2009). Less recent literature reports Iodine-125 and Iodine-123 use to label benzamides for imaging purpose in melanoma (Moins, 2001; Brenner, 1999; Larish, 1998; Nicholl, 1997) and for other brachytherapy applications in eye-melanoma (Stannard, 2000).

"Oxygen" : second in the rank.

The word "oxygen" occurs 7.4% of melanoma-manuscripts while Table 1 shows that only two epithelioma manuscripts contain "oxygen" in the title.

According to the most recent literature, oxygen is most often mentioned as part of Reactive Oxygen Species (ROS), active in melanoma set-up. The antioxidant pattern has been found altered in experimental melanoma (Lazescu, 2013) and in simvastatin-treated melanoma cells undergoing a p53/p21 –mediated senescence (Guterres, 2013); the ROS pool can be produced by NADPH oxidase enzymes (NOX family), representing a promising target for melanoma treatment (Liu-Smith, 2014). ROS have been found to mediate the pro-angiogenic potential of melanoma cells (Schaafhausen, 2013; Vartanian, 2007); ROS mediate the *in vitro* apoptosis and growth inhibition of A375 human melanoma cells and other melanoma cells, induced by several different agents (Huang, 2014; Huang, 2012; Chakraborty, 2013; Ghosh, 2013; Mayola, 2011; Zhang, 2010; Morrison, 2010; Chou, 2009; Wang, 2008; Verhaegen, 2006) and of B16F10 mouse melanoma cells migration properties (Im, 2012). Blocking ROS production has been shown to reduce the anti-

melanoma activity of Cucurbitacin B (Zhang 2011) while decreasing ROS promotes melanoma growth (Huang 2010). An interesting study shows that the melanoma apoptosis induced by non-thermal atmospheric pressure dielectric barrier discharge (DBD) exposure is ROS-dependent (Sensenig, 2011), while another study suggests that the known low anti-oxidant enzymes expression in males may explain the known males dis-advantage in melanoma survival as compared to females (Joosse, 2010). Altogether, these studies suggest oxygen and ROS as relevant potential therapeutic targets in melanoma (Fruehauf, 2008; Fried, 2008; Tuma, 2008).

Less numerous studies investigate the effects of oxygen tension in melanoma; low-oxygen tension, a condition that can be found within tumors, may alter the expression of heat shock proteins (Shipp, 2012) and may promote melanoma development (Adams, 2006), while hyperbaric oxygen therapy is reported for choroidal melanoma treatment (Gall, 2007). Singlet oxygen generation has been shown to mediate the photodynamic-dependent impairment and the potential photodynamic therapy (PDT) of melanoma cells (Burguete, 2009).

"Ruthenium" : third in the rank.

The word "ruthenium" occurs in 5.9% of melanoma-manuscripts while Table 1 shows that "ruthenium" word does not occur in the title of any epithelioma manuscript.

According to the most recent literature, and similarly to iodine, ruthenium in melanoma is mostly mentioned for Ruthenium-106 -based brachytherapy in choroidal melanoma (Kwon, 2013; Perri, 2012; Razzaq, 2012; Marconi, 2013; Lee, 2012; Russo, 2012; Yarovov, 2012).

Other studies show potential therapeutic applications of non-radioactive ruthenium in melanoma field. In fact, ruthenium has been shown to exert nitric oxide-mediated tumoricidal action on melanoma (Carneiro, 2014) also in cooperation with nickel, copper and zinc (Sweigert, 2012); a ruthenium-porphirin complex shows toxic properties toward melanoma cells upon tungsten-lamp irradiation (Rani-Beeram, 2008) and a ruthenium-imidazolium complex inhibits melanoma metastases in an *in vivo* model (Gava, 2006).

"Boron" : fourth in the rank.

The word "boron" occurs in 5.6% of melanoma-manuscripts while Table 1 shows that "boron" word does not occur in the title of any epithelioma manuscript.

According to the most recent literature, boron is invariantly cited in melanoma manuscripts for the Boron Neutron Capture Therapy (BNCT), exploiting boron carriers accumulating within melanoma tissue and then irradiated with neutron beams. BNCT has shown to induce BCL2 and caspase-3 mediated apoptosis as well as cell-cycle arrest in mouse melanoma cells (Faiao-Flores, 2013a, Faiao-Flores, 2013b; Faiao-Flores, 2012) as well as oxidative stress, free radicals production and

growth inhibition in melanoma cells (Faiao-Flores, 2011), suggesting boron-containing complexes as potentially useful in melanoma treatment (Bonjoch, 2008; Morita, 2006, Meijer, 2005).

"Calcium" : fifth in the rank.

The word "calcium" occurs in 5.4% of melanoma-manuscripts, while Table 1 shows that only one epithelioma manuscript contains "calcium" in the title.

According to the most recent literature, calcium is essential in a variety of melanoma cells reactions, including melanoma vasculogenic mimicry (Vartanian, 2011) and S100B- p90 ribosomal S6 kinase (RSK) complex formation, which affects cell viability, modulates MAPK signaling and prevents RSK action on nuclear targets (Hartman, 2014; Lin, 2010). Increased cytosolic calcium levels are required for the specific anti-melanoma activity of BIL, a snake venom derived lectin (Aranda-Souza, 2014) and gap-junction dependent calcium sequestration increases melanoma resistance to chemotherapy (Lin, 2010). Intra- and extra-cellular calcium levels have been shown to control melanoma growth, migration and response to therapy via Orai1 and STIM2 activity (Stanisz, 2014), or via matrix-metalloproteinase activity (Long, 2013), or via 1,3- dichloro-2-propanol (DCP) (Park, 2010), or via PKC phosphorylation (Dissanayake, 2008), or via honeybee-venom dependent melanoma apoptosis (Tu, 2008), or via phospholipase D and acidic sphingomyelinase pathways (Kato 2007). Further, TRPV1, TRPM8, TRPA1 and CB1 expression have been shown to control calcium transients and to act as potential drug targets in melanoma (Mergler, 2014). T-type calcium channels play a key role in melanoma progression and T-type channel blockers have been shown to arrest cell cycle, inhibit autophagy and induce cell-death (Das, 2013), suggesting T-type channels as potential therapeutic targets in melanoma (Das, 2012). Cholesterol-enriched membrane micro-domains (rafts) control melanoma growth in a calcium dependent way (Fedda-Medula, 2008) opening new hypotheses on lipid control in melanoma (Wang, 2013). On the other hand, the role of the enzyme transglutaminase type 2 (EC. 2.1.3.2.1.3, a calcium-dependent cross linking enzyme with several other enzymatic functions) in melanoma development and progression was reported both *in vitro* and *in vivo* (Yang, 2014, Facchiano 2013).

Finally, calcium-supplementation, associated to vitamine D-supplementation, has been reported to reduce melanoma risk in women with non-melanoma skin cancer history (Tang, 2011).

"Carbon" : sixth in the rank.

The word "carbon" occurs in 4.5% of melanoma-manuscripts, while Table 1 shows that only one epithelioma manuscript has "carbon" in the title.

According to the most recent literature, carbon mostly appears as a component in advanced technologies or materials used for melanoma therapies, such as carbon-ion radiotherapy application (Karasawa, 2014; Demizu, 2014; Toyama, 2013; Inubushi, 2013; Jingu, 2011), carbon-dioxide laser

in melanoma cutaneous metastases (Elfatoiki, 2014; Mc Leod, 2012; Oni, 2009), carbon nanotubes for diagnostic purpose or promising topical applications (Siu, 2014; Naderi, 2013; Chaudhuri, 2010) or carbon nanoparticles as promising novel cytotoxic vectors (Grudzinski, 2013).

"Sodium" : seventh in the rank.

The word "sodium" occurs in 3.9% of melanoma-manuscripts, while Table 1 shows that "sodium" word absents in the title of epithelioma manuscripts.

According to the most recent literature, sodium appears as a key component of several therapeutic agents formulation, such as the promising tasisulam sodium (Hamid, 2014; Kirkwood, 2011), dantrolene sodium as useful alternative in patients intolerant to meperidine (Azari, 2012), sodium arsenite showing antitumor action in both melanoma and neuroblastoma cells (Ivanov, 2011; McNeely, 2008). A more specific sodium action in melanoma biology has been shown in a study demonstrating that the alpha1-sodium-pump expression correlates with the Breslow index in melanoma patients, indicating this pump as a potential therapeutic target (Mathieu, 2009).

"Zinc" : eighth in the rank.

The word "zinc" occurs in 3.6% of melanoma-manuscripts, while Table 1 shows that "zinc" word appears in the title of only one epithelioma manuscript.

According to the most recent literature, zinc is a component of different molecules with strong anti-melanoma action, such as zinc nanoparticles (Alarifi, 2013; Bolfarini, 2012; Maduray, 2011) or zinc-porphyrins for photoinduced melanoma toxicity (Sweigert, 2012; Kolarova, 2005).

Additionally, a zinc-finger structure has been observed in a number of melanoma-related molecules, such as zinc-finger protein 28 (Yajima, 2009) and promyelocytic leukemia zinc finger (PLZF) transcription factor (Felicetti, 2008; Shiraishi, 2007).

"Iron" : ninth in the rank.

The word "iron" occurs in 3.3% of melanoma-manuscripts while Table 1 shows that "iron" word appears in the title of only one epithelioma manuscript.

According to the most recent literature, iron appears as molecular component of melanoma-toxic iron-containing nanoparticles (Grudzinski, 2013; Cengelli, 2010; Balivada, 2010) or iron-containing molecules (Franke, 2010), able to induce iron-dependent oxidative damage of DNA (Corti, 2009). Interestingly, melanotransferrin, i.e. melanoma tumor antigen p97, is a iron-binding molecule playing a direct control on growth and tumorigenesis of melanoma cells (Suryo Rahmanto, 2007; Kang 2005).

"Technetium" : tenth in the rank.

The word "technetium" occurs in 3.2% of melanoma-manuscripts, while Table 1 shows that "technetium" word does is absent in epithelioma manuscripts.

According to the most recent literature, technetium is invariantly cited for its uptake at melanoma sites, shown to be related to Breslow thickness (Masiero, 2013), or to specific receptors (Yang, 2012; Yang, 2010).

Conclusion

In the present study we report that iodine, oxygen, ruthenium, boron and calcium are the 5 chemical elements mostly common in the title of melanoma manuscripts, highlighting the role such elements may play in the pathogenesis or diagnostic studies of melanoma.

Further, the chemical elements mostly present in melanoma- , epithelioma- or squamous cell carcinoma- manuscripts are all different (namely, iodine, radium and platinum), while sodium is the mostly present in "skin" manuscripts, highlighting different biological roles of such chemical elements.

Executive summary

Investigating the occurrence of chemical elements in the disease-specific manuscripts may help summarize the known biological functions of chemical elements, within the effort to investigate the impact chemical elements have on the human health.

The systematic approach followed in the present study represents a novel linguistics-based methodology to investigate biological functions of chemical elements and to collect literature data in an ordered, systematic manner.

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Tables

Table 1 Number of manuscripts having in title "melanoma" OR "epithelioma" OR "squamous cell carcinoma" OR "skin", AND each chemical element (in alphabetic order).

Vertical categories: melan (melanoma); epith (epithelioma); sq cell car (squamous cell carcinoma); skin (skin).

	name	melanoma	epithelioma	squamous cell carcinoma	skin		name	melanoma	epithelioma	squamous cell carcinoma	skin
1	Actinium	0	0	0	0	60	Neodymium	5	0	2	14
2	Aluminium (Aluminum)	0	0	1	20	61	Neon	1	0	0	17
3	Americium	0	0	0	1	62	Neptunium	0	0	0	0
4	Antimony	5	0	0	7	63	Nickel	1	0	1	87
5	Argon	10	0	2	32	64	Niobium	0	0	0	1
6	Arsenic	18	3	10	181	65	Nitrogen	13	6	3	115
7	Astatine	1	0	1	0	66	Nobelium	0	0	0	0
8	Barium	0	0	3	4	67	Osmium	1	0	0	8
9	Berkelium	0	0	0	0	68	Oxygen	61	2	25	493
10	Beryllium	0	1	0	27	69	Palladium	8	0	0	4
11	Bismuth	0	0	0	8	70	Phosphorus	24	1	0	47
12	Bohrium	0	0	0	0	71	Platinum	22	0	60	14
13	Boron	46	0	6	11	72	Plutonium	0	0	0	12
14	Bromine	0	0	0	9	73	Polonium	0	0	0	7
15	Cadmium	0	0	0	28	74	Potassium (Kalium)	11	0	5	103
16	Caesium (Cesium)	0	2	0	11	75	Praseodymium	0	0	0	0
17	Calcium	45	1	18	263	76	Promethium	0	0	0	1
18	Californium	0	0	1	3	77	Protactinium	0	0	0	0
19	Carbon	37	1	19	230	78	Radium	0	38	7	36
20	Cerium	0	0	0	2	79	Radon	2	3	0	20
21	Chlorine	0	0	1	14	80	Rhenium	9	0	0	0
22	Chromium	2	0	0	75	81	Rhodium	2	0	0	0
23	Cobalt	18	3	4	50	82	Roentgenium	0	0	0	0
24	Copper	18	1	7	91	83	Rubidium	1	0	0	4
25	Curium	0	0	0	0	84	Ruthenium	49	0	0	9
26	Darmstadtium	0	0	0	0	85	Rutherfordium	0	0	0	0
27	Dubnium	0	0	0	0	86	Samarium	1	0	0	0
28	Dysprosium	0	0	0	0	87	Scandium	0	0	0	0
29	Einsteinium	0	0	0	0	88	Seaborgium	0	0	0	0
30	Erbium	0	0	0	60	89	Selenium	14	1	9	52
31	Europium	0	0	0	2	90	Silicon	3	0	0	21
32	Fermium	0	0	0	0	91	Silver	7	0	6	105
33	Fluorine	10	0	5	3	92	Sodium	32	0	11	784
34	Francium	0	0	0	0	93	Strontium	7	1	4	16
35	Gadolinium	4	0	0	19	94	Sulfur (Sulphur)	16	1	0	149
36	Gallium	23	0	3	16	95	Tantalum	5	0	1	3
37	Germanium	0	0	0	0	96	Technetium	25	0	1	4

38	Gold	21	0	10	145	97	Tellurium	0	0	0	0
39	Hafnium	1	0	0	0	98	Terbium	0	0	1	0
40	Hassium	0	0	0	0	99	Thallium	3	0	6	13
41	Helium	21	0	0	25	100	Thorium	0	3	0	21
42	Holmium	0	0	0	1	101	Thulium	0	0	0	5
43	Hydrogen	12	0	2	87	102	Tin	0	0	0	5
44	Indium	21	0	1	3	103	Titanium	0	0	0	39
45	Iodine	91	1	14	152	104	Tungsten	0	0	0	1
46	Iridium	1	2	5	9	105	Ununbium	0	0	0	0
47	Iron	27	1	5	97	106	Ununhexium	0	0	0	0
48	Krypton	0	0	0	4	107	Ununoctium	0	0	0	0
49	Lanthanum	1	0	0	6	108	Ununpentium	0	0	0	0
50	Lawrencium	0	0	0	0	109	Ununquadium	0	0	0	0
51	Lead	14	1	0	68	110	Ununtrium	0	0	0	0
52	Lithium	5	0	0	35	111	Uranium	0	0	0	14
53	Lutetium	1	0	0	1	112	Vanadium	0	0	0	1
54	Magnesium	4	0	2	36	113	Xenon	4	0	0	29
55	Manganese	5	0	7	25	114	Ytterbium	0	0	0	0
56	Meitnerium	0	0	0	0	115	Yttrium	5	0	2	20
57	Mendelevium	0	0	0	0	116	Zinc	30	1	14	180
58	Mercury	3	0	0	70	117	Zirconium	0	0	0	6
59	Molybdenum	0	0	1	4						
							totals	827	74	286	4395

Table 2. Values expressed as percentage of total manuscripts in each vertical category and ranked in each vertical category.

Melanoma manuscritps			Epithelioma manuscritps			Squamous cell carcinoma manuscripts			Skin manuscritps		
Rank	**Name**	**% in melanoma manuscr.**	**Rank**	**Name**	**% in epithelioma manuscr.**	**Rank**	**Name**	**% in squamous cell carc. manuscr.**	**Rank**	**Name**	**% in skin manuscr.**
1 th	**Iodine**	11.00	*1 th*	**Radium**	51.35	*1 th*	**Platinum**	20.98	*1 th*	**Sodium**	17.84
2 nd	**Oxygen**	7.38	*2 nd*	**Nitrogen**	8.11	*2 nd*	**Oxygen**	8.74	*2 nd*	**Oxygen**	11.22
3 th	**Ruthenium**	5.93	*3 th*	**Arsenic**	4.05	*3 th*	**Carbon**	6.64	*3 th*	**Calcium**	5.98
4 th	**Boron**	5.56	*4 th*	**Cobalt**	4.05	*4 th*	**Calcium**	6.29	*4 th*	**Carbon**	5.23
5 th	**Calcium**	5.44	*5 th*	**Radon**	4.05	*5 th*	**Iodine**	4.90	*5 th*	**Arsenic**	4.12
6 th	**Carbon**	4.47	*6 th*	**Thorium**	4.05	*6 th*	**Zinc**	4.90	*6 th*	**Zinc**	4.10
7 th	**Sodium**	3.87	*7 th*	**Caesium (Cesium)**	2.70	*7 th*	**Sodium**	3.85	*7 th*	**Iodine**	3.46
8 th	**Zinc**	3.63	*8 th*	**Iridium**	2.70	*8 th*	**Arsenic**	3.50	*8 th*	**Sulfur (Sulphur)**	3.39
9 th	**Iron**	3.26	*9 th*	**Oxygen**	2.70	*9 th*	**Gold**	3.50	*9 th*	**Gold**	3.30
10 th	**Technetium**	3.02	*10 th*	**Beryllium**	1.35	*10 th*	**Selenium**	3.15	*10 th*	**Nitrogen**	2.62
11 th	**Phosphorus**	2.90	*11 th*	**Carbon**	1.35	*11 th*	**Copper**	2.45	*11 th*	**Silver**	2.39
12 th	**Gallium**	2.78	*12 th*	**Calcium**	1.35	*12 th*	**Manganese**	2.45	*12 th*	**Potassium (Kalium)**	2.34
13 th	**Platinum**	2.66	*13 th*	**Copper**	1.35	*13 th*	**Radium**	2.45	*13 th*	**Iron**	2.21
14 th	**Gold**	2.54	*14 th*	**Iron**	1.35	*14 th*	**Silver**	2.10	*14 th*	**Copper**	2.07
15 th	**Helium**	2.54	*15 th*	**Iodine**	1.35	*15 th*	**Boron**	2.10	*15 th*	**Hydrogen**	1.98
16 th	**Indium**	2.54	*16 th*	**Phosphorus**	1.35	*16 th*	**Thallium**	2.10	*16 th*	**Nickel**	1.98
17 th	**Arsenic**	2.18	*17 th*	**Lead**	1.35	*17 th*	**Fluorine**	1.75	*17 th*	**Chromium**	1.71
18 th	**Cobalt**	2.18	*18 th*	**Sulfur (Sulphur)**	1.35	*18 th*	**Iron**	1.75	*18 th*	**Mercury**	1.59
19 th	**Copper**	2.18	*19 th*	**Selenium**	1.35	*19 th*	**Iridium**	1.75	*19 th*	**Lead**	1.55
20 th	**Sulfur (Sulphur)**	1.93	*20 th*	**Strontium**	1.35	*20 th*	**Potassium (Kalium)**	1.75	*20 th*	**Erbium**	1.37
21 th	**Lead**	1.69	*21 th*	**Zinc**	1.35	*21 th*	**Cobalt**	1.40	*21 th*	**Selenium**	1.18
22 th	**Selenium**	1.69	*22–117 th*	**all others**	<0.01	*22 th*	**Strontium**	1.40	*22 th*	**Cobalt**	1.14
23 th	**Nitrogen**	1.57				*23 th*	**Barium**	1.05	*23 th*	**Phosphorus**	1.07
24 th	**Hydrogen**	1.45				*24 th*	**Gallium**	1.05	*24 th*	**Titanium**	0.89
25 th	**Potassium (Kalium)**	1.33				*25 th*	**Nitrogen**	1.05	*25 th*	**Magnesium**	0.82
26	**Argon**	1.21				*26*	**Argon**	0.70	*26*	**Radium**	0.82

th						*th*			*th*		
27 th	**Fluorine**	1.21				*27 th*	**Hydrogen**	0.70	*27 th*	**Lithium**	0.80
28 th	**Rhenium**	1.09				*28 th*	**Magnesium**	0.70	*28 th*	**Argon**	0.73
29 th	**Palladium**	0.97				*29 th*	**Neodymium**	0.70	*29 th*	**Xenon**	0.66
30 th	**Silver**	0.85				*30 th*	**Yttrium**	0.70	*30 th*	**Cadmium**	0.64
31 th	**Strontium**	0.85				*31 th*	**Aluminium (Aluminum)**	0.35	*31 th*	**Beryllium**	0.61
32 th	**Lithium**	0.60				*32 th*	**Astatine**	0.35	*32 th*	**Helium**	0.57
33 th	**Manganese**	0.60				*33 th*	**Californium**	0.35	*33 th*	**Manganese**	0.57
34 th	**Neodymium**	0.60				*34 th*	**Chlorine**	0.35	*34 th*	**Silicon**	0.48
35 th	**Antimony**	0.60				*35 th*	**Indium**	0.35	*35 th*	**Thorium**	0.48
36 th	**Tantalum**	0.60				*36 th*	**Molybdenum**	0.35	*36 th*	**Aluminium (Aluminum)**	0.46
37 th	**Yttrium**	0.60				*37 th*	**Nickel**	0.35	*37 th*	**Radon**	0.46
38 th	**Gadolinium**	0.48				*38 th*	**Tantalum**	0.35	*38 th*	**Yttrium**	0.46
39 th	**Magnesium**	0.48				*39 th*	**Terbium**	0.35	*39 th*	**Gadolinium**	0.43
40 th	**Xenon**	0.48				*40 th*	**Technetium**	0.35	*40 th*	**Neon**	0.39
41–117 th	**all others**	<0.40				*41–117 th*	**all others**	<0.01	*41–117 th*	**all others**	<0.39