S-block elements: pharmacological properties and potential medical applications of alkali and alkaline earth metals (#100012)

First submission

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- 1. BASIC REPORTING
- 2. STUDY DESIGN
- 3. VALIDITY OF THE FINDINGS
- 4. General comments
- 5. Confidential notes to the editor
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Use these criteria points to structure your review. The full detailed editorial criteria is on your guidance page.

BASIC REPORTING

- Clear, unambiguous, professional English language used throughout.
- Intro & background to show context.
 Literature well referenced & relevant.
- Structure conforms to <u>PeerJ standards</u>, discipline norm, or improved for clarity.
- Is the review of broad and cross-disciplinary interest and within the scope of the journal?
- Has field been reviewed recently. It there a good reason for this review (different viewpoint, audience etc.)?
- Introduction adequately introduces the subject and makes audience and motivation clear.

STUDY DESIGN

- Article content is within the <u>Aims and Scope</u> of the journal.
- Rigorous investigation performed to a high technical & ethical standard.
- Methods described with sufficient detail & information to replicate.
- Is the Survey Methodology consistent with a comprehensive, unbiased coverage of the subject? If not, what is missing?
- Are sources adequately cited? Quoted or paraphrased as appropriate?
- Is the review organized logically into coherent paragraphs/subsections?

VALIDITY OF THE FINDINGS

- Impact and novelty is not assessed.

 Meaningful replication encouraged where rationale & benefit to literature is clearly stated.
- Conclusions are well stated, linked to original research question & limited to supporting results.
- Is there a well developed and supported argument that meets the goals set out in the Introduction?
- Does the Conclusion identify unresolved questions / gaps / future directions?

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Τ	p

Support criticisms with evidence from the text or from other sources

Give specific suggestions on how to improve the manuscript

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Organize by importance of the issues, and number your points

Please provide constructive criticism, and avoid personal opinions

Comment on strengths (as well as weaknesses) of the manuscript

Example

Smith et al (J of Methodology, 2005, V3, pp 123) have shown that the analysis you use in Lines 241-250 is not the most appropriate for this situation. Please explain why you used this method.

Your introduction needs more detail. I suggest that you improve the description at lines 57-86 to provide more justification for your study (specifically, you should expand upon the knowledge gap being filled).

The English language should be improved to ensure that an international audience can clearly understand your text. Some examples where the language could be improved include lines 23, 77, 121, 128 – the current phrasing makes comprehension difficult. I suggest you have a colleague who is proficient in English and familiar with the subject matter review your manuscript, or contact a professional editing service.

- 1. Your most important issue
- 2. The next most important item
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I commend the authors for their extensive data set, compiled over many years of detailed fieldwork. In addition, the manuscript is clearly written in professional, unambiguous language. If there is a weakness, it is in the statistical analysis (as I have noted above) which should be improved upon before Acceptance.

S-block elements: pharmacological properties and potential medical applications of alkali and alkaline earth metals

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Background: The periodic table contains the s-block elements in groups 1 and 2. In the periodic table, they reside in the first 2 columns. S-block consists of 14 elements that include, hydrogen (H), lithium (Li), helium (He), sodium (Na), beryllium (Be), potassium (K), magnesium (Mg), rubidium (Rb), calcium (Ca), cesium (Cs), strontium (Sr), francium (Fr), barium (Ba), and radium (Ra). Because their valence electrons are in the s-orbital, these elements are known as s-block elements. Alkali and alkaline earth metals are used extensively in synthetic and technical chemistry. Because of its numerous applications, structural chemistry has received a great deal of attention, and a growing number of target molecules have been identified during the last ten years. Methodology: Articles were searched using the following search engine: PubMed, Google Scholar, Worldwide Science and Research Gate, etc. Result: S-block components are vital to life as they are essential for metabolism, synthesis of proteins and brain development as well. The diverse uses and effects of alkali metals and alkaline earth metals in the field of medicine and research has been discussed in review. **Conclusion:** Lastly, review covers the historical background and pharmacological potential of s-block elements and their properties, uses, and potential medical applications such as mood stabilization, neuroprotection, antiinflammatory activity, diagnostic imaging, vasodilatory activity, and cardio protective activity.

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35 Abstract

- 36 **Background**: The periodic table contains the s-block elements in groups 1 and 2. In the periodic
- table, they reside in the first 2 columns. S-block consists of 14 elements that include, hydrogen
- 38 (H), lithium (Li), helium (He), sodium (Na), beryllium (Be), potassium (K), magnesium (Mg),
- rubidium (Rb), calcium (Ca), cesium (Cs), strontium (Sr), francium (Fr), barium (Ba), and radium
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- 47 proteins and brain development as well. The diverse uses and effects of alkali metals and alkaline
- 48 earth metals in the field of medicine and research has been discussed in review.
- 49 **Conclusion:** Lastly, review covers the historical background and pharmacological potential of s-
- 50 block elements and their properties, uses, and potential medical applications such as mood
- 51 stabilization, neuroprotection, anti-inflammatory activity, diagnostic imaging, vasodilatory
- 52 activity, and cardio protective activity.

1. Introduction

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- The ancient Greek philosophy of nature is where the idea of components first appeared (1).
- 55 Empedocles (5th century B.C.) asserted that all matter was composed of the four basic "elements"
- of fire, air, water, and earth, which were brought together and divided by the two "active forces"
- of love and conflict (2, 3). Only 13 elements in the contemporary sense of the word were known
- up to the 17th century, and by known we mean that they had been employed in a relatively pure
- 59 condition. An avalanche of elemental discoveries began in the second half of the 18th century and
- has continued to this day. There are now 112 elements (2, 4, 5).
- The elements in the periodic table are arranged such that elements with comparable electron
- 62 configurations are grouped together (6). Blocks can be created from elements in comparable
- 63 groups or columns according to the electron orbital that the valence electrons of those elements

- occupy (7). There are four distinct electron orbitals represented by the four blocks: s, d, p, and f (8).
- Deep roots may be found in the 18th and 19th centuries in the investigation of s-block constituents
- 67 (9). The narrative starts in the late 18th century with the publication of Antoine Lavoisier's seminal
- 68 study on chemical elements and their compounds (10, 11). Group 1 of the periodic table is
- 69 occupied by the alkali metals, which include hydrogen, lithium, helium, sodium, potassium,
- 70 rubidium, cesium, and francium. These are soft, glossy, low melting, extremely reactive metals
- 71 (apart from hydrogen), that tarnish when exposed to air (12). These elements display a remarkable
- 72 reactivity, especially with water, and their qualities became increasingly evident via the efforts of
- pioneers such as Sir Humphry Davy, who separated numerous alkali metals using electrolysis (13).
- 74 The alkaline earth metals of Group 2, which include beryllium, magnesium, calcium, strontium,
- barium, and radium, also attracted interest as the 19th century went on. Chemists such as Antoine
- 76 Bussy and Sir Humphry Davy were instrumental in identifying and defining these components
- 77 (14). These elements' compounds dissolve in water to generate basic (pH greater than 7) or alkaline
- 78 solutions, thus the term "alkaline (15). These substances are effective electrical conductors. When
- 79 first cut, they have a grey-white brilliance, but they tarnish easily in the air (16).
- 80 Synthetic and technical chemistry make significant use of alkali and alkaline earth metals (17, 18).
- 81 Because of its many uses, structural chemistry has attracted a lot of attention, and throughout the
- past ten years, a growing number of target molecules have been identified (19, 20). While alkaline
- earth metals are metals that produce alkaline oxides and hydroxides and are found in the earth's
- crust, alkali metals are not found in nature in their free state (21).

2. Survey Methodology

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- 86 A comprehensive search for relevant literature was conducted using multiple databases including
- 87 PubMed, Google Scholar, Worldwide Science, and ResearchGate. The search strategy involved
- 88 specific keywords and combinations related to the pharmacological properties and medical
- 89 applications of alkali and alkaline earth metals. The search terms included: s-block elements, alkali
- 90 metals, alkaline earth metals, pharmacological properties, medical applications, hydrogen, lithium,
- 91 sodium, potassium, rubidium, cesium, francium, beryllium, magnesium, calcium, strontium,
- 92 barium, and radium. Articles that addressed the pharmacological characteristics of alkali and
- 93 alkaline earth metals and detailed their possible therapeutic uses were considered for inclusion in

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the review. To ensure the relevance and accessibility of the information, only articles published in English were considered. Additionally, the availability of full-text versions of the articles was a prerequisite for inclusion in the review. On the other hand, articles were excluded from the review if they were not available in full text. Publications in languages other than English were also excluded to maintain consistency in language comprehension and analysis. Furthermore, articles that did not focus on the pharmacological properties or medical applications of the target elements were deemed irrelevant and thus excluded from the review. Relevant data from the included studies were extracted and reviewed, encompassing information on the historical background, pharmacological properties, medical applications, and potential therapeutic benefits of the s-block elements. The review explored the uses of these elements in various areas such as mood stabilization, neuroprotection, anti-inflammatory activity, diagnostic imaging, vasodilatory activity, and cardioprotective activity, among others. The search resulted in numerous publications detailing the various applications and properties of alkali and alkaline earth metals. Key findings from these studies include the role of hydrogen in reducing oxidative stress and inflammation, and the effectiveness of lithium in mood stabilization and neuroprotection. Sodium and potassium were found to have crucial functions in maintaining electrolyte balance, muscle contraction, and cardiovascular health. Additionally, rubidium and cesium were highlighted for their diagnostic and therapeutic uses in medical imaging and cancer treatment. Furthermore, the anti-inflammatory, antioxidant, and neuroprotective properties of helium were also identified. The literature review underscores the significant pharmacological potential and diverse medical applications of s-block elements. These findings advocate for the ongoing research and development of therapies that utilize alkali and alkaline earth metals to treat various health conditions.

3. Pharmacological potential of S-block elements

3.1. Hydrogen

The English chemist Henry Cavendish discovered hydrogen in 1766 (22). Hydrogen is made up of diatomic molecules of H₂. At 75% by weight, or 88% of all atoms in the cosmos, it is the most plentiful element; hydrogen and helium together make up 99% of the universe's "normal" matter (23). It is acknowledged that molecules such as molecular hydrogen are inert and nonfunctional in human bodies. Strong oxidants like hydroxyl radicals in cells react with H₂, which has been shown to have potential uses in both therapeutic and preventative measures (24). Given how quickly H₂

diffuses into tissues and cells, it offers a variety of benefits with wide-ranging impacts (25). H₂
promotes energy metabolism and has anti-inflammatory and anti-apoptotic properties (26).
Research on hydrogen has advanced quickly in recent years due to the growing evidence that
molecular hydrogen is a particularly effective therapy for numerous illness models, including
ischemia-reperfusion damage (27). It has been demonstrated that hydrogen is beneficial whether
consumed as a gas as well as when administered orally, intravenously, or topically as a liquid
treatment (28, 29).

3.1.1. Antioxidant activity

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Given how quickly H₂ diffuses into tissues and cells, it offers a variety of benefits with wide-132 133 ranging impacts (30). Reactive oxygen species (ROS) are very reactive oxygen-containing molecules that have the ability to harm tissues and cells (31). Diatomic hydrogen has been 134 135 suggested as a new type of antioxidant that preferentially lowers harmful reactive oxygen species 136 levels (32). H₂ (orally eaten or breathed; usually as 0.8 mM H₂-saturated water) has been shown 137 in several studies recently to have positive effects in a variety of animal models of neurological, inflammatory, and ischemia-reperfusion damage (24). Oral H₂ saturated water therapy has been 138 shown to enhance glucose and lipid metabolism in individuals with diabetes mellitus or impaired 139 glucose tolerance in the clinic; encouraging outcomes have also been shown in the reduction of 140 inflammation in patients receiving hemodialysis and in the treatment of metabolic syndrome (27). 141 According to research, H₂ may have antiapoptotic, anti-inflammatory, and antiallergenic benefits 142 in addition to its specific antioxidant capabilities (33). 143

3.1.2. Anti-inflammatory activity

It has been demonstrated that molecular hydrogen lowers pro-inflammatory cytokine levels, which are signaling molecules that contribute to the inflammatory response (34). Hydrogen could reduce inflammation by adjusting the expression of these molecules. Certain inflammatory signaling pathways, such the nuclear factor-kappa B (NF-κB) pathway, may be inhibited by hydrogen (35). One transcription factor that is essential for controlling inflammatory and immunological responses is NF-κB (36).

3.1.3. Neuroprotective activity

Treatment with hydrogen reduces the size of infarcts, enhances cognitive performance following traumatic brain damage, protects against the loss of dopaminergic neurons in Parkinson's disease,

- has antioxidant benefits in Alzheimer's disease, and lessens oxidative stress in newborn hypoxic-
- ischemic encephalopathy (37, 38).
- 156 **3.2.** Lithium
- 157 The element's name comes from the Greek word "lithos", which means stone (39). The soft, silvery
- metal lithium has a very low density, interacts violently with water, and tarnishes easily in air (40).
- 159 Although it was only produced in small amounts, lithium was one of the three elements created
- 160 during the Big Bang (41).

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3.2.1. Mood Stabilization activity

- Since its introduction in psychiatry at the end of the 1940s, the monovalent cation lithium has been
- the first-choice medication for treating people with bipolar disorder (BD) (42). It lowers the risk
- of suicide and is useful in the treatment of moderate-to-severe acute mania as well as a preventative
- measure against repeated manic and depressive episodes. Additionally, it can strengthen the
- efficacy of antidepressants when used to treat major depressive disorder (43). Bipolar disorder and
- certain forms of depression are treated with lithium salts (such as lithium carbonate, Li₂CO₃),
- which are also used to enhance the effects of other antidepressants (44).

3.2.2. Suicidal prevention activity

- Most bipolar disorder patients should be offered lithium as their first treatment, especially if they
- exhibit suicidal thoughts or behaviors, and they should be given enough information regarding the
- drug's possible long-term advantages as well as negative effects (45). Many people are able to take
- 173 lithium without the need for antipsychotics or antidepressants, which could have serious long-term
- negative effects or worsen the illness, respectively (46). Treatment with Li substantially lowers
- 175 "impulsive-aggressive" behavior, a susceptibility factor linked to bipolar disorder and suicide, by
- targeting the serotoninergic system specifically (47).

3.2.3. Neuroprotective activity

- 178 Lithium modulates neurotransmitters, calcium, potassium, and other neurotrophic and
- 179 neuroprotective proteins and supports protective signaling pathway in neuronal cells. According
- 180 to clinical reports, lithium might be a useful supplement to treat Parkinsonism and help regulate
- the "on-off" phenomena (48). By downregulating tau proteins, lithium at doses of 1.25, 2.5, 5, and
- 7.5 mM protects neurons from the harmful eff of amyloid beta (Aβ) and apoptosis (49, 50).
- Lithium prevents apoptosis from occurring, which has neuroprotective properties (49, 51-53). The

- neuroprotective effects of lithium are mediated through the inhibition of intrinsic and/or extrinsic apoptotic mechanisms (54, 55).
 - 3.2.4. Anti-inflammatory activity
- By preventing the synthesis of two important inflammatory cytokines, interleukin (IL)-1 beta and
- tumor necrosis factor (TNF)-alpha, lithium has the abilities reduce inflammation. The way that
- 189 lithium prevents neurodegeneration during neuroinflammatory events is reinforced by these
- 190 processes (56-58).

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- 191 **3.3.** Helium
- August 18, 1868, saw the discovery of helium in the form of a brilliant yellow line (59). After
- 193 hydrogen, helium is the second-most plentiful and lightest gas in the universe. Numerous uses for
- helium exist in biomedicine (60). It is a monoatomic gas that has no color or smell (61). Helium
- finds several uses in arc welding, cryogenics, MRI scanners, gas pressurizing, and the cooling of
- superconducting magnets. Deep sea diving decompression sickness has historically been less
- 197 common when helium is utilized (62).

3.3.1. Diagnostic activity

- 199 A medical imaging method called magnetic resonance imaging (MRI) is used in radiology to look
- 200 into the architecture and physiology of the body in both healthy and sick conditions (63). It has
- been discovered that liquid helium, which boils at 4.2 K, is helpful for producing superconducting
- 202 magnets, which are necessary for nuclear magnetic resonance and nuclear resonance imaging (64).
- Due to the medical profession's ability to employ magnetic resonance imaging (MRI) to diagnose
- complicated disorders, the usage of liquid helium in MRI is constantly growing (65).

3.3.2. Vasodilatory activity

- 206 It has been found that helium increases collateral circulation in the heart (66) and strengthen the
- 207 pulmonary arteries' natural vasodilatory response to breathed nitric oxide (67). It may be applied
- 208 to the evaluation of airflow distribution and anatomical alterations in the lung parenchyma,
- 209 including fibrosis and emphysema. The 2007 recommendations released by the National Heart,
- 210 Lung, and Blood Institute also acknowledged heliox (a gas combination of helium and oxygen) as
- a critical adjuvant in the treatment of severe exacerbations of asthma (68). When children with
- 212 severe asthma exacerbations were treated, pulsus paradoxus, peak flow, and dyspnea were
- 213 improved with inhalational heliox therapy (69). Helium has therapeutic effects because of its faster

- 214 flow rate and lower turbulent flow, which enable gases to enter the distal alveoli deeper, produce
- 215 larger minute quantities, and enhance breathing (70).

216 3.3.3. Neuroprotective activity

- 217 Research on neurological disorders has been done to assess the possibility of low temperature
- 218 atmospheric pressure plasma based on helium in treating conditions like Parkinson's and
- Alzheimer's disease, which are linked to amyloid fibrils (71, 72). It has been discovered that in
- vitro, amyloid fibrils can fragment into smaller units when exposed to low temperature
- 221 atmospheric pressure plasma (73).

3.3.4. Anticancer activity

- There are other consequences of atmospheric pressure helium plasma jet on live cells (74, 75). It
- has been shown that plasma interactions with several cancer cell types cause cell death, which may
- be related to the generation of reactive oxygen species (ROS) (76-80). Helium plasma at
- 226 atmospheric pressure has been used recently to treat human lung cancer cells in vitro (74). It has
- 227 shown promise in the treatment of cancer cells, blood coagulation, sterilization, and teeth
- 228 whitening (81-83).

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- Helium-based non-thermal atmospheric plasma jets have been investigated in depth in a number
- of cancer types, and in vitro antitumor effects have been noted on carcinogenic cell lines associated
- with skin (melanoma), brain (glioblastoma), colon, liver, lungs, breast, cervix, bladder, oral and
- ovarian carcinoma, and leukaemia (73, 84).

233 **3.4. Sodium**

- The word "soda," which appears in several sodium compounds like washing soda, sodium
- bicarbonate, and sodium hydroxide, is where the word "sodium" originates (85). The Latin name
- for the element, natrium, is where the sign "Na" originates. In the crust of the Earth, it ranks as the
- fourth most plentiful element (86). To transmit nerve impulses, contract and relax muscles, and
- maintain the ideal balance of water and minerals, the human body needs a tiny quantity of sodium
- 239 (87). It is estimated that 500 mg of salt every day is required for these essential processes (88).

3.4.1. Electrolyte regulation

- The main solute preserving water in the extracellular compartment is sodium. Total body sodium
- 242 is a prerequisite for both total body water and extracellular volume. Thus, maintaining sodium

balance is essential for controlling volume (89). Changes in the sodium balance cause variations in plasma volume, which are mostly detected by changes in the circulatory system (90). The most common form of IV fluid for both replacement and maintenance has historically been normal saline (91).

3.4.2. Blood pressure regulation

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Blood pressure management requires the careful maintenance of salt and fluid balance, and changes to this equilibrium can result in the development of hypertension (91). Since sodium is the primary cation in extracellular fluid, any alteration in sodium excretion through the urine would result in an increase in the amount of intravascular fluid, which would raise blood pressure and possibly cause hypertension (92).

3.4.3. Sodium muscularity activity

Sodium makes it easier for calcium ions to enter muscle fibers, which releases ATP, the body's energy storage (93). Proper muscle activity and electrical impulse transmission depend on the sodium and potassium ion balance (94). Moreover, magnesium is necessary for muscular contraction, and sodium promotes the dephosphorylation of ATP and ADP in the presence of magnesium (95). Consequently, sodium is a necessary element for preserving the best possible health, especially during the contraction of muscles (96).

260 **3.5. Potassium**

"Potash" is the root word of the term potassium. For a very long time, potassium carbonate and potassium hydroxide have been combined to create potash (97). In earlier ages, ashes in pots were used to make potash. Potassium is a soft, silvery metal that tarnishes quickly in air and interacts quite strongly with water (98).

3.5.1. Electrolyte balance

Potassium is essential for maintaining the body's electrolyte and fluid balance (99). Its participation in a number of physiological processes contributes to the maintenance of appropriate electrolyte concentrations, fluid distribution, and cellular function (100). Intake can be reduced to the point of total loss, often due to famine. The kidneys filter potassium, and the amount expelled in urine is controlled to preserve equilibrium (101). Studies have also looked at electrolyte imbalance changes that occur with mental illnesses; cyclic mood disorders, such manic-depressive illness (102).

3.5.2. Acid-Base balance

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- 274 Potassium, in conjunction with sodium, control the body's and tissue's acid-base and water balance
- 275 (103). It acts as a buffer to balance out access basses or acids, assisting in the stabilization of the
- internal environment of the organism (104).

3.5.3. Cardioprotective activity

- 278 In the heart, potassium is essential for the passage of electrical impulses (105). Maintaining a
- 279 normokalaemia condition is crucial for the prevention of potentially significant consequences and
- 280 for the preservation of cardiovascular health, particularly in individuals who are at-risk for
- cardiovascular disease (106). Serum K⁺ values kept between 4.0 and 5.0 mmol/L seem to be both
- safe and likely to offer stability in a variety of cardiovascular processes (107). Increased
- 283 consumption of potassium-rich foods is linked to a decreased incidence of stroke and may also
- lessen the risk of congenital cardiac conditions and overall cardiovascular disease (108). These
- 285 findings corroborate suggestions to increase intake of foods high in potassium in order to prevent
- vascular disorders (109).

287 **3.6.** Rubidium

- 288 An alkali metal in Group 1 of the Periodic Table is rubidium. Its physical and chemical
- characteristics often fall between those of cerium and potassium (110). Rubidium is not the major
- 290 metallic element in any minerals. Rubidolite and pollucite are the minerals that contain rubidium
- 291 (111). In general, rubidium is classified as having a low level of toxicity. There are health dangers
- related to chemicals called rubidium (112). Rubidium is mostly used in research. Pharmaceuticals
- and medical procedures both employ rubidium isotopes (113).

3.6.1. Cardiac imaging

- 295 In particular, coronary artery disease is one cardiovascular illness for which rubidium is used in
- 296 diagnostic and treatment (114). A radioactive isotope of rubidium called rubidium-82 is utilized
- as a positron-emitting radiotracer in cardiac imaging. Rubidium-82 PET (Positron Emission
- 298 Tomography) imaging is the name of this application (115). It is frequently used to evaluate blood
- 299 flow to the heart muscle in myocardial perfusion imaging. When evaluating the myocardial
- 300 perfusion of individuals with known or suspected coronary artery disease, rubidium-82 PET
- 301 imaging is especially helpful (116).

3.6.2. Neurological research

Rubidium's ability to mirror the behavior of potassium has made it a useful ion in neurological studies (117). Rubidium influx has been utilized by researchers as a measure for neurotransmitter release because rubidium ions may enter neuron terminals and imitate the actions of potassium (118). Rubidium has been used in combination with electrophysiological methods, such as patch-clamp recordings, to investigate the electrical characteristics of neurons (119). Evaluation of rubidium's effects on membrane potential, action potentials, and other electrophysiological parameters may be part of these investigations (120). A few studies have looked at rubidium's possible neuroprotective benefits (121). Alzheimer's disease can be strongly predicted by changes in brain rubidium levels. Rubidium 82/86 PET imaging may be able to detect Alzheimer's disease in its early stages (117). It has been claimed that lithium and rubidium have neuroprotective effects on disorders of the central nervous system, such as mania and depression (122).

3.6.3. Diagnostic marker for brain tumor

Positron emission tomography (PET) has made considerable use of rubidium-82 as a diagnostic marker for brain tumors; greater absorption of the tracer indicates a breakdown in the integrity of the blood-brain barrier (BBB) (123).

3.7. Cesium

In 1860, Gustav Kirchoff and Robert Bunsen made the discovery of cesium (124). The soft alkaline metallic element cesium has a silver-white color and atomic number 55. As the isotope 133Cs, it is the rarest naturally occurring alkali metal. With a cesium oxide content ranging from 5% to 32%, pollucite is the most widely used commercial source of cesium (125). Cesium in radioactive forms (134Cs and 137Cs) is also present in the environment. When cesium was radioactive and had potential for radiation therapy and carcinogenesis, it first attracted interest (126). When cesium metal comes into touch with flesh, it may burn people severely (127). Cesium has limited practical uses in neurology because of its possible toxicity. Serious health concerns, including as cardiovascular, gastrointestinal, and neurological disorders, can result from cesium poisoning (128). As a result, using cesium therapeutically is quite rare in traditional medicine and calls for great caution (129).

3.7.1. Anticancer activity

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- 331 It has been proposed that using cesium chloride as a cancer treatment, often known as "high pH
- therapy," will have anticancer effects by increasing intracellular pH and inducing apoptosis (130).
- 333 Since the 1980s, anticancer efficaciousness for steady cesium treatment has been asserted. Studies
- 334 conducted in vivo have demonstrated a substantial reduction in tumor volume following the
- treatment of oral gavage or intraperitoneal injection of calcium chloride (131). Prostate cancer has
- been treated using 131Cesium brachytherapy (132).

3.8. Francium

- Marguerite Perey made the discovery of francium in 1939 (133). It is the lustrous metal in its purest
- form, existing at room temperature as a liquid as opposed to a solid. It emits a lot of radioactivity.
- With a maximum half-life of just 22 minutes, it is a radioactive metal that is heavy and unstable
- 341 (134). The chemical characteristics of francium and cesium are comparable (135). After astatine,
- 342 it is the second rarest element in the crust of the Earth. It is the most chemically reactive alkali
- metal since it is the least electronegative element among all of the elements (136). There is no
- known biological function of francium in human life. Due to its volatility and scarcity, francium
- has no commercial use. It is exclusively utilized for research. Its use as a potential diagnostic tool
- for various malignancies has also been examined, although this use has been judged unfeasible. Its
- only toxicity is from its radioactivity, which can harm nuclear material and cells (137).

3.9. Beryllium

- Wohler made the first isolation of beryllium in 1828 (138). It is a lightweight alkaline earth metal
- with a steel-gray color. It is the only metal with the unusual quality of being almost X-ray
- 351 transparent (139). It is harmful when breathed or applied topically, and it can cause dermatitis,
- acute pneumonitis, and chronic lung disease (140). Breathing problems, chest discomfort, or
- 353 shortness of breath may be the initial symptoms of a severe or potentially fatal acute beryllium
- exposure (141). In conclusion, beryllium is not used in pharmaceutical applications as any possible
- therapeutic advantages are outweighed by its hazardous qualities (142).

3.9.1. Chronic beryllium disease (CBD)

- 357 Berylliosis, sometimes referred to as chronic beryllium disease (CBD), is a granulomatous illness
- brought on by beryllium exposure (143). Granulomas, or aberrant inflammatory nodules, are
- formed in the lungs and other regions of the body as a result of a systemic illness (144). The most

- 360 frequent symptoms are cough, fever, night sweats, and exhaustion, although the clinical course
- might vary. The beryllium lymphocyte proliferation test (BeLPT), bronchoalveolar lavage (BAL),
- and granulomatous inflammation on lung biopsy are the mainstays of a conclusive diagnosis of
- 363 berylliosis (145).

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3.10. Magnesium

- Magnesia, a location in Greece, is where magnesium compounds were initially found. In the crust
- of the earth, magnesium is the seventh most common element (146). It is an alkaline Earth metal
- that occurs in minerals and rocks in the natural world (147). Just 1% of the magnesium in the body
- 368 is found in the blood, with the majority of the mineral being in high metabolic tissues such the
- muscles, brain, heart, kidneys, and liver (148). The human body uses magnesium (Mg^{2+}) for a
- 370 variety of processes, including blood pressure, neuromuscular transmission, and muscle
- contraction (149, 150). Furthermore, the creation of nuclear materials, the generation of energy,
- active transmembrane transport for other ions, and bone growth all depend on magnesium (151).
- 373 Moreover, a variety of illnesses have been linked to magnesium shortage (152).

3.10.1. Cardiovascular health

- 375 Magnesium is essential for preserving heart health (153). Magnesium affects vascular tone,
- 376 peripheral vascular resistance, and endothelial function in addition to its significant involvement
- 377 in the control of heart rhythm. An increased risk of cardiac arrhythmia is linked to
- 378 hypomagnesemia. Additionally, hypomagnesemia raised the risk of postcardiac surgery for atrial
- 379 fibrillation. Individuals with congestive heart failure are more likely to have low potassium and
- 380 magnesium levels in their blood (154).

3.10.2. Maintain heart rhythm

- 382 Ion channels, such as those that control the electrical activity of the heart, depend on magnesium
- 383 to operate properly. It contributes to the preservation of a regular heartbeat and aids in the
- 384 stabilization of cell membranes (155). Sufficient magnesium levels can promote the heart's general
- electrical stability and help avoid arrhythmias, or irregular heartbeats (156).

3.10.3. Blood pressure regulation

- 387 Blood pressure management is aided by magnesium. It facilitates blood channel dilating, which
- lowers peripheral resistance and increases blood flow (157).

3.10.4. Anti-inflammatory effects

- 390 Cardiovascular disorders are linked to chronic inflammation (158). Due to its anti- inflammatory
- 391 qualities, magnesium may help lower inflammatory processes in the cardiovascular system and
- 392 promote heart health (159, 160).

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3.10.5. Preventing Coronary Artery Spasms

- Coronary artery spasms are abrupt contractions of the coronary arteries that might lower cardiac
- blood flow. Magnesium can help avoid these spasms (161). Magnesium may help to avoid these
- spasms by encouraging the relaxation of smooth muscles (162).

3.10.6. Protecting Against Ischemia-Reperfusion Injury

- 398 The possible preventive benefits of magnesium against ischemia-reperfusion injury, a condition in
- 399 which blood flow is momentarily obstructed and then restored have been investigated. The heart
- may be shielded from such damage by magnesium's capacity to lower inflammation and oxidative
- 401 stress (163, 164).

3.10.7. Laxative effect

- 403 It is commonly known that magnesium and sulphate have laxative properties (164). Patients
- 404 commonly self-treat constipation using over-the-counter medications, such as magnesium
- 405 hydroxide (Milk of Magnesia) or magnesium citrate (165-167).

406 3.10.8. Migraine prevention

- 407 Magnesium is a cheap, safe, and well-tolerated migraine preventive alternative, according to the
- 408 NCBI (168). Acute headaches, such as tension-type headaches, migraines, and cluster headaches,
- 409 may also benefit from its use. One kind of magnesium that is frequently used to stop migraines is
- 410 magnesium oxide (169, 170).

3.10.9. Pre-eclampsia prevention

- 412 A lot of people use magnesium sulphate to avoid eclamptic seizures (171). In preeclamptic women,
- 413 MgSO₄ is more effective than phenytoin, nimodipine, diazepam, and placebo for eclamptic seizure
- 414 prevention (172). Additionally, magnesium sulphate may function as a central anticonvulsant or
- preserve the blood-brain barrier while preventing the development of cerebral edema (173-176)

3.10.10. Bone health

- Given its importance to bone health, magnesium may be a useful nutrient in the fight against osteoporosis and bone loss (177, 178). A magnesium deficit may impact bone by lowering bone
- 419 mineral density, boosting osteoclasts and decreasing osteoblasts that interfere with vitamin D,
- 420 causing oxidative stress and inflammation, and ultimately leading to bone loss (179).

421 3.11. Calcium

- London in 1808, Cornish chemist Sir Humphry Davy made the discovery of calcium. Its name
- comes from the Latin word "calx," which means "lime" (limestone is a calcium ore) (180). A soft
- element, calcium is a member of the alkali earth metal family. Of all the metallic components that
- make up the human body, it is the most prevalent (181). There is no toxicity to calcium. It is a
- 426 necessary mineral for the growth of strong bones and teeth, as the primary component of bones is
- 427 calcium phosphate (182-184). Calcium shortage can lead to osteoporosis, osteopenia,
- 428 hypocalcemia, and other illnesses (185). Although calcium is not a medicine in and of itself,
- 429 supplements and products containing calcium are utilized for a variety of pharmacological
- objectives (186). For adults, the recommended daily intake (RDI) of calcium is 1,000 mg daily
- 431 (187).

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432 **3.11.1. Bone health**

- 433 In addition to being essential for maintaining healthy bones, calcium is frequently used to treat and
- 434 prevent diseases including osteoporosis and osteopenia (188). In order to increase bone density
- and lower the risk of fractures, doctors commonly prescribe calcium supplements together with
- vitamin D, particularly for people who are deficient in these nutrients or who are at risk for bone-
- related illnesses (189, 190). Early adult peak bone mass is determined by the amount of calcium
- an individual consumes, which also impacts skeletal calcium retention during growth (191). In
- later age, calcium also helps to prevent osteoporotic fractures and bone loss (192).

3.11.2. Antacids

- 441 An ionic substance called calcium carbonate is used as an antacid or calcium supplement to treat
- 442 the symptoms of acid reflux, heartburn, and sour stomach. It is a simple substance that works by
- balancing the acidic effects of hydrochloric acid in stomach secretions (193).

3.11.3. Cardiovascular health

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- A family of drugs known as calcium channel blockers is used to treat a number of cardiovascular
- diseases, such as hypertension (high blood pressure) and certain arrhythmias (194). These drugs
- 447 function by obstructing the calcium channels in the heart and blood vessels, which causes the
- smooth muscle to relax and the blood vessels to dilate (195).

3.12. Strontium

- 450 First found in a mine in 1790, strontium was separated in 1808. An alkaline earth metal, strontium
- 451 is a delicate silver-white yellowish metallic element that is very chemically reactive (196). This
- 452 silvery metal is a non-radioactive element that occurs naturally. Strontium possesses physical and
- chemical characteristics comparable to those of its two vertical neighbours in the periodic table,
- calcium and barium (197). The bones contain 99 percent of all the strontium in the human body.
- 455 Its pharmacological uses are mostly related to the treatment of osteoporosis (198, 199). Because
- of its radioisotopes, strontium has become more important in nuclear medicine, primarily for the
- palliative and pain-relieving treatment of bone metastases (200).

3.12.1. Osteoporosis treatment

- The most significant cation in bones is strontium, which can fight osteoporosis by promoting the
- 460 proliferation of osteoblast cells and preventing bone reabsorption (199). In osteoporotic
- 461 individuals, strontium ranelate lowers the fracture rate and raises bone calcium (201). In the bone
- 462 structure, strontium-coated halloysite nanotubes (SrHNTs) strengthened the bone and stimulated
- osteoblasts to produce new bone (202). It has the ability to load drugs, lower bone reabsorption,
- and exhibit antibacterial action (203).

3.12.2. Dentistry

- 466 Strontium has the ability to both strengthen bones and shield teeth against decay (204). It has also
- been discovered that strontium-substituted hydroxyapatite (SrHAp) nanoparticles enhance the
- 468 process of tooth remineralization by raising the ALP activity, which is linked to the cloning process
- 469 in hard tissues (205, 206).

3.12.3. Anticancer activity

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- 471 Strontium nanoparticles, or SrNPs, find applications in chemosensory medicine, bioimaging, and
- cancer treatment (207). Chemosensing, medication delivery, cancer treatments, and biomedical
- imaging all employ strontium-suspended vesicles (208).

2.12.4. Antimicrobial activity

- 475 Gram-positive and gram-negative bacteria were both susceptible to the antibacterial properties of
- 476 strontium cerium oxide (SrO-CeO₂) nanoparticles (209, 210). Gram-negative bacteria are more
- 477 likely to attach themselves to SrO-CeO₂-combined NPs (211). Strontium oxide nanoparticles
- 478 (SrONPs) displayed excellent antibacterial activity against gram-negative bacteria such as Proteus
- vulgaris, Psudomonas aeruginosa, Morganella morganii, and Klebsiella pneumonia than that of
- 480 the gram-positive bacteria (212, 213).

481 3.12.4. Analgesic activity

- Due to its radioisotopes, strontium has become more important in nuclear medicine, primarily for
- the palliative and pain-relieving treatment of bone metastases (214, 215).

484 3.12.5. Barium

- One of the alkaline-earth metals in group 2 (IIa) of the periodic table is barium (Ba) (215). It is a
- prevalent element in the crust of the Earth, occurring naturally in one oxidation state (+II) and at
- a concentration greater than that of most other trace elements (216). The most prevalent minerals
- 488 of Barium are hollandite and barite, and they are typically related to potassium in geochemical
- 489 processes (217). Barium is mostly known for its poisonous qualities, and it is not thought to have
- 490 any substantial therapeutic effect. When consumed or breathed, barium compounds can cause
- 491 toxicity by interfering with cellular functions, especially by inhibiting potassium channels (218).

3.12.6. Anti-ulcer activity

- Barium oxide (BaBG) is a novel bioactive glass that may be used as an anti-ulcer agent (219). In a
- 494 number of ulcer models, including ethanol, aspirin, gastric ulcers caused by pyloric ligation,
- 495 duodenal ulcers caused by cysteamine, and ulcers that heal when exposed to acetic acid, BaBG
- 496 was found to greatly minimize ulcerative damage (220). BaBG has been shown to neutralize
- 497 stomach acid, promote cell proliferation, and provide a physical barrier of protection over the

gastro-duodenal epithelial cell (221). It also increased the pH of the stomach, exhibiting antacidlike effects (219) .

3.12.7. Diagnostic activity

Since barium sulphate is mostly employed as a contrast agent in medical imaging rather than for therapeutic purposes, it is not usually recognized for its pharmacological properties in the conventional sense (222). Most frequently, barium sulphate is used as a contrast agent in treatments like barium enema and swallow (223). The esophagus, stomach, and intestines are highlighted in these imaging investigations, which aid in the visualization of the gastrointestinal system. Barium sulphate is appropriate for this use since it is insoluble and inert (223). It covers the lining of the gastrointestinal tract during imaging examinations. The organs and tissues under examination are more visible because to this covering (224, 225).

3.12.8. Radium

The heaviest of the Group 2 (IIa) alkaline-earth metals in the periodic table is radium (chemical symbol Ra) (226). The discovery was made by Marie and Pierre Curie in 1898. It is created when uranium decays, releasing gamma, beta, and alpha ionizing radiation (227). In an aqueous solution, it produces the colorless radium cation, which is very basic and does not form complexes. As a result, the majority of radium compounds are basic ionic compounds (228). It exists in trace amounts in rocks, soil, and water in the natural environment. Radon is a radioactive gas that is created when some of the atoms in radium decay and release radiation (229-231). One type of anticancer medication is radon. In terms of radium isotopes, Ra-226 and Ra-228 are the most prevalent (232). The chemistry of radium is comparable to barium, which is widely employed as a substitute due to the high radiation of radium (233).

3.12.9. Anti-cancer activity

The first and only alpha-emitting radiopharmaceutical to be approved for clinical use by the FDA and EMEA for treating metastases linked to metastatic castration-resistant prostate cancer (mCRPC) is [223Ra] radium chloride (Xofigo®; previously alpharadin) (234-236). Six intravenous doses totaling 50 kBq kg-1 and 223 RaCl₂ are given, with a four-week interval between each administration. After entering the body, 223Ra²⁺ will work as a Ca²⁺ imitator and form complexes with the mineral hydroxyapatite at locations where bone is actively growing, which happens in metastatic bone tissue at a faster pace. Through a multimodal method, 223radium kills

- 528 tumor cells as well as osteoblasts and osteoclasts, the effector cells of pathological bone
- metabolism (237). It may also stimulate local immunological responses against tumors (238).

3.12.10. Ankylosing spondylitis treatment

- Radium chloride was first used to treat ankylosing spondylitis in 1948 (239). A course of ten
- weekly injections, totaling roughly 50 MBq, was administered to most patients. For ankylosing
- spondylitis patients, positive clinical outcomes were documented, indicating a sustained effect and
- a decrease in the requirement for analysesic and anti-inflammatory medications (240).

4. Conclusion

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- In conclusion, the s-block elements, including the alkali metals and alkaline earth metals, exhibit
- 537 diverse and significant roles in health, disease, and medical research. From neurological research
- 538 to anticancer activity, these elements have shown potential therapeutic applications, such as
- 539 lithium's neuroprotective effects and cesium's investigation for anti-cancer properties.
- Additionally, the pharmacological potential of these elements extends to the applications of helium
- 541 in human life and medical treatments. Overall, this comprehensive overview highlights the
- 542 multifaceted potential of s-block elements in medicine and research. These findings would
- 543 motivate us to carry out additional analysis and testing to show the effectiveness of s-block
- elements as prospective options in medicine.

545 Acknowledgements

546 Not applicable

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Table 1(on next page)

S-block elements (symbols and letters)

1 Table 1: S-block elements (symbols and letters)

Н	He	Li	Na	K	Rb	Cs
Hydrogen	Helium	Lithium	Sodium	Potassium	Rubidium	Cesium
Fr	Be	Mg	Ca	Sr	Ba	Ra
Francium	Beryllium	Magnesium	Calcium	Strontium	Barium	Radium