

LITHIUM MINERAL WATER

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Abstract

Hydrological surveys showed that Romania basement contains a variety of balneary resources located within on the surface crust. Mineral waters are spread over more than 20% of the country at different depths, with a wide range of physical, chemical and therapeutic properties depending on their genesis.

Balneary resources are represented mainly by therapeutic minerals that the physicochemical properties answer the needs of medical and prophylactic maintenance, enhancement and restoration of health, work capacity and physical and mental comfort of the individual.

The surface waters arising from a natural source or updated by drilling and whose physical and chemical characteristics that may exert dynamic pharmaco-therapeutic are considered therapeutic mineral waters. Mineral waters are waters that have a variable content of salts, gas, minerals, radioactive elements, which gives them therapeutic properties. In the past, name of mineral water was attributed to all shallow or groundwater mineral water that could be used for therapeutic purposes. In recent years, mineral water that could be used for therapeutic purposes have been given the name of curative water.

Lithium arouses a great scientific interest because, although his structure is so simple, easy to analyze, with chemical and physical properties well established the myriad of the effects on biological systems by influencing many cellular processes and molecular and the mechanism of action are still unclear generates a mystery that modern science attempting to decipher.

LITIU 1mM Ziua 7

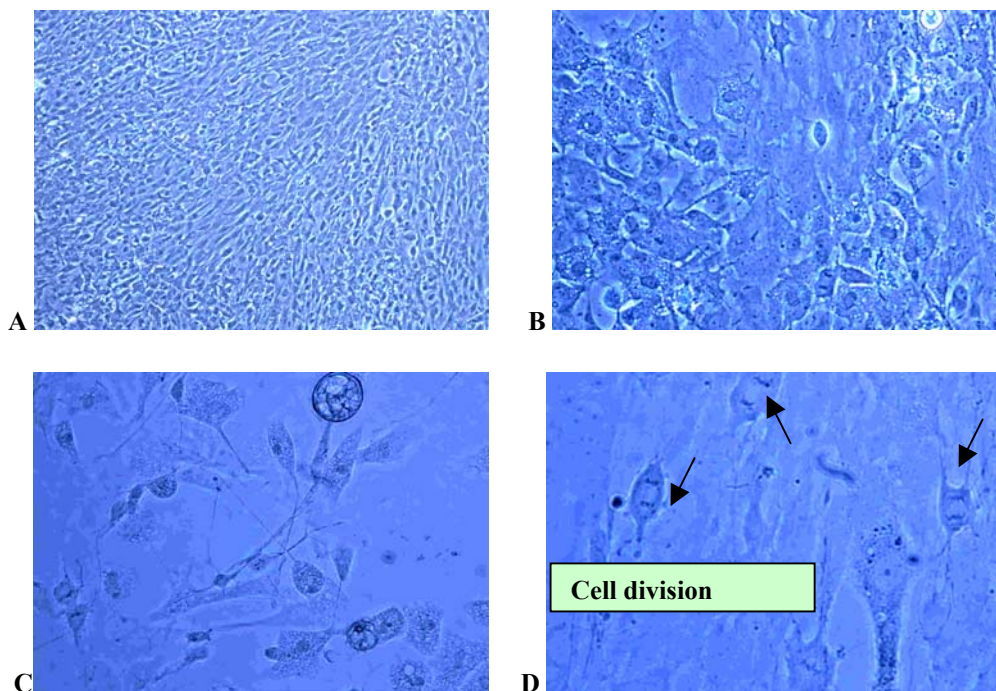


Fig. 16 Microscopy aspect of 7 days of culture treated with 1 mM LiCl
(A- x10 - island of cells, B- x30, C- x40, D- x40)

In vivo and *in vitro* studies have shown that lithium exerts multiple effects on receptor signaling mediated by neurotransmitters, ion transport, signaling cascades, hormonal regulation, and diurnal rhythm of gene expression (Cyrus et al, 2006). Unfortunately, the molecular mechanisms responsible for these effects are still a subject of debate. Biochemical mechanisms of action of lithium appear to be multifactorial and interrelated with functioning of several enzymes, hormones and vitamins, as well as factors of growth and transformation (Schrauzer, 2002).

Acute effects of lithium are mediated through inhibition of enzymes involved in two distinct but interactive signal paths - the path of protein C kinase and glycogen synthase 3 β kinase cascade - which converge at the level of gene transcription.

The expression of some genes, including transcription factors, is significantly changed by chronic administration of lithium. Chronic lithium treatment increases the neuroprotective bcl2 protein expression, leading to an interesting possibility that some effects of lithium to be mediated through effects neurotrophic / neuroprotective (Ikonov and Manji, 1999).

In centre of Romania, in the county with the same name, located in the Brasov Depression, at the western foot of the Vrancea mountains at an altitude ranging between 550 and 600m, 31 km east

of the city of Saint George, is located Covasna city – an important center for bottling mineral water.

The medicinal mineral water known as Maria water is bottled in Malnas Bai resort. Malnas Bai resort is situated in the gorge that separates the mountains Bodoc from Baraolt Mountains, about 22 km from St. George. Climate has no large thermal amplitudes, the average annual temperature is 70 C and average annual rainfall of 600 mm. The resort formation dates since 1759 and after 1865 and its reputation reached abroad

Maria mineral water is a water bicarbonate, chloride, sodium, carbonated, hypotonia, used for internal cure and packaging.

Maria medicinal mineral water is bottled since 1904 when it was recommended to treat various digestive disorders such as digestive (chronic gastritis with hyperacidity, gastric and duodenal ulcers, chronic colitis, chronic constipation), shares hepatobiliary (dyskinesia bile, chronic hepatitis, chronic pancreatitis, chronic cholecystitis not calculated or calculated), associated diseases: neurasthenia, migraine, emotional disturbances.

Maria medicinal water from Malnas Bai, containing 8 mg per liter of lithium been applied in clinical and experimental research in the treatment of migraine and affective disorders, diseases that have entered the therapeutic spectrum of water in the past.

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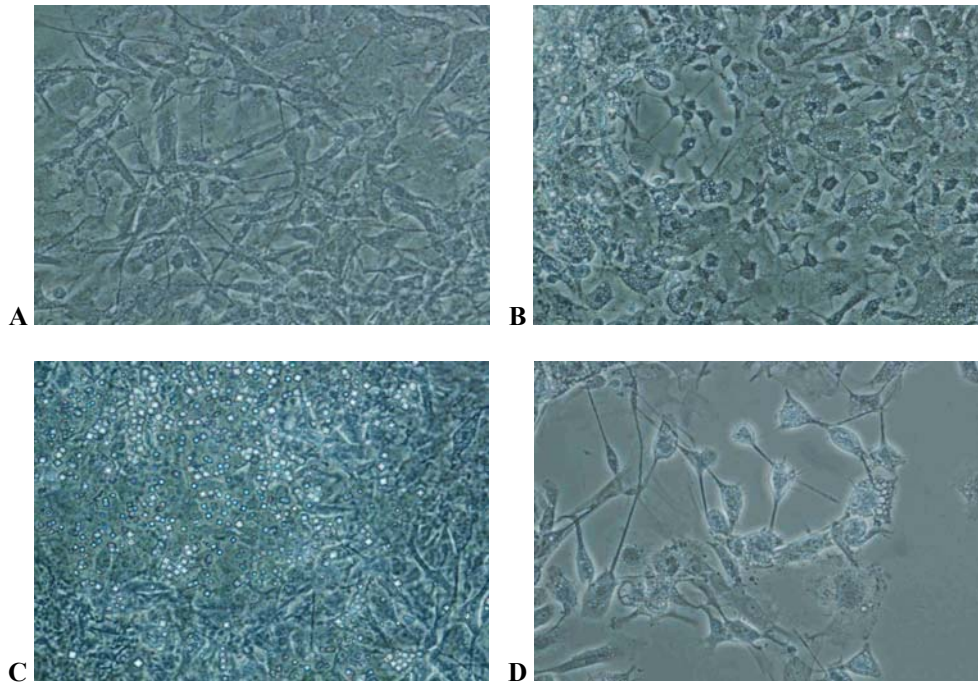


Fig. 24 Microscopy aspect of 12 days of culture treated with LiCl 2mM (A- x40, B- x30, C - x30, D- x40)

Lithium effects on the nervous system have been intensively studied thanks it for use in the treatment of manic-depressive psychosis (Gilles and Bannigan, 1997, Lenox and Hahn, 2000).

Treatment with lithium chloride began from the day 6 of cultivation of glial cells after lag phase, which corresponds to cell multiplication start, to cell islands formation and pronounced cell differentiation.

Treatment with lithium chloride involves using a growing medium prepared with a quantity of lithium chloride corresponding to 1 and 2-mM lithium concentrations. According to the used protocol, the preparation of lithium chloride medium involves obtaining a stock solution of 20 mM lithium chloride in DMEM medium, from which the specific volume is used to obtain the desired concentrations.

Medium change and the treatment application with lithium of 1 and 2 mM concentration, occurs at a frequency of three days of cultivation.

Concentration of 1 mM lithium corresponds to therapeutic serum level of lithium, achieved in the treatment of manic-depression, a level that should be closely monitored so as not to be exceeded.

Concentration of 2 mM lithium is a toxic dose to the body, as demonstrated most of studies conducted till now in various research centers that focused on the effects of lithium.

Biological effects of lithium can be divided into: short-term effects (manifested shortly after

application and probably mediated by complex cellular available) and long-term effects (assumed to be based on selective changes of gene expression that occur after a delay of several days to weeks). Many short-term effects of lithium appear to be specific to cells or tissues. Examples include short-term stimulatory effects of corticotropin secretion induced by lithium of rat anterior pituitary cells and a massive release of glutamate of the brain sections treated with lithium. Inhibitory effects of short-term treatment with lithium are evidenced by the secretion of aldosterone induced by angiotensin II adrenal glomerular cells and the rate of relaxation that follows the induction of cholinergic smooth muscle contraction. Inhibitory effects of short-term treatment with lithium are evidenced by the secretion of aldosterone induced by angiotensin II of adrenal glomerular cells and the rate of relaxation that follows the induction of cholinergic smooth muscle contraction.

Among the long-term phenotypic changes may be mentioned changes induced by lithium on the circadian rhythm and of course behavior changes in patients with bipolar disorder appeared after 2-3 days or few weeks.

Chronic lithium treatment on laboratory rats leads to a running persistent deficit at some behavioral tests (active and visual avoidance of the maze), taking into account that the memory deficit in a task space is transient.

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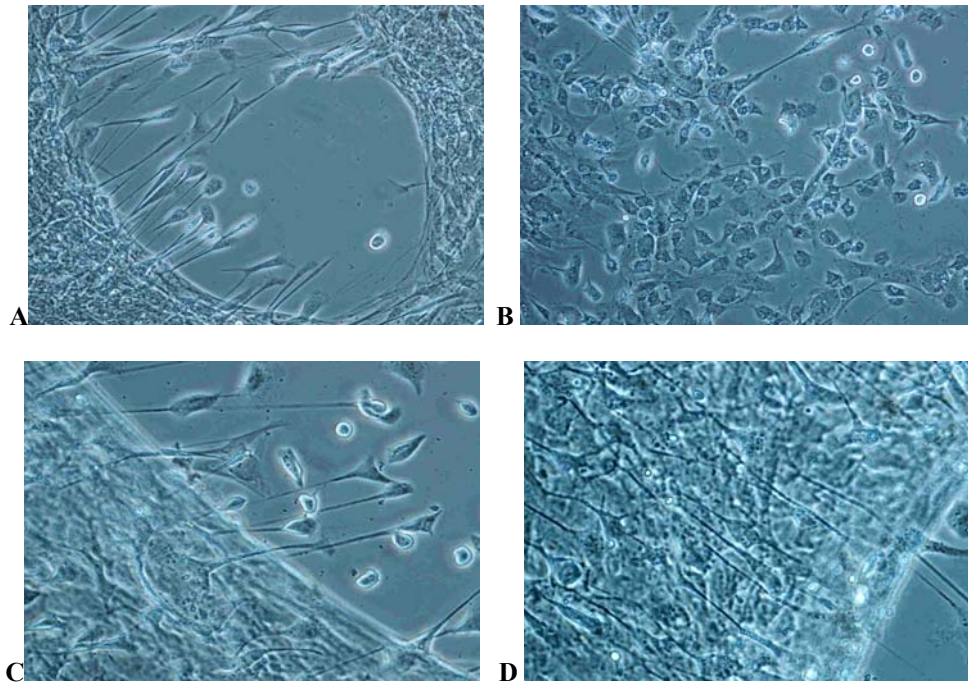


Fig. 38 Microscopy aspect of 14 days of culture treated with MARIA water 25% (A- x30, B- x30, C - x30, D- x40)

Glial cells grown in the presence of lithium-rich mineral waters is the experimental model to verify hypotheses on their role in improving the growth parameters of glial cells *in vitro*.

Maria mineral water treatment involves the preparation of media for cultivation replacing a part of double distilled water necessary for the process of obtaining with Maria mineral water. The experimental treatment involves the use of media with 50% and 25% Maria mineral water, which basically means the replacement of 50% and 25% respectively of necessary double distilled water with Maria mineral water from Malnas-Spa.

A third alternative case for tracking the water effects is represented by adding of variant with 25% Maria mineral water to a concentration of 1 mM LiCl to monitor the effect of increasing the total amount of lithium in water.

Sterilization of culture media prepared with Maria mineral water and used for the treatment of glial cell cultures is performed by nitrocellulose filtration membrane with pore diameter of 0.2 μ m.

Medium change and the treatment with Maria mineral water of 50%, 25% and 25% + 1 mM LiCl concentration, occurs at a frequency of two to three days of cultivation

The treatment with Maria mineral water began from the day 6 of cultivation of glial cells after lag phase, which corresponds to the start

islands cell formation and to pronounced cellular differentiation.

Choosing water concentration was correlated with the physiological capacity of water ingestion of the organism, under the assumption that in blood may be replaced within 24 hours maximum 25% of serum with water consumed daily (1.5 - 2 liters of water a day), to be filtered and removed the salts through kidney, digestive and skin.

Maria mineral water of 50% concentration is chosen only to experimental pursue to investigate the effect of this high level has on the glial cells *in vitro*. This level has no therapeutic value, because the body has no way to have a such quantity of consumed water.

From the experimental point of view, the 50% concentration represents a positive control of the effects that Maria mineral water may have on cells.

Preliminary experimental data of our studies have shown that by replacing 100% of double-distilled water needed in the technological process of preparing the medium for the cultivation of glial cells culture, culture destruction occurs in 48-72h after application.

Was found that Maria mineral water can not provide the minimum conditions for survival of glial cells *in vitro*.

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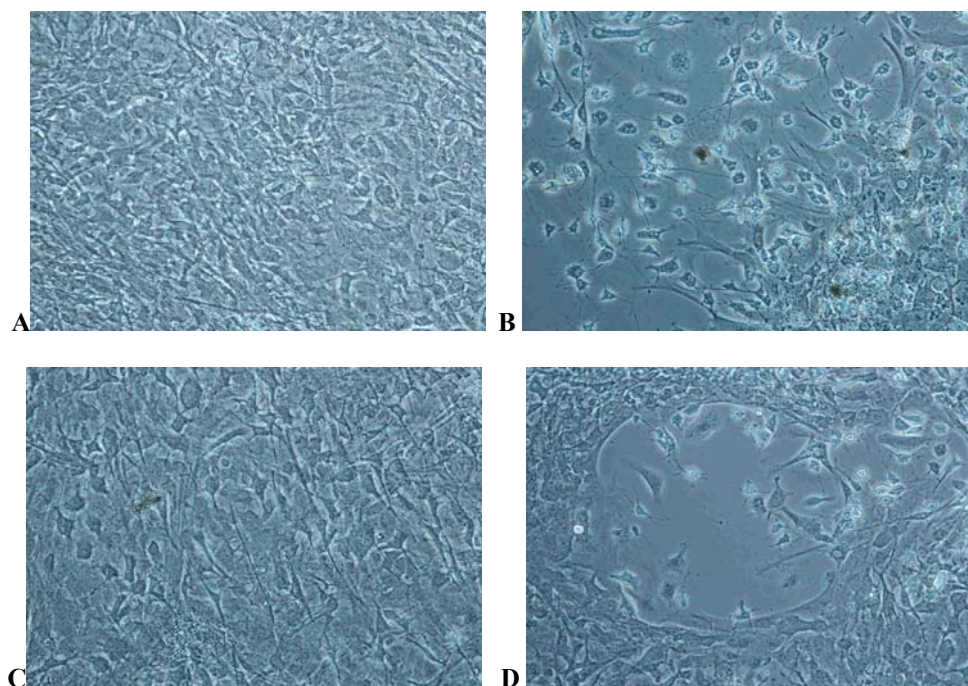


Fig. 39 Microscopy aspect of 15 days of culture treated with MARIA water 25% (A- x 15, B- x 15, C- x 20, D-x 15)

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