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## **Drinking mineral waters: biochemical effects and health implications – the state-of-the-art**

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**Abstract:** Spring mineral water might have the properties favourable to health, which should be assessed by clinical and pharmacological analyses. Efforts have recently been made to approach the study of the validity of spring mineral water curative therapies by advanced biochemical research on both animal models and humans. Owing to the paramount interest and the growing recent use of drinking mineral waters, a need for a rigorous scientific approach arises. The therapeutic action of drinking mineral waters has been demonstrated to have important biochemical implications. However, some adverse events during health resorts cure must be considered and investigated. This paper reviews the state-of-the-art on the biochemical studies related to the effects of drinking mineral water. In the light of the review of the literature on the matter, we conclude that further studies are necessary to avoid any possible implication for public health connected with mineral water misuse.

**Keywords:** biochemical effects of mineral waters; drinking mineral water; mineral waters; spring therapy.

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## 1 Introduction

Thermal waters have been used for hydrotherapeutic purposes in the Mediterranean region since the second century BC; however, the first epidemiological data relating water consumption with health and digestion appeared only in twentieth century (Loisy and Arnaud, 1967). The consumption of natural mineral water has increased enormously during the past few years. Water is the base of all drinks, and it supplies essential minerals. Mineral waters contain different types of substances dissolved, namely minerals and other biological compounds. Modern science has developed new classification approaches of the different mineral waters by chemical and chemical-physical analysis and the evaluation of metabolic variations by different biochemical parameters. Mineral water’s ‘special’ mineral composition might have the properties favourable to health, which should be assessed by clinical and pharmacological analyses. This health benefits

were studied, particularly in Eastern European spas (Loisy and Arnaud, 1967; Brzecki et al., 1978). Mineral waters have been used in human nutrition, especially in the different stages of life, during physical activity and in the presence of some morbid conditions ([www.benessere.com/terme/acqua/index.html](http://www.benessere.com/terme/acqua/index.html)). The use of drinking mineral waters as therapeutic and preventive remedies for many diseases affecting the respiratory tract, skin, liver, intestine, gynaecological apparatus and osteo-articular system has been demonstrated. Water intake favours the digestive solubility of foodstuffs and improves intestinal physiology (Grassi et al., 2002). Most authors (Garzon and Eisenberg, 1998; Bonfante et al., 1999; Bortolotti et al., 1999b; Capurso et al., 1999; Serio and Fraioli, 1999; Fraioli et al., 2001; Bertoni et al., 2002; Grassi et al., 2002; Fioravanti et al., 2003; Petracchia et al., 2005) have suggested that thermal waters are valid tools in the treatment of illnesses such as functional dyspepsia, irritable bowel syndrome and functional disorders of the biliary tract, because carbonated waters stimulate the secretion and motility of the digestive tract (Schoppen et al., 2004; Gasbarrini et al., 2006). Furthermore, salt-rich mineral waters enhance the conversion of cholesterol into bile acids and their subsequent secretion (Capurso et al., 1999; Bertoni et al., 2002; Grassi et al., 2002). Spring mineral therapy with sulphurous water can provide beneficial effects in chronic inflammatory disorders with an immunologic pathogenesis by inhibiting the immune response at a local level. The influence of drinking water composition on the risk of myocardial infarction has also been studied. The few available biochemical studies showed the effects on animal models and human. Spring mineral waters have anti-oxidant, hypocholesterolaemic activity and may affect calcium metabolism (Toussaint et al., 1986, 1988). For example, sulphurous mineral water was found to have anti-oxidant properties and a positive effect on the oxidative defence mechanism on both rabbits and rats, respectively (Albertini et al., 1996, 1999a). Magnesium-sulphate-sulphurous spring mineral water has been demonstrated to have a very good hypocholesterolaemic activity and a protective effect against oxidative lipid damage. The oral intake of water containing calcium increases serum calcium and inhibits intact parathyroid hormone secretion (Cantalamesa and Nasuti, 2003). However, results vary depending on the type of water mineralisation (Toussaint et al., 1988; Aptel, Cance-Rouzaud and Grandjean, 1999; Neimark, Davvdov and Lebedev, 2003; Nerbrand et al., 2003). Epidemiological studies carried out over the past 10 years found the relations between the mineral content of drinking water and the Cardiovascular Disease (CVD) mortality rate in various countries (Sauvant and Pepin, 2000; Schoppen et al., 2004). Some studies demonstrated a positive geographical correlation between stroke-associated mortality and river water acidity (Neri, Mandel and Hewitt, 1972; Punsar et al., 1975; Huel et al., 1978; Flaten and Bolviken, 1991).

Some adverse events during health resorts cure were observed and investigated. These adverse events have been described as the general or neurological outcome such as asthenia and malaise, but have never been studied in relation to the biochemical spring mineral water activity. We therefore urge more biochemical studies to determine the validity of mineral water drinking therapy and whether there are unforeseen adverse effects of mineral waters for some populations. Researchers should determine which chemical forms present in mineral waters are best absorbed and most effective. It is also important to better understand the interrelation of various water and food constituents and individual risk factors.

## 2 Natural mineral waters: the European Community Directives

The conservation and the healing properties of mineral water are recognised by the Ministry of Health after clinical and pharmacological trials, and certain mineral waters may be useful in providing essential micro-nutrients, such as calcium; however, the World Health Organization (WHO) retains that the evidences to support the beneficial effects of consuming mineral waters are not yet enough and thus, as a consequence, WHO 'Guidelines for Drinking Water Quality' do not make the recommendations regarding minimum concentrations of essential compounds (<http://www.who.int/fsf>). Nevertheless, the European Council Directive 80/777/EEC of 15 July 1980 on the approximation of the laws of the Member States relating to the exploitation and marketing of natural mineral waters (Official Journal L 47 of 20.02.1981) was amended by the European Parliament and Council Directive 96/70/EC of 28 October 1996. The Directives concern the water extracted from the ground of a Member State and recognised as the natural mineral water by the responsible authority. They also concern the water extracted from the ground of the Third-World countries. The Directives define the characteristics of natural mineral waters (Table 1), the treatments and additions that may be made to them and the conditions of exploitation of springs. Member States, which recognise a mineral water as such, must justify that decision, which is published, and inform the Commission thereof. The list of the recognised mineral waters is published in the *Official Journal of the European Communities* (Table 2). The Directives lay down very precise rules on the labelling and packaging of natural mineral waters. The Directive 96/70/EC also sets the validity of the certification of water extracted from the ground of a Third-World country at 5 years (<http://europa.eu.int/scadplus/leg/en/lvb/l21129.htm>).

A Member State may temporarily restrict or suspend the trade in a natural mineral water that does not comply with the provisions of the Directives or which poses a risk to public health. It must give reasons for its decision. The Directive provides for the option of treating the natural mineral waters with ozone-enriched air or other treatments and lays down the authorisation procedure for such treatments. The term 'spring water' must meet the conditions of exploitation and microbiological conditions applicable to natural mineral waters and the provisions of Directive 80/778/EEC, in particular with regard to the physical and chemical parameters and undesirable substances. Thus, in Italy (D.Lgs 339/1999 and 31/2001), like mineral water, spring water must not be purified but used only as it gushes out from the source (Dabeka et al., 2002; Petrelli et al., 2003).

**Table 1** European Commission Directives defined for natural mineral waters (<http://europa.eu.int/scadplus/leg/en/lvb/l21129.htm>)

|   |   |
|---|---|
| Directive 80/777/EEC amended by the European Parliament and Council Directive 96/70/EC (18/10/1996) | Defines the provisions applicable to the marketing and exploitation of natural mineral waters.  |
| Directive 2003/40/EC  | Establishes the list, concentration limits and labelling requirements for the constituents of natural mineral waters and the conditions for using ozone-enriched air for the treatment of natural mineral waters and spring waters. |
| Directive 80/778/EEC  | Defines the conditions of spring water exploitation, in particular to the physical and chemical parameters and undesirable substances.  |

**Table 2** List of natural mineral waters recognised by Member States (<http://europa.eu.int/scadplus/leg/en/lvb/l21129.htm>)

| <i>Member States</i> | <i>Number of sources</i> |
|----------------------|--------------------------|
| Belgium              | 37                       |
| Germany              | 688                      |
| Greece               | 37                       |
| Spain                | 123                      |
| France               | 65                       |
| Ireland              | 4                        |
| Italy                | 390                      |
| Luxembourg           | 4                        |
| The Netherlands      | 10                       |
| Austria              | 18                       |
| Portugal             | 19                       |
| Finland              | 1                        |
| Sweden               | 2                        |
| Denmark              | 6                        |
| UK                   | 94                       |

### 3 Drinking mineral water classification

There are several categories of drinking waters. Drinking mineral waters belong to some of these categories. Natural mineral waters are characterised by their purity at the source and by their constant mineral content. There are different criteria used to identify the different types of waters, the chemical–physical analyses (temperature, density, pH, radioactivity, etc.) the chemical analyses (dry residues, ozone, sulphydrometric grade, gasses dissolved, etc.) and the general characteristics (colour, taste, limpidity, etc.). Based on the total salt content in grams after evaporation of 1-litre mineral water dried at 180°C (dry residues), mineral waters can be classified as: waters with a very low mineral content, waters low in mineral content, waters with a medium mineral content and strongly mineralised waters. In Italy, the most used classification is still that proposed by Marotta and Sica (1933), which is the one subordinated to the authorisation for the oral use of the mineral waters. Based on ion composition, mineral waters can be classified as: bicarbonate waters, sulphate waters, sodium chloride or salt water, sulphurous waters, etc. (Table 3). According to these parameters, mineral waters can be classified as follows:

- oligomineral and low mineralised water
- sulphurous water
- salt-bromine-iodine water
- radioactive water
- salt water

- sulphate water
- bicarbonate and carbonic waters
- ferrous arsenic water.

**Table 3** Ion content describing the different types of mineral water  
([www.benessere.com/terme/acqua/index.html](http://www.benessere.com/terme/acqua/index.html))

| <i>Ion content</i>   | <i>Types of mineral water</i>           |
|--|---|
| $\text{Na}^+$ , $\text{Cl}^-$ , $\text{I}^-$ , $\text{Br}^-$                                       | Salt water, salso-bromo-iodic           |
| $(\text{CaCO}_3)$ $\text{H}_2\text{CO}_3$ , $\text{HCO}_3^-$ , $\text{Mg}^{2+}$ , $\text{Ca}^{2+}$ | Bicarbonate, carbonic, calcic, alkaline |
| $(\text{CaSO}_4)$ $\text{SO}_4^-$ , $\text{Ca}^{2+}$ , $\text{Mg}^{2+}$                            | Sulphate, calcic, magnesian             |
| $\text{SO}_4^-$ , $\text{Cl}^-$ , $\text{HCO}_3^-$   | Sulphate                                |
| $\text{H}_2\text{S}$ , $\text{NH}_4^+$   | Sulphurous                              |

### 3.1 *Oligomineral and low mineralised water*

Oligomineral waters are poor in mineral content (dry residue not higher than 50 mg litre<sup>-1</sup> and not higher than 500 mg litre<sup>-1</sup> for low mineralised and oligomineral waters, respectively) for two main reasons: their rapid flow through the sub-soil hinders the mineralisation processes and the contact with dense rocks that hardly transfer substances in solution. Some low mineralised waters are radioactive, and this fact strengthens their biological and therapeutic effects. The therapeutic use of oligomineral water should be performed on everyday basis to be effective, and the spring therapy with oligomineral water in thermal centres are then useful for different reasons. The characteristics of the water as it gushes are peculiar and potentiate the treatment. Oligomineral waters are hypotonic and stimulate diuresis ([www.italiantourism.com/spas.html](http://www.italiantourism.com/spas.html); [www.benessere.com/terme/acqua/index.html](http://www.benessere.com/terme/acqua/index.html); Scalabrino, Buzzelli and Raggi, 1998). The effects of these waters do not depend exclusively on their hypotonic characteristics but depend on their mineral content as well; many of these traces elements act as catalisators of enzymatic reactions of important biochemical pathways.

### 3.2 *Sulphurous water*

Sulphurous waters contain at least 1 mg litre<sup>-1</sup> sulphydric acid ( $\text{H}_2\text{S}$ ) and should preferably be ingested as they gush (Rajchel et al., 2002; Searcy and Peterson, 2004). Depending on the pH of the water, the  $\text{H}_2\text{S}$  is present as a whole molecule (low pH) or dissociated as  $\text{H}^+$  +  $\text{HS}^-$  (alkaline water). Italian sulphur mineral waters usually exhibit pH values below 8. When they are bottled, stocked, conserved and opened, they loose their gasses. Sulphurous waters may also contain other elements such as sulphate, sodium, bicarbonate, calcium, etc. Because of the toxicity of  $\text{H}_2\text{S}$ , only sulphur-bacteria and few other microorganisms can survive in sulphurous water. These waters are the most studied and their biological effects are well known on skin, respiratory and vaginal mucous membrane and gastroenteric system (Ibadova, Lopatinskii and Shaidenko, 1997; Costantino, Rossi and Lampa, 2003; Lopalco et al., 2004).

### 3.3 *Salt-bromine-iodine water*

This type of mineral water is of seawater origin. It contains mostly sodium chloride, iodine and bromine, these latter are present as  $I^-$  and  $Br^-$ . Other important curative elements such as calcium, magnesium, sulphate, bicarbonate and sulphur are also present. In the absence of bromine, these waters are defined salt-iodine. Salt-bromine-iodine waters are well known for their anti-inflammatory activity and are used in a variety of pathological conditions, such as diseases of the gastrointestinal system (Dartois and Casamitjana, 1991; Staffieri et al., 1998; Evandri and Bolle, 2001). They can be radioactive at the spring. Ionic concentration may vary and thus we may find hypotonic, isotonic and hypertonic salt-bromine-iodine waters.

### 3.4 *Radioactive water*

Radioactive waters have radioactivity as the main characteristic, since they contain traces of different radioactive elements: radium, radon, uranium, etc. The most important radioactive element (and the one present at highest concentration) for clinical therapy is the radon. Radon is easily absorbed by the mucous membrane and skin, and is eliminated in a short period of time (only few hours). Its therapeutic property derives from alpha radiation with weak penetrating characteristic and good ionising capacity. A mineral water is classified as radioactive water when it contains at least 1 nC (nanocurie) corresponding to 2.75 UM (Mache Unit) per litre. Nevertheless, some authors believe that the radioactivity should reach 50–80 UM to be effective during a therapy. Since the half-life of radon activity is 3.825 days, it is suggested to drink these waters as they gush from the spring to avoid the element decay and thus the therapeutic properties decrease. Based on the radioactivity, this type of mineral water is classified as low radioactive (up to 30 nC litre<sup>-1</sup>), average radioactivity (between 30 and 150 nC litre<sup>-1</sup>) and high radioactivity (above 150 nC litre<sup>-1</sup>). The therapeutic property of radioactive waters seems related to the energy released by the radioactive elements that yield excitation and ionisation properties. The therapeutic uses of radioactive waters concerns the treatment of osteo-articular diseases, gout and of diuresis stimulation (Gans, 1985; Bartoli et al., 1989; Amrani and Cherouati, 1999). Effects on central nervous systems, gynaecological functions and immune system (autoimmune syndromes) have also been observed.

### 3.5 *Saltwater*

They have the same origin than the salso-bromo-iodic waters. As stated by their name, these waters have an important concentration of sodium and chloride but often contain sulphate also. These waters can be used for hydropinic therapy when either bicarbonate or iodine is also present. Salt waters can be either hypo-, hyso- or hyperthermal waters inducing different biological effects. Their use is particularly indicated for hydropinic therapy for disease of the gastrointestinal system (Bortolotti et al., 1999a).

### 3.6 *Sulphate water*

In this type of waters, the predominant element is the sulphur that is present in natural mineral waters as sulphate ion ( $SO_4^{2-}$ ). We can also find other elements such as bicarbonate, calcium, magnesium, chloride, arsenic. The most commonly used sulphate

waters are constituted of bicarbonate, calcium and magnesium (named sulphate-bicarbonate and sulphate-alkaline earthy, respectively). The presence of other elements in sulphate waters gives the possibility to classify them in other classes as, for example, salt waters. These waters are enriched of calcium sulphate ( $\text{CaSO}_4$ ) when they pass through the soil. The bicarbonate-sulphate alkaline earthy, sulphate-calcic, sulphate-alkaline earthy, sulphate-bicarbonate-calcic waters are the most commonly used for clinical therapy. These waters are particularly indicated for the treatment of liver, kidney, gastro-enteric and respiratory diseases (Cristalli, Abramo and Pollastrini, 1996; Grossi et al., 1996).

### 3.7 *Carbonic water*

Carbonic waters are the most diffuse in nature. In earth, there is a prevalent concentration of bicarbonate as compared with calcium, sulphate, sodium and magnesium. Carbonic waters originate by infiltrating in a calcic soil. Calcium and magnesium bicarbonate are derived from the reaction with  $\text{CO}_2$ . The  $\text{CO}_2$  is commonly present in both the volcanic soil (deep origin) and the atmosphere. Carbonic waters are prevalently characterised by the presence of the  $\text{HCO}_3^-$  ion. In bicarbonate-alkaline waters an important concentration of sodium and potassium are present, while the bicarbonate-alkaline earthy waters are rich in calcium and magnesium. Furthermore, among these elements, in bicarbonate waters other elements are also commonly present: sulphate, chlorine, iron, bromide, iodide, etc. Bicarbonate waters are prevalently used in the hydropinic therapy for curing cardio-circulatory and respiratory diseases (Schorr, Distler and Sharma, 1996; Coen et al., 2001).

Carbonic waters (often belonging to the bicarbonate water category) are characterised by the presence of an elevated concentration of free  $\text{CO}_2$  (containing at least  $300 \text{ mg litre}^{-1}$ ). Another classification of this type of water has been established depending upon the therapeutic properties: light carbonic water ( $300\text{--}500 \text{ ml litre}^{-1}$  of free  $\text{CO}_2$ ); medium carbonic water ( $300\text{--}1,000 \text{ ml litre}^{-1}$  of free  $\text{CO}_2$ ) and strong carbonic water ( $>1,000 \text{ ml litre}^{-1}$  of free  $\text{CO}_2$ ).

### 3.8 *Ferrous arsenic water*

The classification of these waters as ferrous arsenic is due to the high probability to observe these two elements associated in mineral waters. In fact, there are ferrous waters or arsenic waters in a few cases only. Other elements are also present as traces in these category of waters: copper, manganese, lithium, zinc, nickel, cobalt, aluminium. There are two principal types of ferrous waters: sulphate-ferrous/ferric waters and bicarbonate-ferrous waters. The sulphate-ferrous/ferric waters are very concentrated and are arsenic-rich. The pH is very low (below 3, and in some cases below 1) for the presence of sulphate and phosphate acids. However, the presence of elevated concentrations of arsenic in water may reflect contaminated soil by both industrial and non-industrial sources, and is often considered a marker of environmental contamination. Most of the Italian thermal waters contain the arsenic element at a concentration ranging from 0.20 to  $0.68 \text{ mg litre}^{-1}$  (Conti, 1997).

The bicarbonate-ferrous waters are arsenic-poor. They are not stable since the oxygen can induce the precipitation of iron by forming hydroxide. In this case, the pH is of about 6 and they have important haemopoietic properties (Marullo and Abramo, 1999).



#### **4 Therapeutic effects of mineral waters**

Based on the biological activity, mineral waters can be classified as: diuretic waters, cathartic waters and waters with anti-phlogistic properties. Several clinical and epidemiological studies are carried out on the outcome of drinking mineral waters therapy in human populations of different age and health conditions. The results of these studies are reported below.

Clinical studies on the effect of sodium chloride- and sodium bicarbonate-rich mineral water on blood pressure and parameters of glucose and lipid metabolism in elderly normo-tensive individuals showed that the consumption of sodium chloride-rich mineral water can abolish the blood pressure reduction induced by dietary salt restriction. It is generally recommended that individuals reduce their salt intake to control hypertension. However, some data indicate that low salt intake increases cholesterol levels, implying increased cardiovascular risk. Conversely, sodium bicarbonate-rich mineral water in conjunction with a low-salt diet may have a beneficial effect on calcium homeostasis. Increased sodium concentrations in the drinking water led to an increase in mean arterial pressure and systolic blood pressure in fourth- and fifth-grade school children (Schorr, Distler and Sharma, 1996). Blood pressure in the neonate is increased by a high sodium intake via drinking water as well. Milk powder formulae have a low content of sodium, almost identical to that of breast milk. However, the final sodium concentration in the milk formula depends upon the concentration of sodium in the diluting water, which varies remarkably. Diluting milk formula with tap water containing a high concentration of sodium will result in the infant being fed a high-salt diet. To equilibrate with breast milk, the formula should be diluted with low-salt water (Schorr, Distler and Sharma, 1996).

Studies on CVD suggested that drinking water is an important vehicle for the supply of minerals (Pomeranz et al., 2002). Among the various non-pharmacological tools for controlling cholesterolaemia, besides a low cholesterol diet, hydropinic treatment with mineral waters of a particular chemical-physical composition can be used. Hydropinic therapy with sulphate-alkaline spring water has been shown capable of markedly reducing increased cholesterolaemic and lipaemic levels by increasing the lipoprotein metabolism (Toussaint et al., 1986, 1988). In particular, studies carried out on the effect of the spring mineral water from Montecatini (Italy) on bile acid extraction and lipid and apolipoprotein serum levels suggested that salt-rich spring water treatment reduces serum- and LDL-cholesterol levels in subjects with mild hypercholesterolaemia, through a mechanism of increased excretion of faecal bile acid sterols (Foschi and Arena, 1990). Studies on the therapeutic effects of sulphurous-arsenical-ferruginous waters on aspecific phlogosis of the upper respiratory tract showed a decreased resistance and increased nasal respiratory flow, normalised mucociliary transport, decreased bacterial layer and increased plasma cells in rhinocytogram. An increase in albumin, non-secretory immunoglobulin and the secretory portion of secretory immunoglobulin A in the nasal mucosa has been observed too. Also the gastrointestinal system, which is a target of psychic and physical stresses displaying symptoms or diseases, may be favourably addressed with the aid of mineral waters. This treatment has proved effective in secretory and motility disorders of the biliary tree, allowing a rapid functional recovery (Bergmann and Bergmann, 1995; Scalabrino, Buzzelli and Raggi, 1998; Matz, Orion and Wolf, 2003).

The calcic and magnesian-sulphate-sulphurous spring mineral water presents various pharmacological actions, such as the improvement of the chronic inflammation of the upper respiratory airways by aerosol vapour inhalation. Besides, calcic and magnesian-sulphate-sulphurous spring mineral waters are commonly used in balneotherapy for the treatment of rheumatic and various dermatologic conditions, such as psoriasis, atopic dermatitis and acne vulgaris (Cantalamesa and Nasuti, 2003). The therapeutic action of sulphurous water is related to its anti-inflammatory, keratoplastic and anti-pruriginous effects.

Previous studies have shown an inverse relation between magnesium in drinking water and the risk of dying from Ischemic Heart Disease (IHD) (Luoma et al., 1983; Marx and Neutra, 1997). The importance of magnesium and calcium in drinking water in relation to morbidity and mortality from acute myocardial infarction has been the object of various studies although not all the reports show the same results (Nerbrand et al., 1992; Hall and Jungner, 1993; Rubenowitz et al., 2000). Some studies have also shown an inverse relationship between waterborne calcium and IHD (Allwright, Coulson and Detels, 1974), but in other studies no such relationship was seen (Linderman and Assenzo, 1964). This study suggested that magnesium in drinking water is associated with lower mortality from acute myocardial infarction, but not with the total incidence.

Calcium is an important factor in the prevention of additional risk of stone formation. The content of calcium in waters used for hydration may vary from very low to relatively high concentration. Therefore, the effect of drinking mineral waters of different calcium concentrations on lithogenic risk factors has been studied in normal volunteers. The water intake for hydration consisted of an oligomineral water with a low calcium content,  $<20 \text{ mg litre}^{-1}$ , or of a bicarbonate alkaline water with a high calcium content,  $370 \text{ mg litre}^{-1}$ . It has been concluded that increased water intake between meals to prevent renal stone recurrence should preferably be achieved with a relatively low calcium water and calcium-rich mineral waters should be avoided (Coen et al., 2001). A normal dietary calcium intake to reduce intestinal oxalate absorption is essential to avoid the recurrence of calcium oxalate stone formation. It is also important in the prevention of osteopenia in idiopathic hypercalciuria. The calcium content of waters used for hydration may vary from very low to relatively high, and is an important factor in the prevention or additional risk of stone formation (Weder and Egan, 1991).

## **5 Biochemical effects of mineral waters**

It must be pointed out that very little are the studies on the biochemical effects of mineral waters; and due to the very high diffusion of hydropinic therapy in our, as well as in other, western and eastern European countries, the need of implementing such studies is highlighted here.

Some authors underlined the importance of hydropinic treatment with calcic and magnesian-sulphate-sulphurous spring mineral water from the biomedical point of view, because it could represent an alternative approach in the interventions aimed at ameliorating biological injury deriving from hypercholesterolaemia. To evaluate the ability to reduce total and erythrocyte plasma membrane cholesterol by using calcic and magnesian-sulphate-sulphurous spring mineral water, a few studies have been performed on rats fed with a cholesterol-rich diet (Nasuti et al., 2005). In these studies, the rate of haemolysis was reduced in those erythrocyte suspensions in which cholesterol was

increased, even if the enzymatic activity of glutathione peroxidase and catalase decreased. Literature reports have demonstrated that this type of water, which contains  $\text{SO}_4^{2-}$ ,  $\text{Ca}^{2+}$  and  $\text{Mg}^{2+}$  ions, has a very good hypocholesterolaemic activity, because it is able to decrease the Low-Density Lipoprotein (LDL) level in blood. Toussaint et al. (1986, 1988) suggested that, in rats, salt-rich mineral waters enhance the conversion of cholesterol into bile acids and their subsequent secretion. Analogous studies on humans reported important effects of various mineral waters, mostly fizzy bicarbonated mineral waters, on lipoprotein levels (Sharma et al., 1990; Schoppen et al., 2004).

Of particular importance is the study of Stein, Thiery and Stein (2002) aimed at investigating the possible beneficial effects of consuming a carbonated mineral water, rich in sodium, bicarbonate and chloride, on lipoprotein metabolism and determining whether the consumption of such water affects the indicators of Endothelial Dysfunction (ED) such as levels of the adhesion molecules, soluble intercellular cell adhesion molecule-1 (Siam-1) and soluble Vascular Adhesion Molecule-1 (sVCAM-1). ED plays a central role in atherosclerosis (Stein, Thiery and Stein, 2002). This study was conducted on post-menopausal women, who have a more heterogeneous lipid profile, higher levels of adhesion molecules and a greater risk of CVD compared with pre-menopausal women. It was observed that the consumption of 1litre  $\text{day}^{-1}$  of this sodium-rich carbonated water over a 2-month period reduces several CVD risk indexes. Diet may delay the appearance of risk factors for chronic and CVD, especially in post-menopausal women (Schoppen et al., 2003) and, as an essential component of the diet, water intake must be considered. In addition, the subjects presented a marked decrease in fasting serum glucose concentration. This reduction indicates the relationship between lipid metabolism and glucose, suggesting that consumption of the carbonated sodium-rich water studied can play a beneficial role in preventing CVD and the metabolic syndrome (Cezanne et al., 1993).

Some investigations have focused mainly on such ions as magnesium (Rubenowitz, Axelsson and Rylander, 1998; Kiss, Forster and Dongo, 2004) and calcium, and less information concerning the possible roles of bicarbonate, fluoride, and sodium in lipid metabolism is available. Sharma et al. (1990) examined the effects of sodium intake on plasma lipids in healthy subjects. Over a 2-week period, a low-salt diet (20 mmol Na per day) increased the total cholesterol levels by 6% and LDL levels by 9.8%, compared with those of the subjects who consumed a high-salt diet (220 mmol Na per day). Weder and Egan (1991) suggested that more attention should be paid to a potential adverse effect of dietary salt restriction on cardiovascular risk. According to these data, a salt-restriction period may induce higher total cholesterol levels. Increasing salt intake could lower the total cholesterol and LDL-cholesterol levels. Schoppen et al. (2004) presented a study where the majority of the participants consumed a low-salt diet (with a low sodium intake) and were supplied by the carbonated water. Reductions in total cholesterol and LDL-cholesterol levels were also observed. In this study, the high-mineral carbonated water used was alkaline with an osmotic effect (Schoppen et al., 2004), which may affect the absorption and/or excretion of cholesterol. Serum levels of total cholesterol and LDL-cholesterol are regulated by: the intestinal absorption of cholesterol, the conversion rate of cholesterol into bile acids and the bile acid pool. Increasing faecal bile acid loss and reducing the size of the bile acid pool stimulates the synthesis of bile acids from serum cholesterol via 7- $\alpha$ -hydroxylase, which consequently decreases the level of serum cholesterol. Ingestion of the carbonated mineral water probably enhances the transformation of cholesterol into bile acids and their secretion; this is consistent with the

increased faecal bile acid excretion and reduced gall bladder volume reported in hypercholesterolaemic subjects who consumed another salt-rich mineral water (Capurso et al., 1999).

In another study performed on experimental animals (Cantalamesa and Nasuti, 2003), it has been demonstrated that the hydropinic treatment with 'San Giovanni' (Italy) calcic and magnesian-sulphate-sulphurous spring mineral water reduces overall cholesterolaemia and LDL levels by interfering with the entero-hepatic cycle of the bile acids that, not being re-absorbed, are eliminated with the faeces. Thus, it can be suggested that crenotherapy with calcic and magnesian-sulphate-sulphurous spring mineral water could be considered as an alternative treatment to lipid-lowering drugs.

In our previous studies (Albertini et al., 1996, 1999a, 1999b) performed both on animals and human healthy subjects, we observed beneficial effects of sulphurous mineral water thermal therapy. These beneficial effects concerned its anti-oxidant properties on liver and erythrocyte metabolism, evaluated by biochemical oxidative enzymatic markers (Albertini et al., 1996; Scheidleder, Holzer and Marktl, 2000). Our studies (Albertini et al., 1996, 1999b, 2001), support the hypothesis that the ingestion of sulphurous mineral water can interfere with Glyceraldehyde-3-Phosphate Dehydrogenase (GAPDH) activity by limiting of the availability of cellular Nicotinamide Adenine Dinucleotide [ $\text{NAD}^+(\text{H})$ ]. However, the presence of unstable haemoglobin was found in our treatment, and probably it is related to erythrocyte GAPDH, Glucose-6-Phosphate Dehydrogenase (G6PDH) enzyme activity inhibition (Colussi et al., 2000). In fact, these latter are both involved in the methaemoglobin-reducing reaction as a biochemical carrier between NADH, Nicotinamide Adenine Dinucleotide Phosphate (NADPH) and methaemoglobin, explaining the increased methaemoglobin concentration observed and the possible impairment in methaemoglobin reducing system: a decreased presence of NADH and NADPH. The fact that after 1 week of treatment most of the volunteers reported that some adverse events (asthenia, cephalgia) can be the consequence of the biochemical effects observed: decreased GAPDH and G6PDH activity and increased methaemoglobin concentration (Albertini et al., 1999b). These data can thus give supplemental information on the adverse events and explain the clinical symptoms observed. Furthermore, we suggest to use GAPDH enzyme assay to monitor the risk to undergo adverse events.

## **6 Conclusion**

Mineral water drinking treatments consist of administering mineral water, especially oligomineral and bicarbonate water, to treat a large number of disorders including problems connected with the liver, intestine and digestive system. Here the term mineral water refers to the water containing significant levels of dissolved mineral salts that have been absorbed from the soil and terrain with which the water comes into contact over the course of its journey. These mineral salts imbue the water with curative properties (something that cannot be said, however, of the ordinary mineral tap waters). The therapeutic use of water as a drink, in accordance with the uses prescribed subsequent to a medical visit, is one of the most important forms of thermal treatment. This is because it encourages and stimulates the metabolic balance and the functional regeneration of the body, which is all too often run down by the stress of modern living. Thermal waters have been used for hydrotherapeutic purposes in the Mediterranean region since ancient

times, as can be seen from archaeological findings, literary and scientific writings. These treatments have, for the most part, been left unaltered over 24 centuries since the age of the ancient Greek philosophers, through various historical periods. As time went by, the use of the experimental methods led to an innovative approach in using thermal waters for therapeutic purposes and new treatments are now being introduced. It is obvious that Italy's richness in thermal and mineral waters, combined with the mildness of the climate and the beauty of the scenery, have made it a favourite venue for 'health care tourism'. Since the past century, hotels with extensive facilities have grown up around spas, which have established international reputations. Abano, Salsomaggiore, Levico, Chianciano, Montecatini, Fiuggi and Ischia are just a few of the names among the many which are known throughout the world and which attract millions of visitors every year. The question here is to review, on the basis of scientific evidences, the health and the biochemical effect of mineral waters. There is no doubt that, as reported from the majority of the examined literature on the matter, mineral water drinking therapy has beneficial health effect on humans and a few biochemical studies to support these findings have also been published; however, the biochemical reports are too scanty to furnish any scientific theory to address the health impact of thermal hydropinia, and a need for more rigorous scientifically oriented studies is definitely evidenced. In addition, the fact that some adverse health effects are also observed during mineral water drinking therapy cannot be underestimated and should be further investigated by biochemical approach.

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