

## Original Article

# Hydrotherapy, balneotherapy, and spa treatment in pain management

Tamás Bender<sup>1</sup>, Zeki Karagülle<sup>2</sup>, Géza P. Bálint<sup>3</sup>, Christoph Gutenbrunner<sup>4</sup>, Péter V. Bálint<sup>3</sup> and Shaul Sukenik<sup>5</sup>

(1); Polyclinic of Brother of St. John of God Hospitals, 7 Árpád fejedelem St, Budapest, Hungary 1025

(2); Department of Medical Ecology and Hydroclimatology, Medical Faculty, Istanbul University, Istanbul, Turkey

(3); National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

(4); Institute for Balneology and Medical Climatology in the Clinic for Physical Medicine and Rehabilitation, Hannover Medical School, Hannover, Germany

(5); Soroka University Hospital, Faculty of Health Sciences, Ben Gurion University, Beer Sheva, Israel

✉; **Tamás Bender Email:** [bender@mail.datanet.hu](mailto:bender@mail.datanet.hu) **Phone:** +36-1-3360266  
**Fax:** +36-1-3360266

**Received:** 23 December 2003 **Accepted:** 3 May 2004 **Published online:** 15 July 2004

**Abstract:** The use of water for medical treatment is probably as old as mankind. Until the middle of the last century, spa treatment, including hydrotherapy and balneotherapy, remained popular but went into decline especially in the Anglo-Saxon world with the development of effective analgesics. However, no analgesic, regardless of its potency, is capable of eliminating pain, and reports of life-threatening adverse reactions to the use of these drugs led to renewed interest in spa therapy. Because of methodologic difficulties and lack of research funding, the effects of 'water treatments' in the relief of pain have rarely been subjected to rigorous assessment by randomised, controlled trials. It is our opinion that the three therapeutic modalities must be considered separately, and this was done in the present paper. In addition, we review the research on the mechanism of action and cost effectiveness of such treatments and examine what research might be useful in the future.

**Keywords** Balneotherapy-Hydrotherapy-Water treatment

---

## Introduction

The use of water for medical treatment is probably as old as mankind. Until the middle of the last century, spa treatment, including hydrotherapy and balneotherapy, remained popular; but this went into decline, especially in the Anglo-Saxon world, with the development of effective analgesics. However, no analgesic, regardless of potency, is capable of eliminating pain, and reports of life-threatening adverse reactions to the use of these drugs led to a renewal of interest in spa therapy.

Confusion persists regarding hydrotherapy and balneotherapy. The former employs simply water, while the latter uses natural thermal mineral water. Spa therapy employs a number of different treatment modalities, including hydrotherapy and balneotherapy, and creates a special therapeutic <sup>1</sup> atmosphere <sup>2</sup> of its own through the change in environment and lifestyle.

Because of methodologic difficulties and lack of research funding, the effects of <sup>3</sup>water treatments <sup>4</sup> in pain relief have rarely been subjected to rigorous assessment by randomised, controlled trials. However, the few which have been done indicate that pain can be relieved in inflammatory and noninflammatory rheumatic diseases, chronic low back pain, and fibromyalgia. Pain relief in several trials has lasted 3 to 9 months.

The placebo effect of spa therapy certainly plays an important role. The mechanisms of action of water treatments—especially the special effects claimed for natural mineral waters—remain largely unknown. Human life has certainly been full of physical and psychologic pain ever since Adam and Eve were driven from the Garden of Eden [1]. Pleasure, it is well known, reduces pain [2]. In postindustrial societies, chronic pain syndromes appear to be on the ascendant, owing to <sup>5</sup>unpleasant <sup>6</sup> psychologic and mechanical factors [3, 4].

After a short historical review, this study discusses evidence of the pain-relieving effects of hydrotherapy, balneotherapy, and spa treatment. It is important to appreciate the difference between these three modalities. Hydrotherapy consists of the use of ordinary water. Balneotherapy on the other hand employs natural thermal mineral water, whether at a spa or not. Spa treatment consists of a <sup>7</sup>cocktail <sup>8</sup> of different treatments including hydrotherapy, balneotherapy, and <sup>9</sup>holiday atmosphere <sup>10</sup>. These terms have often been used interchangeably, even in the best systematic reviews [5, 6, 7]. It is our opinion that the three therapeutic modalities must be considered separately [8, 9, 10], and this is done in the present paper. In addition, we review research on the mechanisms of action and cost effectiveness of such treatments, and we consider what research might be useful in the future.

---

## Taking the waters

The use of water treatments in spas in the ancient world has been admirably reviewed by Jackson [11]. Large quantities of warm water for bathing and immersion were rarely available in ancient times and, not surprisingly, were often considered a donation from gods. The concept of mineral waters' divinity was supported by their sulphurous smell, different feeling to the skin, and diarrhoea when taken orally.

Water therapy was an integral part of the therapeutic armamentarium of Aesculapius, Hippocrates, Galen, and Celsus [11]. Patients admitted to the healing temples of Aesculapius first washed in a large pool before being admitted to the 'wards'. Floating on water and immersion were found useful in relaxing of muscles [12, 13]. Roman authors recognised several classes of thermal and medicinal waters not dissimilar to those of today: sulphur, alum, bitumen, alkaline, and acid [11]. A host of different disorders was deemed appropriate for treatment, some of which are dealt with in modern spas, especially pain arising from musculoskeletal disorders.

Roman baths and spas were centres not only for cleansing, exercising, and medical treatment but also for relaxation and meeting friends and colleagues. This Roman heritage persisted not only in Britain and Europe but also in the United States of America until the first half of the last century [14]. Nowadays, when warm water is readily obtained from taps in every household, the question arises of whether warm mineral water is of any importance. Does hydrotherapy using warm tap water offer any benefits that balneotherapy with warm mineral water does not? Does the full cocktail of spa therapy have any advantage over hydrotherapy or balneotherapy?

---

## Hydrotherapy

According to the law of Archimedes, some exercises in water are made easier, while others such as walking are more difficult [15]. Pain may be relieved due to the effects of pressure and temperature on nerve endings [16] and as a result of muscle relaxation [12]. Recently, Geytenbeek [17] reviewed more than 500 papers, 34 of which fulfilled criteria for further analysis. Eighteen of them assessed pain relief, ten of which provided moderate- to high-quality evidence. Four trials were on patients with osteoarthritis of the hip, two on rheumatoid patients, two on patients with low back pain, and one each on patients with ankylosing spondylitis and fibromyalgia. In all but one trial, the pain was significantly reduced compared to control groups. The trials suffered by not being double-blind, since the patients receiving hydrotherapy exercised in pools while controls exercised on dry land. In one of the trials, the control group sat in the pool but did not exercise, and it showed no improvement. Water immersion for 60 min reduced proximal interphalangeal joint circumference in patients with rheumatoid arthritis as well as controls [18, 19].

Hall et al. found that a seated immersion group had no benefits over a land-exercising, relaxation-treated group, confirming their hypothesis that the exercise component of hydrotherapy is of central importance in reducing pain and joint tenderness [20].

---

## Balneotherapy

Balneotherapy uses natural thermal mineral waters. The definitions of these waters is based on the sum of the cations of Na, K, Ca, and Mg and the anions of SO<sub>4</sub>, Cl, and HCO<sub>3</sub> exceeding 1 g/l [9, 21]. The amounts of NH<sub>3</sub>, NO, and NO<sub>2</sub> must be negligible, and the waters must be bacteria-free. Some elements, such as iodine, require contents of 1 mg/l or more. It was presumed that most mineral ingredients would be absorbed through the skin, which is an active immune organ and may play an important role in the mechanism, but to date this has not been confirmed [22].

The adjective ‘thermal’ requires that the natural spring or well water is 20°C or higher. Balneotherapy alone is difficult to study, since it is usually part of total spa therapy. However, it has been possible to compare the effects of balneotherapy with those of warm tap water in double-blind trials in osteoarthritis of the knees [23, 24] and in rheumatoid arthritis [25]. In other controlled but not double-blind trials, ambulatory balneotherapy was tried in local patients for chronic low back pain [26, 27, 28] and fibromyalgia [29]. In this way, the effect of a ‘spa atmosphere’ was excluded.

---

## Spa therapy

The word ‘spa’ comes from the name of a Belgian town where a thermal spring was discovered in the fourteenth century [14]. The problem in assessing the value of spa therapy is its complexity. Patients receive treatment not only with thermal mineral water but also other modalities such as massage, electrotherapy, and exercise. Spa treatment usually consists of a health holiday lasting some 2–3 weeks. The placebo effect is therefore considerable [8, 30, 31], and if it ‘pleases’, the pain is reduced, and the patient’s general well-being improves, then arguably it is of value irrespective of trial results from randomised, controlled trials. Such trials of balneotherapy at spas have indicated significant improvements in osteoarthritis [32, 33], fibromyalgia [34, 35, 36], chronic low back pain [27, 28, 32], psoriatic arthritis [37], ankylosing spondylitis [38], and rheumatoid arthritis [39, 40, 41, 42]. The authors in these studies were fully aware of the difficulties in defining control groups, but overall it appears that patients treated with balneotherapy did have advantages over controls, especially in the long term. In one trial of patients with rheumatoid arthritis, balneotherapy proved somewhat inferior to cyclosporin therapy after 2 months. The satisfaction of both patients (93.9% vs 40%) and doctors (90% vs 44%) favoured spa treatment [42]. Pleasure seems to indicate overwhelming objective improvement! In none of the studies was balneotherapy at spas associated with any serious side effects.

---

## Mechanisms of action

### Hydrotherapy

Buoyancy, immersion, resistance, and temperature all play important roles. According to the gate theory, the pain relief may be due to the pressure and temperature of water on the skin [16]. Water immersion induced an increase in methionine-enkephalin plasma levels and, conversely, suppressed plasma  $\beta$ -endorphin, corticotropin, and prolactin levels [43]. Muscle relaxation [12, 13] and reduced joint swelling [18, 19, 20] may also play a role. Significant improvements in mood and tension may contribute to the results [20]. Reilly and Bird found that group therapy in a community swimming pool was more effective than individual treatment in the pool of a hospital. This was probably due to concentrating on health improvement and well being, instead of disease, and to encouraging social interaction [44].

### Balneotherapy

One might expect that minerals are absorbed through the skin with balneotherapy or application of mud packs, but there is little evidence of this [19]. Shani et al. [45] in Israel noted, however, increased serum concentrations of bromine, rubidium, calcium, and zinc in psoriatic patients after bathing in the Dead Sea. Whether these chemicals have any biologic effect is not known. There are data, however, that sulphur can be absorbed through the skin and may have an analgesic effect [46, 47, 48]. Gutenbrunner et al. found that sulphur baths reduced pressure-induced, temperature-induced, and spontaneous pain in both normal subjects and patients with rheumatoid arthritis [48]. In Freund's adjuvant-induced chronic arthritis of rats, swelling was reduced by sulphurous baths better than in tap water, although the difference did not reach the level of significance [49]. Radon also penetrates the skin and even can be inhaled during radon bath treatment. This substance might have anti-inflammatory and analgesic effects [50]. It has been reported that plasma levels of  $\beta$ -endorphin are raised after 2 hours of bathing in mineral water at 39 C [51] and that mud packs reduce serum concentrations of PGE<sub>2</sub> and LTB<sub>4</sub> [52].

### Spa treatment

Perhaps the most important aspect of spa therapy is the psychologic effect of removal from the stress of home and work. This effect has long been recognised in patients after admission to hospital, and in rheumatoid arthritis the benefit of hospitalisation in terms of pain relief far exceeds that of antirheumatic drugs, with the exception of large doses of corticosteroids [53].

Spa therapy undoubtedly has a strong placebo effect. It has been noted that pain is relieved more in patients admitted in October and November than in April and June [54]. This may just reflect more severe pain in the former, with greater delta values of response [55].

A number of Anglo-Saxon authors [30, 31, 56, 57] regard spa resorts as excellent places for rehabilitation encouraging the self-efficiency and self-advocacy of the patients. Those receiving spa therapy experienced not only reduced pain and improved function but also experienced greater physical and mental quality of life and less anxiety and depression [28, 39]. The mechanism of action of these effects may be adaptive modifications in regulatory systems, especially of autonomous functions, and behavioural changes [21, 58].

---

## Cost benefit of spa treatment

The question arises of whether the benefits of spa treatment outweigh the costs. Allard et al. [59] showed that health care costs increased in patients who had spa treatment. In the well-designed study of van Tubergen et al. [60], spa treatment of Dutch ankylosing spondylitis patients was cost-effective even when carried out in Austria.

---

## Conclusions

It is our belief that hydrotherapy, balneotherapy, and spa resort treatment should be considered separate entities, similar to the classification of simple, nonsteroidal anti-inflammatory, and opioid analgesics or to different classes of antidepressants. Further, properly designed, controlled, clinical trials are required in various arthritic and rheumatic diseases and other conditions which continue to be treated in spas. There are major difficulties in conducting such studies, especially making them double-blind and obtaining appropriate placebo controls. This applies particularly to the 'cocktail' of spa treatments. However, in studies of nonsteroidal antirheumatic analgesics in patients with rheumatoid arthritis, the fact that patients were not double-blinded did not invalidate the result [61]. The important decision is to pose clear questions and answer them as best one can. Thus, the long-term effects of balneotherapy are encouraging and justified on a cost-benefit basis. The physiologic effects of the various therapeutic modalities used in spas require further study. Financial support for such studies and the necessary therapeutic trials remains a problem.

---

## References:

1. Genesis 14–24, Chap. 3. The New American Bible. Fireside, Wichita
2. Stevens MJ, Heise RA, Pfof KS (1989) Consumption of attention versus affect elicited by cognition in modifying acute pain. *Psychol Rep* 64:284–286 [ChemPort](#) [PubMed](#)
3. Andersson HI, Ejlertsson G, Leden I, Rosenberg C (1993) Chronic pain in a geographically defined general population: studies of differences in age, gender, social class and pain localisation. *Clin J Pain* 9:174–182 [ChemPort](#) [PubMed](#)
4. Macfarlane GJ (1999) Generalized pain, fibromyalgia and regional pain: an epidemiological view. *Baillieres Best Pract Res Clin Rheumatol* 13:403–414 [crossref](#) [ChemPort](#) [PubMed](#)
5. van Tubergen A, van der Linden S (2002) A brief history of spa therapy. *Ann Rheum Dis* 61:273–275 [crossref](#) [PubMed](#)
6. Verhagen AP, de Vet HC, de Bie RA, Kessels AGA, Boers M, Knipschild PG (1997) Taking baths: the efficacy of balneotherapy in patients with arthritis. A Systematic review. *J Rheumatol* 24:1964–1971 [ChemPort](#) [PubMed](#)
7. Verhagen AP, de Vet HC, de Bie RA, Kessels AG, Boers M, Knipschild PG (2000) Balneotherapy for rheumatoid arthritis and osteoarthritis. *Cochrane Database Syst Rev* 2:CD000518 [PubMed](#)
8. Balint G, Bender T, Szabó E (1993) Spa treatment in arthritis. *J Rheumatol* 20:1623–1625 [ChemPort](#)
9. Sukenik S, Flusser D, Abu-Shakra M (1999) The role of spa therapy in various rheumatic diseases. *Rheum Dis Clin North Am* 25:883–897 [ChemPort](#) [PubMed](#)
10. Bender T, Balint PV, Balint GP (2002) A brief history of spa therapy. *Ann Rheum Dis*:61:949
11. Jackson R (1990) Waters and spas in the classical world. *Med Hist Suppl* 10:1–13 [PubMed](#)
12. Kjellgren A, Sundequist U, Norlander T, Archer T (2001) Effects of flotation-REST on muscle tension pain. *Pain Res Manag* 6:181–189 [PubMed](#)
13. Garrett G (1997) Hydrotherapeutic applications in arthritis rehabilitation. In: Becker BE, Cole AJ (eds) *Comprehensive aquatic therapy*. First edn. Butterworth-Heinemann, Boston, pp 103–122
14. De Vierville JP (1997) Aquatic rehabilitation: an historical perspective. In: Becker BE, Cole AJ (eds) *Comprehensive aquatic therapy*. First edn. Butterworth-Heinemann, Boston, pp 1–16
15. Becker BE (1997) Biophysiological aspects of hydrotherapy. In Becker BE, Cole AJ (eds) *Comprehensive aquatic therapy*. First edn. Butterworth-Heinemann, Boston, pp 17–48
16. Melzack R, Wall PD (1965) Pain mechanism: a new theory. *Science* 150:971–979 [ChemPort](#) [PubMed](#)



17. Geytenbeek J (2002) Evidence for effective hydrotherapy *Physiotherapy* 88:514–529
18. Grahame R, Hunt JN, Kitchen S, Gabell A (1978) The diuretic and natriuretic effect of water immersion—a possible rationale for balneotherapy. *Ann Rheum Dis* 37:567
19. O'Hare JP, Heywood A, Dodds P, Corral RJM, Dieppe P (1984) Water immersion in rheumatoid arthritis. *Br J Rheumatol* 23:117–118
20. Hall J, Skevington SM, Maddison PJ, Chapman K (1996) A randomized and controlled trial of hydrotherapy in rheumatoid arthritis. *Arthritis Care Res* 9:206–215 [ChemPort](#) [PubMed](#)
21. Gutenbrunner C, Hildebrandt G (1998) Textbook of balneology and medical climatology [German]. Springer, Berlin Heidelberg New York Tokyo
22. O'Hare JP, Heywood A, Summerhayes C et al (1985) Observations on the effect of immersion in Bath spa water. *Br Med J (Clin Res Ed)* 291:1747–1751
23. Szucs L, Ratko I, Lesko T, Szoor I, Genti G, Balint G (1989) Double-blind trial on the effectiveness of the Puspokladany thermal water on arthrosis of the knee-joints. *J R Soc Health* 109:7–9 [ChemPort](#) [PubMed](#)
24. Kovacs I, Bender T (2002) The therapeutic effects of Cserkeszolo thermal water in osteoarthritis of the knee: a double blind, controlled, follow-up study. *Rheumatol Int* 21:218–221 [SpringerLink](#) [PubMed](#)
25. Sukenik S, Neumann L, Buskila D, Kleiner-Baumgarten A, Zimlichman S, Horowitz J (1990) Dead Sea bath salts for the treatment of rheumatoid arthritis. *Clin Exp Rheumatol* 8:353–357 [ChemPort](#) [PubMed](#)
26. Konrad K, Tatrai T, Hunka A, Vereckei E, Korondi I (1992) Controlled trial of balneotherapy in treatment of low back pain. *Ann Rheum Dis* 51:820–822 [ChemPort](#) [PubMed](#)
27. Guillemin F, Constant F, Collin JF, Boulange M (1994) Short and long-term effect of spa therapy in chronic low back pain. *Br J Rheumatol* 33:148–151 [ChemPort](#) [PubMed](#)
28. Constant F, Collin JF, Guillemin F, Boulange (1995) Effectiveness of spa therapy in chronic low back pain: a randomized clinical trial. *J Rheumatol* 22:1315–1320 [ChemPort](#) [PubMed](#)
29. Evcik D, Kızılay B, Gökçen E (2002) The effects of balneotherapy on fibromyalgia patients. *Rheumatol Int* 22:56–59 [SpringerLink](#) [PubMed](#)
30. Fam AG (1991) Spa treatment in arthritis: a rheumatologist's view. *J Rheumatol* 18:1775–1777 [ChemPort](#) [PubMed](#)
31. Bell MJ (1991) Spa therapy in arthritis: a trialist's view. *J Rheumatol* 18:1778–1779 [ChemPort](#) [PubMed](#)
32. Nguyen M, Revel M, Dougados M (1997) Prolonged effects of 3 week therapy in a spa resort on lumbar spine, knee and hip osteoarthritis: follow-up after 6 months. A randomised controlled trial. *Br J Rheumatol* 36:77–81 [crossref](#) [ChemPort](#) [PubMed](#)
33. Wigler I, Elkayam O, Paran D, Yaron M (1995) Spa therapy for gonarthrosis: a prospective study. *Rheumatol Int* 15:65–68 [ChemPort](#) [PubMed](#)



34. Yurtkuran M, Çelikta M (1996) A randomized, controlled trial of balneotherapy in the treatment of patients with primary fibromyalgia. *Phys Rehab Kur Med* 6:109–112
35. Neumann L, Sukenik S, Bolotin A et al (2001) The effect of balneotherapy at the Dead Sea on the quality of life of patients with fibromyalgia syndrome. *Clin Rheumatol* 20:15–19 [\[SpringerLink\]](#)  
[ChemPort](#) [PubMed](#)
36. Buskila D, Abu-Shakra M, Neumann L et al (2001) Balneotherapy for fibromyalgia at the Dead Sea. *Rheumatol Int* 20:105–108 [\[SpringerLink\]](#)  
[ChemPort](#) [PubMed](#)
37. Elkayam O, Ophir J, Brener S et al (2000) Immediate and delayed effects of treatment at the Dead Sea in patients with psoriatic arthritis. *Rheumatol Int* 19:77–82 [\[SpringerLink\]](#) [ChemPort](#) [PubMed](#)
38. van Tubergen A, Landewe R, van der Heijde D et al (2001) Combined spa-exercise therapy is effective in patients with ankylosing spondylitis: a randomized controlled trial. *Arthritis Rheum* 45:430–438 [crossref](#)  
[PubMed](#)
39. Franke A, Reiner L, Pratzel HG, Franke T, Resch KL (2000) Long-term efficacy of radon spa therapy in rheumatoid arthritis--a randomized, sham-controlled study and follow-up. *Rheumatology (Oxford)* 39:894–902
40. Sukenik S, Buskila D, Neumann L, Kleiner-Baumgarten A, Zimlichman S, Horowitz J (1990) Sulphur bath and mud pack treatment for rheumatoid arthritis at the Dead Sea area. *Ann Rheum Dis* 49:99–102 [ChemPort](#)  
[PubMed](#)
41. Elkayam O, Wigler I, Tishler M et al (1991) Effect of spa therapy in Tiberias on patients with rheumatoid arthritis and osteoarthritis. *J Rheumatol* 18:1799–1803 [ChemPort](#) [PubMed](#)
42. Yurtkuran M, Yurtkuran MA, Dilek K et al (1999) A randomised controlled study of balneotherapy in patients with rheumatoid arthritis. *Phys Rehab Kur Med* 9:92–96
43. Coruzzi P, Ravanetti C, Musiari L, Biggi A, Vescovi PP, Novarini A (1988) Circulating opioid peptides during water immersion in normal man. *Clin Sci (Lond)* 74:133–136
44. Reilly KA, Bird HA (2001) Prophylactic hydrotherapy. *Rheumatology (Oxford)* 40:4–6
45. Shani J, Barak S, Levi D et al (1985) Skin penetration of minerals in psoriatics and guinea-pigs bathing in hypertonic salt solutions. *Pharmacol Res Commun* 17:501–512 [ChemPort](#) [PubMed](#)
46. Andrejew SV, Selenskaja VS (1991) Das Verhalten des in den Körper aus dem Sulfidbad eindringenden Schwefels. In: Pratzel HG, Bühring M, Evers A (eds) *Schwefel in der Medizin*. Demeter, Gräfelfing, pp 35–41
47. Pratzel HG, Aigner UM, Weinert D, Limbach B (1992) .Zur analgetischen Wirksamkeit eines Schwefelmoorbades bei weichteilrheumatischen Beschwerden. Eine randomisierte Doppelblindstudie. *Phys Rehab Kur Med* 2:92–97

48. Gutenbrunner C, Kopetzki K, Neues-Lahusen M, Gehrke A (1999) Wirkungen natürlicher thermoindifferenten Schwefelbäder auf Hautdurchblutung und Schmerzempfindlichkeit bei Gesunden und Patienten mit chronischer Polyarthritis. *Akt Reumatol* 24:117–123
49. Karagülle MZ, Tütüncü ZN, Aslan O, Basak E, Mutlu A (1996) Effects of thermal sulphur bath cure on adjuvant arthritic rats. *Phys Rehab Kur Med* 6:53–57
50. Jöckel H (1997) Praktische Erfahrungen mit der Radontherapie. In: Pratzel HG, Deetjen P (eds) *Radon in der Kurortmedizin*. Geretsried:ISMH 84–91
51. Kappel M, Gyhrs A, Galbo H, Pedersen BK (1997) The response on glucoregulatory hormones of in vivo whole body hyperthermia. *Int.J Hyperthermia* 13:413–421 [ChemPort](#)
52. Bellometti S, Galzigna L (1998) Serum levels of a prostaglandin and a leukotriene after thermal mud pack therapy. *J Investig Med* 46:140–145 [ChemPort](#) [PubMed](#)
53. Lee P, Kennedy AC, Anderson J, Buchanan WW (1974) Benefits of hospitalization in rheumatoid arthritis. *Q J Med* 43:205–214 [ChemPort](#) [PubMed](#)
54. Strauss-Blasche G, Ekmekcioglu C, Leibetseder V, Melchart H, Marktl W (2002) Seasonal variation in effect of spa therapy on chronic pain. *Chronobiol Int* 19:483–495 [crossref](#) [PubMed](#)
55. Lee P, Webb J, Anderson J, Buchanan WW (1973) Method for assessing therapeutic potential of anti-inflammatory drugs in rheumatoid arthritis. *Br Med J* 2:685–688 [ChemPort](#) [PubMed](#)
56. Helliwell PS (1989) An appraisal of medicinal spa therapy for rheumatological disorders. *J R Soc Health* 109:3–7 [ChemPort](#) [PubMed](#)
57. Kersly G (1989) The history of spas. *J R Soc Health* 109:2–3
58. Hildebrandt G, Gutenbrunner C (1996) Über adaptive Normalisierung. *Forsch Komplementärmed* 3:236–243
59. Allard P, Deligne J, Van Bockstael V, Duquesnoy B (1998) Is spa therapy cost-effective in rheumatic disorders? *Rev Rhum Engl Ed* 65:173–180 [ChemPort](#) [PubMed](#)
60. van Tubergen A, Boonen A, Landewe R et al (2002) Cost effectiveness of combined spa-exercise therapy in ankylosing spondylitis: a randomized controlled trial. *Arthritis Rheum* 47:459–467 [crossref](#) [PubMed](#)
61. Huskisson EC, Scott J (1976) How double-blind is double blind? And does it matter? *Br J Clin Pharmacol* 3:331–332 [ChemPort](#) [PubMed](#)