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# Multitarget Regulation in Modern Bioregulatory Medicines

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In the history of modern medicine, we have been experiencing many paradigm shifts driven by advancements in scientific knowledge followed by development of new tools to finally demonstrate validity of the underlying hypotheses—the scientific evidence.

One of the shifts painstakingly taking place at the moment is the shift back from reductionist to complex thinking.

In the words of John Holland: “For the last 400 years science has advanced by reductionism. . . . The idea is that you could understand the world, all of nature, by examining smaller and smaller pieces of it. When assembled, the small pieces would explain the whole.”<sup>1</sup>

Biological systems, however, are complex with properties that cannot be explained by assembling all the pieces. They therefore pose a challenge for drug discovery and reductionist thinking, which is thought by some to have a detrimental effect on this process.<sup>2</sup>

Disease processes as well are difficult to reduce to a collection of linear events. Most malignancies are of multifactorial origin and consequently have multiple targets to be addressed when successful treatment is the goal. This also applies to the majority of diseases with immunological and inflammatory pathophysiology such as rheumatoid arthritis or possibly chronic osteoarthritis<sup>3</sup> as well as chronic diseases with hypothesized interaction between more than one organ system such as irritable bowel syndrome and inflammatory bowel disease.<sup>4</sup>

Drug combinations offer a promising strategy to address this issue, as they are generally more specific to cellular contexts than are single agents; however, the concern is that therapeutic synergy will be accompanied by synergistic side effects.<sup>5</sup> Multicomponent medications are medications that go beyond the common model of “one molecule—one target.” More specifically, a multicomponent medication is a formula consisting of more than one active ingredient that can be either molecules or herbal extracts, depending on the complexity of preparation. Examples include any herbal medication (eg, any herbal traditional Chinese medicine preparation) or Sudafed Cough&Cold. Plant materials, through their multicomponent nature and therefore combination chemistry, may be especially

well suited for such a multitarget approach.<sup>6</sup> The use of ultra low\* concentrations of substances offers another avenue for the delivery of nontoxic interventions with novel areas of application. This approach is a therapy pathway for both conventional and alternative medical therapies for reaching the right balance between clinical outcomes and side effects.<sup>7,11</sup>

Bioregulatory medicine is an emergent science concerning itself with complex bioregulatory networks, as well as using multicomponent medicines to manipulate networks and multiple organ systems rather than single targets.<sup>12</sup> In this supplement, some exemplified principles of bioregulatory medicine and its role in the multitarget approach are depicted and data from past and ongoing research are presented. To validate these concepts, however, high-quality research in this field is warranted. An interesting role may be played by bioinformatics, which lends itself to compute multiple networks and interactions.<sup>13,14</sup>

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\*The concentration of an ultra low dose differs from substance to substance. In the medications described in this supplement, it either is in the range of 1/10 of its physiological concentration in the case of a so-called metabolic factor, or in plants, it is often dictated by the toxicity of the plant and then included above the so-called first safe dilution. This is normally a 1:10 000 dilution of the plant.