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Can Chemical Drugs for Pain be Substituted by Natural Agents?

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ABSTRACT

It is well known that using chemical agents for pain have side effects and may be a problem. However, they are routinely used in many millions of cases. To the extent that they are over-the-counter, patients buy them at will. Therefore, the question arises whether it is possible to replace these drugs, at least in part, by natural substances without side effects. Three such agents are presented here (BCM95 full spectrum curcumin, Abka frankincense oil extract, Tila Taila black sesame oil), which have defined biochemical effects and interfere with the metabolism of pain perpetuation. The author had positive experience with a combination of these substances.

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Introduction

Pain is the alarm system of our body and therefore vital. Pain is very real and not imaginary, it warns us of a threat, a strong irritation or damage. The information from the tissue is analyzed in the spinal cord - the organism's switching point - and either slowed down, stopped or passed on. If the spinal cord classifies information as important, it passes it on to the brain for review. This is where pain originates. If such information transmissions take place frequently, a pathway develops that leads to permanent pain.

Frequent or persistent pain can interfere with life or even make it a misery. Pain is usually caused by changes in the pH value (local and/or general hyperacidity) and local and/or general silent inflammation. Many people take chemical painkillers for this, e.g. paracetamol, ibuprofen, aspirin, metamizole. When taken over a long period of time, they all not only have side effects, but also damage metabolic processes and organs such as the liver and kidneys. In addition, they increase hyperacidity.

If one looks at the instruction leaflets, one finds for example with the over-the-counter and very well-known means Paracetamol in the instructions for use the references: "do not take more than recommended (overdose warning), adults should not take Paracetamol longer than 10 days against pain". What happens after the 10th day? The organism uses pain as a warning "smoke detector". It wants the cause to be found and stopped. However, the detailed examinations necessary for this are only conditionally applicable in the routine of the millions of pain patients, moreover they are relatively expensive. If the symptoms include redness, heating, swelling, stiffness, the localization is simple, as in the case of activated arthrosis or arthritis. The non-steroidal anti-rheumatic drugs (NSAR), however, affect collagen and chondrocytes. Collagen is responsible for supple ligaments, tendons and skin. Chondrocytes are the only cells that can grow new cartilage tissue. Unfortunately, it must be stated that chronicity is the rule here. Although many patients and also doctors are aware of this, they are usually helpless in the face of the problem. If there were a natural alternative that could be easily used, these would probably be used first. We have set out on a search to offer such an alternative.

Unfortunately, it must be stated that chronicity is the rule here. There is an activation of molecules such as NF-kb, 5-LO, COX-2 and Delta 6-Desaturase in the damaged tissue. These keep the process going, like a siren wailing day and night. The body remains in the ongoing process of inflammation and pain. A significant process here is: a relative excess of omega-6 fatty acids activates delta-6 desaturase, arachidonic acid increases, cyclo-oxigenase 2 activates prostaglandin 2, 5-lipo-oxigenase activates leukotrienes, and a silent-inflammation process establishes itself. The body remains in the ongoing process of inflammation and pain. This self-perpetuating process must be interrupted.

NF-kb: It is of great importance for the regulation of the immune response, cell proliferation and cell death. Activation of NF-kb is considered critical for the development of inflammation [1,2]. Cyclooxygenase-2 (COX-2) is increased in transcription by NF-κB. NF-κB is thus an intracellular pathway through which TNF-α and IL-1β leads to increased formation of prostaglandin-E2 [3]. Similarly, interleukin-6 is enhanced transcribed by NF-Kb. Natural inhibitors of NF-κB include for example: Allicin, genistein, quercetin, curcumin, ginkgo, EGCG and tocotrienols. These substances are the active ingredients of garlic, soy, onion, turmeric, ginkgo, green tea and red palm oil [4]. Extracts of oregano, coffee, thyme, clove, and walnut have been shown to significantly reduce excessive NF-κB levels both in vitro and in animal studies [5].

5-LO: Arachidonate-5-lipoxygenase (5-LO) is the enzyme that oxidizes arachidonic acid in two steps to the eicosanoid leukotriene A4 [6].

COX-2: Cyclooxygenase-2, also prostaglandin synthase-2 (PGHS-2), is an enzyme that, like cyclooxygenase-1 (COX-1), oxidizes arachidonic acid to the eicosanoid prostaglandin H2 in two steps [7].

Delta 6 D: D6D is a desaturase enzyme, i.e. introduces a double bond in a specific position of long-chain fatty acids. Among them, it converts between various forms of Omega-3 and Omega-6 fatty acids. It is included in the transformation of Omega-6 fatty acids into arachidonic acid [8].

This has been known in Ayurvedic medicine for thousands of years. It is about dampening or blocking the inflammation-triggering enzymes and proteins that cause pain. A connection to other subsequent chronic diseases such as dementia or Alzheimer's cannot be denied.

Following are some substances that are able to influence and possibly clear up the problem
They are:
1. BCM-95 full spectrum curcumin
2. Abka frankincense extract
3. Tila Taila black sesame oil

Let's take a closer look at them.

BCM95 Full Spectrum Curcumin (BCM95®)
Patented Curcuma extract Curcugreen™, also known as BCM 95®, with particularly good bioavailability thanks to the incorporation of the original essential oils of the curcuma root. It banishes the inflammatory agents by inhibiting the cyclo-oxigenase 2 enzyme. Curcumin (derived from Arabic كركم kourkoum 'saffron') is an intense orange-yellow, naturally occurring chemical compound, from the diarylheptanoids group [9]. Two o-methoxyphenol residues are linked together via an unsaturated chain containing a 1,3-diketone unit [10]. The compound can be counted to the substance group of plant polyphenols. In 1815, Pierre-Joseph Pelletier and Heinrich August von Vogel reported their attempts to isolate the yellow dye from the turmeric plant, which they named curcumin [11]. August Vogel Jr. described a pure but non-crystalline preparation of curcumin in 1842 [12]. In crystalline form, curcumin was first isolated independently in 1870 by F W Daube and Y Iwanof-Gajewsky isolated and studied analytically [13].

Turmeric contains between 2 and 9% curcuminoids. Thereby, curcumin is the main component with more than 50 %, besides other through a keto-enol tautomerism, three possible distinguishable tautomers can be formulated for curcumin. These are, in addition to the diketo tautomer, two degenerate tautomers each of the keto-enol form and - with the inclusion of the phenolic hydroxyl group - of the dienol form compounds, such as demethoxycurcumin and bisdemethoxycurcumin [14,15]. Curcumin, as the main component of turmeric, finds use in traditional Indian and Chinese medicine. In Ayurvedic medicine, it is used to treat respiratory diseases, as well as liver diseases, anorexia, rheumatism, and sinusitis.

Because curcumin is poorly soluble in water, it is absorbed in the gastrointestinal tract at a very low rate [16]. Heating or dissolving it in oil increases the bioavailability of curcumin contained in food [17]. In addition, absorbed curcumin is metabolized very rapidly by the first-pass effect, especially in the kidneys, through sulfation and glucuronidation [18,19]. The resulting metabolites no longer have any medicinal activity and are excreted [20]. Curcumin's half-life is reported to be less than 5 minutes, and the degree of bioavailability is reported to be <1% = very low [21]. Compared to commercially available agents, curcumin would be extremely unstable as a potential agent in vivo and in vitro; pharmacokinetically, it might not reach the desired site of action in the body at all [21]. Several methods are being investigated to improve bioavailability. They are aimed at increasing the stability of curcuminoids as well as their solubility, for example by adding piperine, micellation, complexation with cyclodextrin, liposomal formulations or nanotechnological processes [16]. Some of these are also marketed in food supplements, for example black pepper extract (piperine) [22,23].

Here, the BfR (German Federal Institute for Risk Assessment) points out a potentially liver-damaging effect of combination preparations with piperine [24,25]. In addition, piperine can enhance the effect of drugs. The BVL (German Federal Office of Consumer Protection and Food Safety) and the BfArM (German Federal Institute for Drugs and Medical Devices) point out in a joint statement that with some of these processes a higher systemic availability of curcuminoids or their metabolites can be achieved [25]. These products may then be considered novel foods, since an increase in bioavailability can lead to different toxic effects than with curcumin alone [26].

Anti-inflammatory effect: two metareviews showed that supplementation of curcumin-containing products can reduce CRP levels, an inflammatory marker [27]. The product discussed here excludes the disadvantages mentioned, it has a high absorption, and a high bioavailability. It is only a problem of galenics that has been solved in the meantime by liposomal formulations or nanotechnological processes.

Abka Frankincense Oil Extract
Boswellia (frankincense) contains a compound called A 3-O-Acetyl-11-keto-β-boswellic acid (AKBA for short). ABKA blocks 2 enzymes (5-LOX and COX-2) which are responsible for joint inflammations. It inhibites both inflammatory agents [28].

According to a study published in 2012 by O Werz, boswellic acids reduce the inflammatory response by preventing the synthesis of prostaglandin E2. Prostaglandin E2 is responsible for mediating the immune response. Boswellic acids inhibit the enzyme responsible for its synthesis. Extracts from the resin of the species Boswellia papyrifera proved to be particularly effective - this species occurs predominantly in northeastern Africa (Ethiopia, Somalia, Eritrea) and on the Arabian Peninsula (Yemen, Oman) [29].

Tila Taila Black Sesame Oil
Sesame oil studies reported a reduction of oxidative stress markers and lipid peroxidation [30]. The oil inhibits the enzyme Delta-5 desaturase. Ayurveda: Til or sesame oil is considered best among all vegetable oils. For the medicinal purpose black til oil is mainly recommended. Good quality sesame oil can be used both internally and externally. It is one of the best oils that can be applied on «Vata Vyadhis» such as arthritis, rheumatism, joint swelling. Its internal use is great for improving health, iron level, controlling cholesterol, managing heart diseases, and improving strength [31].

Conclusion
One should conclude from the above data that there are definitely natural means to successfully treat pain, especially joint pain. The mentioned three substances are a selection from other possibilities, for example CBD from hemp should be mentioned here. If the substances are synergistically effective, as is the case here, it makes sense to combine them. However, since the amount of substance per capsule is limited and a minimum effective dose must be

achieved, it is difficult to go beyond three agents in synergy. Therefore, we report here a limitation to three effective substances.

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