Bacillus subtilis as a Homeopathic Remedy

A Well-Known Active Substance with New Accents

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Bacillus subtilis is well-known to the prescriber as part of the SANUM therapy in the form of the UTILIN preparations. In this form, *Bacillus subtilis* is employed as a whole cell preparation.

Immunological test models proved that different fractions of the bacterium possess various immunomodulatory capacities. In all test models, the isolated cell walls showed the strongest stimulating effects, whereby an increase of the phagocytosis was proved as the main effect (by the "smear test of granulocytes", the "chemiluminescence test of granulocytes" as well as by the "carbon-clearance test"). Especially impressive is the so-called "phagocytosis index" as compared to other active substances that are known as immunomodulators:

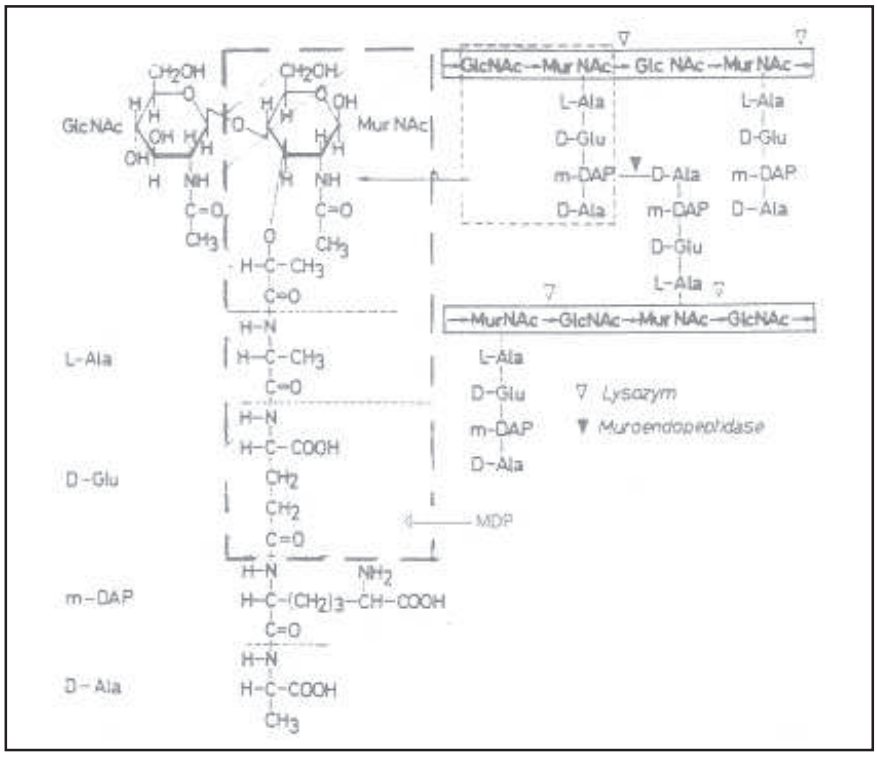

Fig.1: **Hypothetic structure of the murein from *Escherichia coli*.** The heteropolymeric chains consist of an alternating sequence of N-acetyl glucosamine (GlcNAc) and N-acetyl muramic acid (MurNAc) and are linked together in a peptidic way. On the left side of the picture the framed muropeptid MDP is represented as enlargement (from Schlegel: General Microbiology)

B. subtilis: 2.6 (highly effective)
B. cereus: 2.2 (well effective)
B. firmus: 1.9 (well effective)
Mycobacterium phlei: 2.7 (highly effective)
Extracts of Echinacea: 1.5-2.2 (well effective)

Due to the excellent test results with the isolated cell walls of *Bacillus subtilis*, SANUM-Kehlbeck introduced this active substance into the homeopathic therapy system. So far, *Bacillus subtilis* has only been known in homeopathy as a classical nosode. The term of the preparation for this new SANUM remedy is "*BACILLUS SUBTILIS* cell wall".

In the pharmacodynamic view, this preparation represents a decrease of the risk of an allergization, as the allergenic foreign protein components of the bacterial cell were largely separated.

During the registration procedure at the Federal Public Health Department in Germany, it could be proved that the cell wall preparation of 4X does not show any detectable acute intramuscular toxicity with rats, and also does not cause any local toxicity in the sense of an allergic contact dermatitis with guinea pigs. Thanks to these results, the therapeutical range can be interpreted as being very wide.

Results of Bioelectronic Medication Testing

The bioelectronic medication testing delivers the following findings: This preparation is a typical stimulating substance with a broad spectrum of intensive effects, whereby chronic diseases can easily be transferred into acute inflammatory stages. Its main effect aims at the respiratory tract; it also intensively stimulates the thyroid gland. Thus, chronic bronchitis would be a possible indication. Furthermore, a distinct effect upon the ovaries can be stated; here a possible indication could be chronic adnexitis. It launches attacks against tumors and is able to hollow them out from inside. There is also a clear blood cleansing function. Moreover, this medication has a strange "spurring" effect upon the nervous system, leading to a feeling of trepidation and heat waves. Thus, a very important indication would be the syndrome of menopause. The intestinal tract

and the whole metabolism will be rather slowed down resp. calmed down by this remedy. Its unspecific stimulating effect seems to be at least equal to the former UTILIN. Probably, it will even have an intensified effect.

BACILLUS SUBTILIS cell wall is disposable to the prescriber in the potency of 5X in the administration forms of capsules and suppositories.

Bacillus Subtilis Cell Walls - Catabolism in Macrophages

It is well known that bacteria, when administered to mammals, will stimulate unspecific mechanisms of the immunological system. The macrophages work in the front line of the battle between the foreign antigen and the immunological defense; their main task is the phagocytosis of foreign particles, the presentation of antigens and secretion of immunoregulatory messenger substances.

For about 20 years, the minimal chemical structure of bacterial material has been known, which is still able to exercise a so-called adjuvant function, i.e. to strengthen the immunization effect of additionally administered antigens. The pathologist *Freund* developed the adjuvant, that was called after him, in a water-in-oil emulsion. The chemical structure, which can replace *Freund*'s adjuvant, was called MDP (N-acetylmuramyl-L-alanyl-D-isoglutamine or muramyl-dipeptide), see also Picture 1.

Vermeulen & Gray (Infection and Immunity 45, 476-483, 1984) suspected that macrophages were the main point of attack for the MDP. In their article, they report about experiments of digesting isolated *Bacillus subtilis* cell walls with a cell culture from macrophages of a mice strain and of isolating messenger substances to strengthen the immunological system. The radioactively marked cell walls disappeared within a very short time out of the reaction medium, whereas radioactive degradation products of the cell walls were again excreted into the reaction medium.

The following connections have been proven as degradation products by chromatographic purification and isolation, next to other disaccharidepeptides:

Disaccharide-tetrapeptide
(GlcNAc-MurNAc-Ala-isoGln-Dap-Ala)

Disaccharide-tripeptide
(GlcNAc-MurNAc-Ala-isoGln-Dap)

Disaccharide-dipeptide
(G1cNAc-MurNAc-Ala-isoGln).

These glycopeptides can be explained as reaction products of the effect of the macrophage enzyme lysozyme as well as of other enzymes with a peptide-splitting effect, and all of them contain the structure of MDP (MurNAc-Ala-isoGln). The adjuvant activity of all three glycopeptides, is known. Therefore, as the result of these experiments, it can be maintained that through the effect of macrophages upon *Bacillus subtilis* cell walls glycopeptides are released that possess informational character in the immunological reaction process.

The authors emphasize that these results probably can be transferred to many other bacteria as the MDP-structural unit is also contained in their cell walls. However, they point out that the further effect of the cell wall fragments in the mechanisms of the immunological system would be decisive.

Bacillus Subtilis Cell Walls - New Information About the Mechanism of Effectiveness

In addition to the previous presentation of the new preparation *BACILLUS SUBTILIS* cell wall in homeopathy, an article by *Wehner & Gray* shows new aspects on *Bacillus subtilis*. (*Wehner & Gray*: In vitro stimulation of immune functions by lipids derived from macrophages exposed to bacterial peptidoglycan. *The Journal of Immunology* 147, 3595-3600, 1991).

In former tests, the authors demonstrated that a macrophage cell culture of a certain mice strain degrades the so-called peptidoglycan of bacteria within the macrophages into a lycophilic glycopeptide which contains muramine acid (= lactic acid ethers of glucosamine), glucosamine and alanine. The peptidoglycan, also called murein, represents the supporting skeleton of the bacterial cell wall and consists of chains of polymer of N-acetyl glucosamine and N-acetyl muramine acid. The latter is connected via the lactyle group with amino acids typical for bacteria (f.e. m-diaminopimeline acid). Two heteropolymeric chains are linked up at a time by amino acids with two amino groups through peptide bonds. Due to this

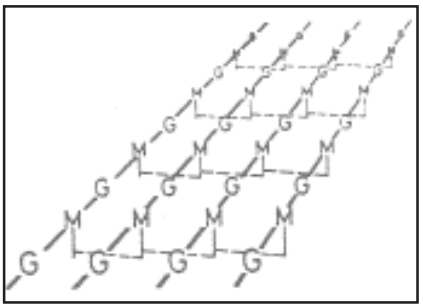

Fig. 2: **Detail of the Murein Net of a Gram-positive Bacterium** (*Staphylococcus aureus*). The tetrapeptide side chains of the n-acetyl muramine acid (M) are connected by pentaglycine chains. The murein net has several layers; it is not yet known whether the transverse netting is so regular as represented in the design, and in which way the individual layers are connected with each other (*Schlegel*).

cross-linkage, the supporting skeleton forms a sack-like gigantic molecule which therefore is also called murein sacculus (See also Fig. 2).

The authors were put before the question whether the lipophile glycopeptide, which results from degradation by macrophages, is responsible for the immunomodulatory properties of the bacterial cell wall. After feeding the macrophages of the cell culture with *Bacillus subtilis* cell walls for their endocytosis, an extract of lipids was obtained from the macrophages. This was fractionated into neutral lipids, glycolipids and phospholipids. The individual fractions were tested for mitogenic activity against mice splenocytes. This model is a detection system for the reaction and extent of the cellmediated immunological response to the presence of antigens. B- and T-lymphocytes are activated and differentiate themselves into effector cells and memory cells (blastogenesis).

As a result, the phospholipid fraction was determined as mitogen. This mitogenic property could not be derived alone from the macrophages when they had acted like phagocytes in eliminating other foreign particles. The authors point out that the phospholipid is an extremely mitogenic component of the macrophages after incubation with *Bacillus subtilis* cell walls. When this phospholipid was encapsulated in liposomes as supporting system and presented to peritoneal macrophages, these were stimulated to produce superoxide and to excrete interleucin-1. The latter acts as a so-called lymphokin, i.e. as a fortifying mediator in the blastogenesis of B- and T-lymphocytes. The secreted superoxide attributes to the microbiocidal and tumoricidal (cytatoxic) effect of activated macrophages.

The chemical identity of the isolated mitogenic phospholipid and the degradation product of *Bacillus subtilis* cell walls in macrophages must still be confirmed, but is most probable according to the author's report. By that it was demonstrated which ways the immunological response follows after the phagocytosis of *Bacillus subtilis* cell walls and the accompanying activation of the macrophages. Thus, the potent immunomodulatory effect of the bacterial preparation of *BACILLUS SUBTILIS* cell wall becomes once more clear.

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