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[**Ouabain - the optimal solution for the problem of myocardial infarction by a well tried herbal substance and a newfound hormone**](http://ouabain.twoday.net/stories/886276/)  **Extracts from the book “Ouabain - the possible victory over myocardial infarction“**  by Rolf-Jürgen Petry\* **(e-mail: strophanthin@web.de )**  (until now only in german language available: Die Lösung des Herzinfarkt-Problems durch Strophanthin"  with a preface from Prof. Hans Schaefer / Heidelberg)  A shorter form of this article is also published at [http://www.infarctcombat.org](http://www.infarctcombat.org/) (see "Heartnews", then position 3), the homepage of a clinic in Sao Paulo which had excellent results with ouabain in acute myocardial infarction (like other clinics and thousands of doctors).  **Content of this article**: --- The therapeutical results of oral and intravenous ouabain in angina pectoris and myocardial infarction (and other diseases)  --- The stimulation of the sodium pump: ouabain and digitalis behave oppositely at the cellular level  --- Ouabain affects several components: heart muscle cells, nerves, arteries, erythrocytes  --- The effect of ouabain in other diseases  --- The false dogma of the bad absorption of orally administered ouabain  --- The detection of ouabain as a new hormone and the criticism of its pretended role as a cause of hypertension  --- The solution of the problem is not wanted: several decades of prejudice and resistance  --- Some mostly unknown pathogenetic aspects of acute myocardial infarction  --- Something about the author and the book  --- 265 References  --- Imprint  Copyright (C) 2007 by Rolf-Jürgen Petry    **Introduction**  One of the most necessary things in the contemporary medicine is to call attention to a topic that seems to be unbelievable at first sight: Ouabain (in german: g-Strophanthin), an extraction of an african plant called “strophanthus gratus“, which since 1991 is discovered as an endogenous substance - a new hormone, prevents angina pectoris and myocardial infarction by 80 - 100 percent without side effects. There is an overabundance of studies and documented experiences - mainly in Germany, Austria and Switzerland, so that its effects are quite obvious, even when the big clinical double-blind study is missing. But there is a mighty inscrutable opposition against the therapy with orally administered ouabain.   Ouabain has a positive effect also in heart failure, hypertension (!), stroke, dementia, arterial occlusive disease (mostly in the legs), glaucoma, sepsis, endogenous depression, asthma bronchiale. The therapeutical sucess is sensational in arterial occlusive disease and dementia. (Because of a lack of time the references aren´t indicated, but this will be made up soon.)  There are two wrong dogmas creating an impermeable wall:  1) Ouabain is like digitalis classified as a cardiac glycoside, with the indications “heart insufficiency“ and “arrhythmia“. Because digitalis has negative effects in angina pectoris and myocardial infarction and the story goes“ that all glycosides act similarly, the outstanding therapeutical results of ouabain don´t attract any attention at all in the medical establishment. Because of the classification as a heart glycoside, in the “Red List“, the german pharmaceutical thesaurus, oral ouabain is associated with all the bad side effects which are noticed in digitalis medication but have never been noticed with the oral ouabain.therapy.  2) In the textbooks is written that ouabain has a very bad oral absorption - but there are over 20 studies which indicate the contrary.  **The worldwide best therapeutical results in angina pectoris and myocardial infarction**  Short preliminary remark: Most references regarding the therapeutic effect are published in German. An important reference in English, which shows the reduction of cardiac pain during a bicycle ergometry by ouabain, is attainable with free full text as PDF on <http://www.pubmedcentral.nih.gov/picrender.fcgi?artid=458511&blobtype=pdf> Another study shows the exact parallel of the effect of oral ouabain with a nitro preparation, the generally accepted medicament used in angina pectoris pain attacks: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=6428911> Both studies are outlined below.  The best example for the indeed excellent therapeutic results of oral ouabain in angina pectoris and myocardial infarction is Prof. R.Dohrmann from Berlin (West), the leader of a public hospital, starting 1975 with this therapy. 1984 Dohrmann and Dohrmann published a study (1) dealing with oral ouabain therapy in unstable angina pectoris. 148 patients with severe stenosis visable in coronary angiography, who received for years all the medicaments modern medicine offers and who are dissatisfied because of continous heart attacks and in part unpleasant side effects, have been switched over (with their agreement after an information discourse) to the therapy with oral ouabain from one day to the other, i.e. the other medicaments including the ß-blockers (!) were discontinued immediately. After one week 122 of 148 patients were completely free from angina pectoris, and after two weeks this success could be seen with 146 patients. They were also free from the side effects of the former medication. The ouabain capsule which is dissolved in the small intestine(\*) is sufficient in many cases (in this study 3 x 1 capsule daily), and when in spite of this prophylaxis there is a heart attack, the capsule for lingual absorption - to break with the teeth (\*\*) surely helps in 5-10 minutes in almost every case. \* Strodival mr® (3 mg) from MEDA GmbH, Wiesbaden / Germany  \*\* Strodival® (3 mg) or Strodival spezial® (6 mg).  **No side effects** The other two patients (of 148) in the study of Dohrmann & Dohrmann 1984 had to stop the therapy because of some irritation of the digestion tract, the only harmless side effect which sometimes occures. Strictly speaking, these “side effects“ (up to diarrhoea and local inflammation of the tongue) are reversible phenomenons that occur only during the absorption of the drug. Once absorbed, there are no side effects reported while the experiences with this medication from 1947 until now are counting several hundred thousand of “patient years“ (number of patients x duration of treatment). There are still about 2000-3000 physicians in Germany who are using orally administered ouabain.  The dosage is declared as 1 - 4 x 3 - 6 mg daily; principally success and demand should regulate the dosage. There is no real danger of overdosage as often seen with digitalis preparations. Even suicide attempts with huge amounts of ouabain capsules (900 mg) miscarried and led only to some days of reversible ECG irritations. (Caution ! Intravenous ouabain only 0,25 mg or 0,125 mg with slow injection !)  By the way it is not a necessary condition to discontinue the former medication: there have never been any interactions between oral ouabain and any other medicine, even not with digitalis, on the contrary the experience shows that oral ouabain reduces the side effects of digitalis, when the latter drug is necessary because of tachycardia (see below, regarding the different molecular mechanism of ouabain and dogoxin). So the careful, perhaps doubtful doctor can initially prescribe oral ouabain additionally, and with the mostly instating improvement of symptoms, he can reduce or leave the former medication.  The study of Dohrmann et al. 1977 (2) deals with lingually applied ouabain (6 mg) to all patients coming to the hospital with severe heart attacks, acute myocardial infarction (AMI) or suspected AMI. In 170 of 264 cases (= 64 %) the attack was totally stopped within 5-10 minutes, in the rest there has just been an AMI in 55 cases, when there is no success to be expected any more, so that only in 15 % of the patients with Angina pectoris (but without AMI) there was no positive result with the first application of ouabain. The above mentioned study (1) shows that the optimal effect of ouabain is reached within some days after repeated intake.  In acute mayocardial infarction (AMI) 1975-1987 Prof. Dohrmann used a new therapy with initially 1) i.v. cortison to stabilize the lysosomal membranes and 2) i.v. k-strophanthin (0,25 mg, repeated every 24 h). Additiononally oral ouabain (lingual absorption, capsule to break with the teeth, 6 mg) was given when there was heart pain in the following days. The quota of nonsurvivors (30 days) after myocardial infarction previously was very high (38,8 %) because in Berlin (West) have been much more elderly people than in the rest of Germany. With this therapy Prof. Dohrmann reached the best rate of survival in whole Europe - in the first year with oral ouabain 17,6 % nonsurvivors (3), and 1987, after 12 years, 15,1 % with experiences with 1056 patients (4). A multicenter study of northern Germany reported a quota of 26 % mortality (30 days) in 1977 (5). Prof. Dohrmann was outnumbered only by Prof.DeMesquita from a clinic in Sao Paolo (6) who used ouabain i.v. from 1972 -1979 in 1037 cases (until ouabain lost the license in Brasilia): they reached 9,6 % mortality during the stay in hospital, which could be reduced to 5-7 days with the ouabain therapy.  Another example is a coal mine in Gelsenkirchen/Germany (7) where the average number of workers dying because of acute myocardial infarction (AMI) in the mine, under the surface of the earth, was 3 every year; the way to the doctor lasted more than half an hour. After the doctors of the mine began with oral ouabain therapy directly in the mine in 1974 - given only when there was an acute heart attack, not prophylactically given -, the mortality concearning AMI was reduced to zero in the following 10 years with this therapy. In two cases there was no possibility to give oral ouabain (accidents) and the workers died. The cases concearning severe angina pectoris attacks and non-mortal cardiac infarctions that forced to drive the workers out of the mine were reduced by 80 % with oral ouabain in 1974-1984.   Salz & Schneider 1985 (8) carried out a placebo controlled doeble-blind study with 30 patients with coronary heart disease. They found after 14 days of prophylactic application of oral ouabain (3 x 6 mg Strodival mr® daily) a highly significant effect on the ECG (elevation of the lowered S-T-segment), the angina pectoris attacks and the subjective state of health in comparison of the verum and the placebo group and also an amelioretion of hypertension. With placebo there was seen a deterioration of all parameters, see table below:  Salz & Schneider 1985, double-blind study  the effect of Strodival® in 16 patients ...........patients without change ...moderate improvement..essential improvement  exercise-ECG..............0........................5...........................11  angina pectoris-attacks..1........................2...........................13  subjective condition......0........................1...........................15   the effext of the placebo in 14 patients ...............................patients with deterioration exercise-ECG...........................12 angina pectoris-attacks...............10 subjective condition...................10   In 1984, the small firm "Herbert Pharma" (the former producer of Strodival® - the only available ouabain medicament nowadays - in Wiesbaden / Germany) had made an inquiry to 3650 doctors with experiences of the oral ouabain therapy (9). Ca. 98,5 % answers were positive, 1,5 % were positive with some limitation and no doctor gave a negative feedback. Reading the released extract, the answeres of 300 physicians, published with full adress, is really convincing; very often they say: "excellently effective", "no side effects", "better than the rest", "I don't see deadly myocardial infarctions any more" and so on... (The small firm hadn´t enough money to corrupt such a great number of physicians to make such definite statements. The author talked to some of them, so that it wasn´t a faked inventory)  Dr. Berthold Kern (Stuttgart), the explorer of the oral ouabain therapy in 1947, had documented very well his experiences from 1947 to 1967 with more than 15.000 patients (10). His patients, who were severely ill above the average, have had only 20 non-fatal myocardial infarctions, a very low number. Also after this period until his retirement 1991 he saw this good success, like the other doctors of his working group in and around Stuttgart and like the thousands of doctors in Germany who had used or are still using this therapy.  The double-blind experiment of Kubicek and Reisner 1973 (69) with angina pectoris-patients under hypoxia showed in 19 of 22 patients a marked improvement of the electrocardiogram (S-T-alterations) - in 7 cases a total normalization - after 6 mg oral Strophoral® (90 % ouabain, 10 % k-strophanthin) in comparison to a control group, and the result of subjective state of health is as follows: control: 18 patients with pain or giddiness and only 4 without trouble. After oral ouabain: Only 4 patients with pain or giddiness and 18 patients are without trouble. A placebo showed no effect. Digitalis had a negative effect, so that some experiments had to stop before the regular end (several drugs in differentiated dosis: Digoxin i.v. 0,4 mg, 0,8 mg, ß-Methyl-Digoxin oral 0,05 mg, 0,2 mg, 0,8 mg). Also Sharma et al. 1972 (70) had similar good results with 0,7 mg i.v. ouabain. After ouabain the patients had much less angina pectoris pain using bicycle exercise. The ECG didn´t change, perhaps because of the very high dosage. This is the corroboration of the therapeutical results reported by Prof. Dohrmann and others, see above.  There are many other articles about the experiences of doctors with orally administered oauabin. Manfred von Ardenne, the great scientist of the German Democratic Republic, made many investigations dealing with ouabain and wrote a review in English language about the therapy with orally administered ouabain (11).  The author could motivate some physicians to use ouabain. Their reports about a good therapeutical success are a good current authentication of the findings in the literature. The anthroposophic “Ita Wegman Klinik“ in Arlesheim / Switzerland are using ouabain since 2002 with the expected success, also the “Neue Wicker Kliniken“ in Bad Nauheim / Germany March 2004.  In Germany intravenous ouabain / k-strophanthin was accepted in acute heart insufficiency for decades until 1992 (13). Later incomprehensibly Digoxin was recommended and nowadays criticised because of too slow onset of action. Anyhow, 35 % of german doctors on emergency classified digoxin as indispensable and 15 % as desirable in 2001 (14). They are adused to use ouabain / k-strophanthin again, the cardiac glycosides with the quickest onset of action.  There are many pharmacodynamical studies dealing with ouabain, which are described in the next but one chapter.  Also with homoeopathic ouabain (D4, Strophactiv® from magnetactiv, Wiesloch / Germany) there is seen a quite good therapeutic success. The blind study of Hupe & Balint 1988 (12) showed that 60 % of the patients with angina pectoris improved their pathological ECK (S-T segment) after Strophactiv®, but only 15 % of the patients of the placebo group. In cases of emergency a regular dose (1 ml) will probably not be sufficient, but there are reports of a good effect of much larger doses, i.e. 25-50 ml (see below the expected blood levels after homoeopathic ouabain).   **Ouabain and digitalis behave oppositely at the cellular level**  The commonly accepted receptor for cardiac glycosides, i.e. ouabain and digitalis and some other substances, is the sodium pump (= Na-K-ATPase), which is present in the wall of every cell in a great number and which is pumping sodium out of the cell and kalium into it. This is very important for many fundamental functions of the cell.   Ouabain is extensively used in many scientific in vitro experiments to block the sodium pump. In all textbooks and articles there is written that cardiac glycosides are inhibitors of the sodium pump. But for all that, this is only the toxilogical and not the physiological part of the truth: The inhibition of the sodium pump occurs only with high concentrations of ouabain (ca. 10(-7) Mol to 10(-3) Mol and higher), which are easily attainable in a laboratory. On the contrary, the low concentrations of ouabain, which are present in the human body after taking the medicine or naturally because of the endogenous nature of ouabain, have the opposite effect. There are over 50 unnoticed and unrefuted studies that report of the stimulation of the sodium pump by low doses of ouabain (ca. 10(-13) Mol to 5 x 10(-8) Mol), the first one to mention is Kurt Repke 1961 (15, with k-strophanthin), the discoverer of the sodium pump. The working group of Prof. Godfraind (Brussels) had made extensive studies on this topic (for example 16). The most important nowadays is Gao et al. 2002 (17) from the University of New York: “Isoform-specific stimulation of cardiac Na/K pumps by nanomolar concentrations of glycosides“ in “Journal of General Physiology“. They report about a stimulation of Na-K-ATPase by ouabain and dihydro-ouabainin guinea pig, canine and human heart cells. In the animal studies there was a stimulation of the high affinity isoforms alpha-2 (guinea pig) and alpha-3 (canine), but not of the low affinity isoform alpha-1 of NA-K-ATPase by up to 107 %. In human heart cells the differentiation is difficult because all isoforms, also alpha1, have equal affinities to ouabain.  Meanwhile some of the leading scientists are accepting the real cellular mechanism of low doses of ouabain, for example Prof. Schoner from Giessen / Germany in his parting lecture 2003: <http://www.vetmed.uni-giessen.de/biochem/schoner/Abschiedsvorlesung/Folie25.PNG> and Prof. Hakuo Takahashi (Osaka, personal communication), Ferrandi and Manunta 2004 (18), Saunders u. Scheiner-Bobis 2004 (19), Hambarchian et al. 2004 (20) and Su et al. 2003 (21). The result of the stimulation of the sodium pump is a reduction of intracellular sodium and also a reduction of intracellular calcium because sodium and calcium are associated via the sodium-calcium-exchanger. For digitalis the data is poor, but it seems to be that digitalis is not able to stimulate the sodium pump (19). This is the explanation for the differences between ouabain and digitalis preparations seen in many pharmaco-dynamical studies (see below) and especially seen in the therapeutical results. Actually oral ouabain can reduce the side effects of digitalis. Older pharmacological animal studies (Hildebrand 1947) show that an injection of a small dosis of ouabain augments the necessary amount of the following deadly dosis.  Two study groups have detected a new receptor for cardiac glycosides inside the cell, at the sarcoplasmic reticulum, the calcium store of the cell (22-23). The effect is a release of calcium. Ouabain acts tenfold weaker than Digoxin at this new intracellular receptor. Furthermore Santana et al. 1998 (24) could show, that already 0,1 nanoMol of digoxin, a concentration below those that are found in the human blood after digoxin medication, have the halfmaximal effect of opening the sodium channels for calcium, letting in 30 percent of the total calcium influx, whereas ouabain needs nearly the hundredfold concentration to achieve this effect. These differences between the actions of ouabain and digoxin are a good additional explanation for the different therapeutical effect of ouabain and digitalis in angina pectoris and cardiac infarction.  The study of Horackova and Mullen 1988 shows a reduction of the Ca++ content of isolated cardiomyocytes with low doses of ouabain, unchanged results with intermediate and a rise with high concentrations of ouabain (25).   **Ouabain affects several components**  In ischemia the activity of the Na-K-ATPase of heart muscle cells is diminished (26-28). This occurs in a situation where the number of sodium pumps is already reduced. The first sentence of Ko et al. 1995 (28) is: “Na-K-ATPase (sodium pump) may play a key role in the prevention of reperfusion injury caused by Ca++ overload.” By stimulating the sodium pump ouabain could prevent the ischemic and reperfused heart from calcium overload and could at least prevent the border areas of infarcted myocardium from necrosis and minimize infarct size.  Because the sodium pump is present in every cell, ouabain can influence not only the heart muscle cells. Because the cells exchange a part of their sodium for calcium, ouabain reduces the inracellular calcium concentration and therefore acts similar to a calcium antagonist. In addition ouabain combines the qualities of a whole train of medicaments.  --- Riehle & Bereiter-Hahn 1994 (29) showed that 10-10 Mol ouabain markedly increase fatty acid oxydation of cardiomyocytes (but not the oxydation of other substrates), which is diminished in ischemia. Gousious et al. 1967 made a study (30) which investigates the influence of ouabain in the isolated heart without ischemia: there was an increase in fatty acid oxidation in absence of increased uptake. In this connection it is interesting that carnitine, which is necessary for the transport of fatty acids into mitochondria and is also a stron stimulator of fatty acid oxydation, is taken up by the cell via Na-K-ATPase (31). Perhaps ouabain could prevent the loss of carnitine which occurs in ischemia (32).  --- The nerve cells as well have sodium pumps, they are even the cells with the highest frequency. Sharma et al. 1980 saw a reduced output of noradrenaline in nerve terminals with low doses of ouabain, no change with intermediate concentrations and an increase with high concentrations of ouabain (33). Gutman and Boonyaviroj 1977 (34) report that only low doses of ouabain are reducing the output of epinephrine and noradrenaline in the adrenal glands, while high concentrations of oauabin have the opposite effect. So the medicament ouabain lowers the level of stress-hormones in the whole body and especially in the myocardium and therefore acts also in the field of a beta-blocker. Agostoni et al. 1994 (35) report about a 50 % reduction of noradrenaline levels in patients with heart insufficiency over 3 months of intravenous k-strophanthin 0,125 mg daily (Digoxin: no effect)  --- Because of the sympathetic nervous system lowering (33-35) and parasympathetic nervous system enhancing effect (36-38) ouabain could dilate the small arteries inside the myocardium which are susceptible for a paradoxical reaction to ischemia: they are further contracting instead of dilating (39), which is mediated by the sympathicus (40).  Furthermore, in the same way ouabain could reduce coronary spasm which can promote the rupture of vulnerable plaques. In this way ouabain could reduce “coronary events”. Perhaps ouabain has also a direct effect on the vulnerable plaques: In the study of Matsumori et al 1997 (41) ouabain caused the quadrupiclation of survival in rats with sepsis because of a suppression of cytokine production (IL-6 and TNF-alpha). Perhaps ouabain could show this effect also in the heart and coronary system and reduce the inflammatory process in the vulnerable coronary plaques.  --- Although in the last years ouabain is regarded as a blood pressure enhancing hormone only based on contradictory 1) studies in vitro, 2) studies with rodents and 3) statistical findings with ouabain-like substances (see below the respective chapter) there is considering evidence that oral ouabain and oral / i.v. k-strophanthin are lowering blood pressure in patients with hypertension (8, 9, 35, 42-44) – but not in normotensive or hypotensive patients (44). Two double blind clinical studies with orally administered ouabain (8) and k-strophanthin i.v.(35) show the in Germany wellknown ouabain effect of blood pressure lowering in patients with hypertension, as do many other reports (most of them in german language only), for example Qi et al. 2001 (42), who report that only i.v. k-strophanthin lowered hypertension and not digoxin. Agostoni et al (35) also observed a lowering of hypertension with k-strophanthin 0,25 mg daily (Digoxin: no effect) in patients with heart failure. Also Pidgeon et al. 1994 (45) demonstrated the reduction of diastolic blood pressure in healthy volunteers after 0,5 mg ouabain i.v..  DeMots et al. 1978 (46) gave the same dosis (1,05 mg / 70 kg, extremely high !!) of ouabain i.v. to patients with coronary artery disease with different velocities (10 sec., 2 min., 15 min.). The two quick injections showed an increase in systemic vasular resistance and a deterioration in myocardial lactate metabolism, whereas the slow injection of ouabain caused the contrary, a tendency towards a reduction of systemic vascular resistance and a profound improval of myocardial lactate metabolism, an effect of ouabain which is wellknown by older german pharamacology, together with a pH improvement.  Saradeth & Ernst 1991 (47) made a randomized, double-blind and placebo-controlled crossover-study with healthy volunteers and found a reduced rise of diastolic blood pressure in exercise after lingually administered ouabain (6 mg).  --- Ouabain is enhancing the blood flow in the myocardium. This was revealed by von Ardenne 1991 (48) in a double blind crossover study using a szintigraphy with 99technetium showing a marked increase in myocardial blood flow by lingual ouabain (12 mg) in patients with angina pectoris. This confirmed the findings of Vatner & Baig 1978 (49) with ouabain i.v. in dogs.  --- Particularly important is the effect of ouabain on the red blood cells. Their diameter (8 micrometers) is bigger than the diameter of the capillaries, which they must pass (3 micrometers). To manage this, the erythrocytes have to make themselves very thin and long, really like a submarine. But because the acid and the oxygen radicals generated in ischemia or even by an overactivity of the sympathetic nervous system (see below, part two of the appendix) reduce the activity of the sodium pump of the erythrocytes, intracellular sodium and subsequent intracellular water accumulates and the erythrocytes become bulging and unflexible (50-52), like it is mimicked by high concentrations of ouabain (52). However, low concentrations of ouabain are able to stimulate the sodium pump of the erythrocytes. Strobelt et al. 1986 found a marked improved flexibility of erythrocytes even at low pH (53). So they get slim enough to pass through the capillaries again. Here ouabain acts principally like an ASS preparation, like Aspirin®. Saradeth & Ernst 1991 (47, double blind, crossover, healthy volunteers) found an enhancement of erythrocyte flexibility after oral ouabain (6 mg).  A disorder of microcirculation could get harmful. Because of the reduced flexibility of the red blood cells, the bloodflow is further reduced and the acid accumulates. That will make the erythrocytes even more immobile and so on – a real vicious circle, that could aggravate an ischemic situation, increase the necrotic area in the case of an acute myocardial infarction and perhaps even initiate the death of single heart muscle cells or even of bigger regions, if the microcirculation in the capillaries is downgrading up to a stasis. This could perhaps be a widely unnoticed mechanism of how a myocardial infarction respectively a myocardial necrosis could be generated. This could take place in such cases when a coronary thrombus is absent. There is a number of studies that report of a relatively low frequency of coronary thrombosis in myocardial infarction (54-66), for example 49 % in Murakami et al. 1998 (54) or 20 % in Doerr et al. 1974 (65, Prof. Doerr was the president of the German Society of Pathology). (For more research results supporting an alternative view of myocardial infarction pathogenesis please see the appendix.)   So the action of ouabain on the red blood cells is very important. With the lingually administered ouabain capsules every patient can help himself in angina pectoris and perhaps even in the case of a beginning acute myoardial infarction, before the ambulance can be present.  --- Pidgeon et al. 1996 (67) report that in sheep intravenous ouabain after 3 weeks caused a reduction of angiotensin II levels, an effect which could also be seen in healthy human volunteers after a single i.v. injection of ouabain (68). Studies in patients are still lacking. Perhaps ouabain could also act like an ACE-inhibitor.  --- Generally speaking, ouabain acts like a nitro-preparation, without two disadvantages that reduce the applicability of nitroglycerin preparations. In the case of acute hypotension with ouabain there is no danger of a further fall of blood pressure, and there is no addiction to the drug - the thousandth capsule is effective like the first ones.  The very good results of the randomized, placebo-controlled double-blind study - Salz & Schneider 1985 (8) in seven doctor´s surgeries and the double-blind studies of Kubicek & Reisner 1973 (69) and Sharma (70) are already presented above.  Belz et al 1984 (71) made a placebo-controlled double-blind crossover-study, which shows that lingually administered ouabain (12 mg) has a constant and significant (in part highly significant) effect on the heart contractility of healthy volunteers that is different from the effect of ouabain i.v. and similar to that of nitroglycerine, that is a negative inotropic effect. Dohrmann & Schlief-Pflug 1986 (72) repeated the above mentioned study with patients which had severe coronary heart disease and instable angina pectoris. Also in these patients lingually administered ouabain had the same effect like Nitrolingual®, that is in 2/3 of the patients a positive inotropic effect and in 1/3 of the patients a negative inotropic effect. Perhaps the different effect of ouabain on heart contractility is due to a different intracellular calcium content, because a calcium overload has a negative inotropic effect (73) and in this case the reduced intracellular calcium content by ouabain could have a positive inotropic effect (73). The latter was also seen in the studies of Piscitello u. Maggi 1973 in patients after orally administered ouabain (74) and Su et al. 2003 in isolated heart preparations (21, with strophanthidin). There are still open questions, because Horackova & Mullen 1988 in myocytes (25) saw a reduction of intracellular calcium with low doses of ouabain, an augmentation with high doses and no change with medial concentrations, but in all cases a positive inotropic effect. In any case, oral ouabain is effective in mild heart insufficiency. In severe cases it was reported (75) that oral ouabain is effective after a transient treatment with intravenous ouabain, which perhaps should be repeated from time to time (several weeks to months). Intravenous k-strophanthin (and probably ouabain) in the therapy of severe heart failure is more potent than oral digoxin. This was shown by the double blind study of Agostoni et al. 1994 (35): Only with k-strophanthin the performance in bicycle exercise rose (by 40 %), the vascular resistance and the noradrenaline blood level fell (the latter by 50 %). Qi et al. 2001 (42) report about an increment in cardiac output of 25 % with digoxin and of 41 % by k-strophanthin and a significant fall of diastolic hypertension only by k-strophanthin.  As we have seen, ouabain combines the actions of several medicaments without their side effects and is the optimal pharmacological solution in the case of angina pectoris and myocardial infarction.  What are the effects of low concentrations of ouabain in ischemia / reperfusion injury? I never have seen an animal study or an in vitro / ex vivo study in this direction at all. I think such an investigation could be a breakthrough !   **The effect of ouabain in other diseases**  There are many other diseases other than angina pectoris, myocardial infarction and heart failure, in which the activity of the sodium pump of the concearning tissues or of the red or white blood cells is lowered: diabetes, cancer, multiple sclerosis, Morbus Parkinson and Alzheimer, epilepsy, dementia, Huntington chorea, schizophrenia, obesity, anorexia nervosa, cataract, acratia, hypothyroidism and hyperthyroidism, inflammable intestinal diseases, arthritis, cystic fibrosis, McArdle´s disease, pulmonary edema, allergies, toxications, sepsis. In this cases low doses of ouabain as a stimulator of the Na-K-ATPase speculatively could have a positive influence. There are almost no studies regarding the effect of ouabain in this diseases up to now. The diseases in which a therapeutic effect of ouabain in patients is documented are cerebral ischemia (76-77), asthma bronchiale (78) and endogenous depression (79).  Hsieh et al. 2003 (80) and other studies report about a rise in intracellular Na+ in patients (80-81) and animals (82-84) with sepsis which perhaps could be the cause of the disturbances of Na-K-ATPase activity - on the one hand a reduction in erythrocytes (81) and erythrocytes, skeletal muscle and liver (85) of patients and in the rat heart (82, 86) and on the other hand a stimulation (the most other references) have been reported. Tang et al. 1993 (87) report about time-dependent changes in rat heart, first a stimulation, then a decrease in Na-K-ATPase activity.  The effect of oral ouabain in patients with sepsis is an open question. Regarding the theoretical background sepsis could be a contraindication because of the stimulation of Na-K-ATPase by low doses of ouabain. Anyway, in several decades of oral ouabain therapy there has never been an announcement of an aggravating effect of sepsis by oral ouabain, but it could be possible that 1) perhaps there has never been an oral ouabain therapy in sepsis or 2) that perhaps a negative effect hasn´t been attributed to a possible oral ouabain therapy. Nevertheless Levy et al. 2005 (88) report about a beneficial effect of ouabain released by microdialysis probes in the skeletal muscle of patients with sepsis, probably in such a high concentration able to inhibit the local Na-K-ATPase. Also other studies report of this mechanism in animals (89-90). A head of department in a german clinic told the author that he has given intravenous Ouabain (0,125 mg or even less) in all cases of acute sepsis from 1975 to 2000 and is sure that because of this medication none of his patients died. The dose rate is so low that one can suppose that it could act like oral ouabain. Maybe that in sepsis low concentrations of ouabain have different effects in skeletal muscles and heart, which cannot be excluded. In any case, regarding the latter there is a number of studies showing an enhanced utilization of lactate after low dosed ouabain - DeMots et al. 1978 (46) and some german studies from 1941 to 1972 (91-98), see also the review of Ardenne 1978 (11, in english). In the study of Matsumori et al 1997 (41) intraperitoneally applied ouabain caused the quadrupiclation of survival in rats with sepsis because of a suppression of cytokine production (IL-6 and TNF-alpha). Some studies attribute the Na-K-ATPase stimulation in sepsis to catecholamines (89, 99-102) which were reduced by low doses of ouabain (33-35). Further studies are necessary.   **The false dogma of the bad absorption of oral ouabain**  The opinion that ouabain is very poorly absorbed (0-4 %) when enteral administered is not valid, as shown in the table below (arranged according to the duration of the study).  Absorption of radioactively labelled Ouabain Study species application time absorption Greenberger et al. 1969 (103), intraduodenal, 30 min,  rat: ouabain: 17 % (+ 11 % in the mucosa), digoxin: 27 % with equal blood levels of both glycoxides  guinea pig: ouabain: 19 %, digoxin: 15 %   Ohlmeier & Ruiz-Torres 1968 (104), rat, intraduodenal, 30 min, 28 %  Forth et al. 1969 (105), cat, intraduodenal, 1 h, 11 %  Forth et al. 1969 (106), intraduodenal, 1 h,  rat: ouabain: 24 % digoxin: 75 % digitoxin: 86 %,  guinea pig: ouabain: 48 %, digoxin: 20 % (!), digitoxin: 59 %   Marzo et al. 1974 (107), guinea pig, intraduodenal, 5 h, ouabain 36 %, k-Strophanthin 38 %  Leuschner & Winkler 2001 (108), guinea pig, oral, 6 h, absorption 45 %, systemic bioavailability 43-50 %  Garbe & Nowak 1968 (109), guinea pig, oral, 7 days, 67 %  There are additional examples reporting of a much higher absorption than the textbooks (110-112).   Citation Forth et al. 1969 (106) p. 207 (translated by the author): “The findings indicate that the polarity (lipid solubility) is not the only important quality of cardiac glycosides regarding their absorption.“  Kitano et al. 1998 (113) refer of a high absorption of radioactively labelled and orally administered ouabain (only 0,03 mg / 70 kg daily) to rats, comparable with that of equimolar digoxin (blood levels after 14 days: ouabain 0,024 nano-Mol, digoxin 0,033 nano-Mol).  1952 Dr. Berthold Kern (114) administered ouabain to patients with artificial anus and analysed the feces with picric acid and KOH, a very sensitive colorimetric method: very little amounts of ouabain (0,02 mg) evoke a marked coloration in the control experiment with only 2 % result variation. In every case there was no ouabain detectable. This affirms the older findings that only 0,7 % (guinea pigs, Lendle 1938 (115)) respectively 0,1 % (cats, Fühner 1929 (116)) were detectable after rectal administration of deadly doses of ouabain.  Lauterbach suggested that there is an active transport process for polar cardiac glycosides like ouabain through the intestinal cells (117-118). As a parallel there is an uptake process per endocytosis into the intracellular compartments of the myocardium (119).  After orally administered 3H-ouabain in humans there are high blood levels of ouabain (up to 8 nMol = 8 x 10-9 Mol , which is far more than claimed for the therapy of heart failure) in the studies of Erdle et al. 1979 (120) - see the diagram below - and Marchetti et al. 1972 (121), which astonishingly never have been cited, for example they are not mentioned in the "Handbook of Experimental Pharmacology" (122). Here only the third respective study of Lahrtz et al. 1968 (123) is mentioned, in which 1) too little of ouabain was given (0,04 mg; a normal therapeutic dose is 3-12 mg) and 2) indeed there was given too little of radioactivity, even below the detection limit, so that a positive result was impossible even if there had been an i.v. application. However, also the effects of orally administered ouabain on human haemodynamics support the finding of a high and linear, not uncertain absorption (Piscitello &b Maggi 1973) (74). Interesting are also the double blind study of Belz et al. 1984 (71) and the study of Dohrmann & Schlief-Pflug 1986 (72).   Investigations with the RIA-method show smaller amounts of ouabain-immunoreactivity in human blood after oral application (0,3 - 0,5 nMol = 2-5 x 10-10 Mol with Strodival® and up to 1,4 nMol = 1,4 x 10-9 Mol with Purostrophan®) (124-125), which were always ruled as a prove for the ineffectiveness of the oral ouabain therapy. But also these concentrations of ouabain are fully within the concentration range that shows a distinct stimulation of the sodium pump, a knowledge that just recently begins to become accepted. Strobach et al. 1986 (126) only investigated the excretion in the urine and found a very low absorption rate for ouabain (1,4 %). But they found an urinary excretion of intravenous ouabain of only 33 % - this is the half of the excretion found in other studies (for example 124-125). This casts doubt on the methods of this study.  Riehle et al. 1991 (with Prof.Bereiter-Hahn, the vice president of the university of Frankfurt on the Main / Germany (127) could show that even a concentration of 10-13 M (= 60 quadrillionth gram in one millilitre) of ouabain has a reproducible effect on cardiomyocytes regarding the oxygen metabolism, in some cases even a concentration of 10-15 Mol did so; both are concentrations that can be produced by diluting but cannot be measured any more by any method. Even after homoeopathic treatment (1 ml Strophactiv®, D4) there are ouabain blood levels expected much higher than 10 -13 Mol, i.e. 1,3 x 10 -10 Mol.   **Only a hair raising inconsistancy or a prearranged deception ?**  The often published statement of the uncertain enteral absorption of ouabain has its only root in a single examination of a ouabain preparation called Purostrophan®, which was available in the 1970ies and showed indeed some fluctuation of the results concerning the blood and urine levels of ouabain. Beside the fact, that this fluctuation wasn´t bigger than that of the commonly used Digitalis medicaments, the author discovered, that the real examination of oral Purostrophan® wasn´t made in the oftenly cited study (124) of Prof. Greeff et al. 1974, the accepted authority at that time, but was made one year before in a dissertation of his institute (125). The peculiarity of this dissertation is, that the examination of Purostrophan® has been made with two different groups of patients: one group took ouabain before and the other group took ouabain after the breakfast. In the text of the dissertation the expected result is written: The group who took the medicine before the breakfast had absorbed more ouabain than the other group. Already in the dissertation the different results were summarized to one diagramm and then were repeated by Prof. Greeff in his study (124) and other articles without citation, so that the origin remained hidden, and also without naming the methodological anomaly. This is the origin of the intensively published statement of an uncertain absorption of ouabain, which was used for the adoption of the prescription requirement. This nonscientific results are published in the same study that reports of the low enteral absorption of ouabain and influenced the majority of the physicians not to prescribe ouabain to their patients. The also tested Strodival® (lingual absorption) showed only minimal deviations, with even minor fluctuation of blood levels than that after i.v.application.   **The detection of ouabain as a new hormone and the birth of a new false dogma**  Since 1991 ouabain is identified as an endogenous compound (128), produced by the adrenal glands and / or by the brain (hypothalamus). By the way, the possibility that ouabain is taken up with the food cannot be excluded - this would be another proof for the good absorption of ouabain. First described as an isomer of ouabain (129-130) which implicates the possibility of different physiological properties, it could be shown that this was an artefact (131-132). Meanwhile it was assured that the endogenous ouabain is completely identical to original plant ouabain (132-134). For all that recently there are new findings, together with reanalysis of the before mentioned studies (132-133) that used 1H-NMR (nuclear magnetic resonance spectrometry), which suggest that perhaps endogenous ouabain could be yet an isomer (with 11ß-hydroxylation), which is very hard to observe in HNMR (135).  Because ouabain antibodies are crossreacting with other substances ( for example 136-145), the results with an immuno-assay should be always verified by a chromatographic method (HPLC). Without HPLC it should not be spoken of ouabain but of OLS (ouabain-like substances) or similar terms. Unfortunately not all working groups pay attention to this important point. In human plasma 9 - 190 picoMol ouabain was found. Some other endogenous cardiac glycosides were identified: digoxin (146-147), dihydro-ouabain (148) proscillaridin (133), 19-norbufalin (149), marinobufagenin (150), telocinobufagenin (151) and other, up to now unidentified compounds (for example 152-153). The ouabain specific binding protein described by the workgroup of Giessen / Germany ( 154-155) turned out to be an artefact (personal communication).  Unfortunately one can observe the birth of a new false tenet: the role of endogenous ouabain as the cause of hypertension, which is based only on contradictory 1) studies with rats, 2) in vitro studies and 3) statistical findings. The extensive clinical observations with ouabain (g-strophanthin) and k-strophanthin which all report about a hypertension-lowering property of these substances (see above) is not known by the international scientists because most of the studies were published only in german language except Agostoni et al. 1994 (35) and Qi et al. 2001 (42). Even Prof. Schoner (Giessen / Germany) didn´t know these facts.   1) The most in vitro studies are using unphysiologically high ouabain concentrations, which are likely causing an inhibition of the sodium pump. Only very few are dealing with physiological low doses of ouabain which stimulate the Na-K-ATPase. For example Saunders & Scheiner-Bobis 2004 (19) noticed a production of (blood vessel contracting) endothelin in human artery endothelial cells by 10 –9 to 10 –8 Mol ouabain, but Woolfson & Poston 1991 (156) report on the one hand of a reduced response of human resistance arteries to acetylcholine and on the other hand of an increased response to (blood vessel relaxing) NO (nitric oxide) by 10 –10 Mol ouabain. Dong et al. 2004 (265) report of a decrease of the delay of NO production after a bradykinin stimulus, i.e. an enhancement of NO production. Woolfson et al. 1991 (157) report that the sequence of pharmacological actions is also important: The response of human resistance arteries to noradrenaline is increased by ouabain (in high concentrations) only when noradrenaline is added before ouabain. When ouabain is added before noradrenaline, the response to noradrenaline conversely is diminished. Such a detail has never been considered in any other study. Low doses of ouabain didn´t alter the response of human arteries to noradrenaline.  The whole net effect seems to be concentration dependent: a good example for the effect of low doses of ouabain on vascular smooth muscle is the study of Branco and Osswald 1986 (36): the authors report of the different actions of three different concentrations of ouabain on dog blood vessels. The two high concentrations caused a constriction (release of noradrenaline), but the low concentration had the contrary effect. Also the studies of DeMots et al. 1978 (46) and Nelissen-Vrancken et al. 1997 (158) show the oppositional effects of high respectively low doses of ouabain..  2) The hypothesis of ouabain as a cause of essential hypertension is based mainly on quite a lot of observations in rodents (mostly rats, 1-2 times mice, the references are widespread in every study and review and here not listed). Exclusively in this species in vivo results supporting the hypothesis are available. It is an old pharmacological knowledge that rodents behave different regarding cardiac glycosides in comparison to other species and humans. So the experiences with rodents are of doubtful value, especially when some studies with very similar protocol (for example over a period of several weeks) do not show a hypertensinogenic action of ouabain (159-161), which is not often cited. Li et al. 1995 (160) are using the same test conditions as Manunta et al. 1994 (162) but don´t notice any hypertension in Sprague-Dawley rats over 4 weks with subcutaneous ouabain infusion (0,7 mg / 70 kg). Tamura et al. 2000 (163) report that a synthetic diet completely without cardiac glycosides causes hypertension in rats, which is prevented by orally administered ouabain in very low dosage (10 microgram / L).  One of the studies (164), in which ouabain caused hypertension in rats, contains a surprising hint for the beneficial therapeutic effects of ouabain. The rats given ouabain showed no cardiac hypertrophy like the rats in the control group. Citation Yuan et al. 1993 (164) p.186: "Ouabain actually may be cardioprotective." There are older studies who also report about the prevention of hypertrophy of heart (165) and adrenals (75). Moskopf & Dietz 1955 (75) report that guinea pigs with orally administered ouabain triplicated their capacity of swimming until exhaustion (the smallest dosis had the biggest effect - 31,5 mg, 63 mg, 94,5 mg / 70 kg). There was no adrenal hypertrophy as noticed in the control group. Similar results with rats are reported by Kuschinsky 1947 (165).  J.M. Hamlyn from one of the leadig workgroups said (166, unpublished data) that rats who had developed hypertension after ouabain had better pelt and were more healthy and agile than the animals without ouabain. Perhaps the hypertension in these rats is not a disadvantage as suggested. A study with these rats concearning the status of health and length of life were interesting.  The studies with other animals (dog, rabbit, sheep) are reporting of an unchanged or even lowered blood pressure after a single dose of ouabain. The sheep used in the study of Pidgeon et al. 1996 (67, double-blind, crossover)) showed a reduction of mean blood pressure, of renin and angiotensin II levels and of sodium excretion after three weeks of 0,25 mg i.v. ouabain daily.  3) Some studies report of statistical correlations between hypertension and ouabain (better: OLS, because all without HPLC) blood levels in patients (for example 167-169). By the way, it should not be forgotten that principally statistical correlations do not prove any causal relations (remembering the simultaneous decline of the number of storks and the number of births). Otherwise a high ouabain / OLS secretion in hypertension could be interpreted as a counteraction against hypertension. Anyway, the biggest recent studies - with J.M. Hamlyn - reveal that normotensive (170) as well as hypertensive persons (171) with a mutation of the adducin gene have higher blood pressure and lower OLS blood levels than those with the unmutated gene, who have lower blood pressure and higher OLS blood levels.  The findings of the study of Gottlieb et al. 1992 (167) are a good argument against overhasty causal interpretaions : The patients with heart insufficiency had higher OLS blood levels than healthy controls. Could therefore ouabain be seen as the cause of heart insufficiency ? The differentiated findings veto this superficial interpretation: Higher OLS levels are found in patients with NYHA I-III, while patients with severe heart insufficiency (NYHA IV) had lower OLS levels. Thus, the higher OLS levels in NYHA I-III could be a physiologic reaction to the disease, while the lower OLS levels in NYHA IV could reflect an exhaustion of the production capacity of the adrenals and the hypothalamus. The fact that ouabain is used in Germany for many decades as a remedy in heart insufficiency pleads for the latter interpretation.  There is considerable clinical evidence that orally administered ouabain attenuates hypertension in patients (8, 9, 35, 42-44) and healthy volunteers (45, 47). On the other hand there are reports by some patients in Germany that oral ouabain is also enhancing hypotension. It is wellknown by the “ouabain doctors“ that in acute heart attack oral ouabain can be given also in cases with very low blood pressure, in which a nitro preparation is dangerous because the possibility of a hypotonic crisis. Perhaps ouabain could be regarded as a blood pressure controling hormone in a physiologically positive manner.  Ouabain was primarily postulated as a natriuretic hormone acting by inhibiting the Na-K-ATPase (sodium pump) in the kidneys and - as a side effect - also in the blood vessels creating hypertension. Meanwhile the natriuretic action of ouabain / OLS could be disproved; in contrast according to Manunta et al. 2001 (172, one of the leading workgroups, with J.M.Hamlyn) there is no difference in OLS blood levels between salt-sensitive and salt-resistant hypertensive patients and ouabain blood levels are elevated in hypertensive patients only in the case of sodium depletion (172). Even the creator of the original hypothesis in 1961 himself, H.D.DeWardener, proclaims already 1997, that ouabain is not a natriuretic hormone (173). Other substances are better candidates (174-175). Also Marinobufagenin has all properties to fulfill the criteria of a natriuretic and blood pressure enhancing hormone (176).  D´Urso et al 2004 (177) report that the rat heart is producing ouabain (verified with HPLC) in ischemia. De Angelis & Haupert 1998 (178) report that rats breathing air with reduced oxygen content had elevated ouabain blood levels.(confirmed by HPLC). This studies remember of the therapeutic effects of orally administered ouabain in angina pectoris and myocardial infarction. Probably the hormone ouabain has a positive physiological function in the heart - and perhaps in other tissues.   **The solution of the problem is not wanted**  Unfortunately there has been a systematic opposition against the excellent therapy with oral ouabain in angina pectoris and myocardial infarction, a German "speciality", so that the numerous published convincing proves were not proclaimed adequately. From 1905 until the 1950ies ouabain i.v. was the german official therapy in heart insufficiency and also partially in angina pectoris and myocardial infarction, which were rare diseases at that time. The exasperated controversity reaches back to ca. 1950, when some of the German universities supported this therapy with which you see results which are unparalleled by any other, even modern medication. The one and only repeated and ruminated “argument“ against ouabain was the pretended bad oral absorption of ouabain. Especially in the 1970ies and 1980ies an International Society for Infarct Combat, renamed as International Society for Infarct Prevention (179), (= “Internationale Gesellschaft für Infarktbekämpfung“ and “...Infarktverhütung“ respectively), which was founded by Dr.med. Berthold Kern, the developer of the oral ouabain therapy, with many doctors and some supporting professors, strived for acknowledgement of the respective facts, but the "suppression fraction" of the medical establishment was too strong, In that time Prof. Gotthard Schettler was the main opposer. In part it seemed to be a private war of Prof. Schettler against Dr. Kern. They knew each other from the 1950ies in Stuttgart, where Dr. Kern had a big practice and Prof. Schettler were the leader of a hospital and counteracted the therapy of Dr. Kern.  In 1971 Prof. Schettler, who was at that time leader ot the German Society for Internal Medicine, invited Dr. Kern to a symposium in Heidelberg to discuss the ouabain therapy. Dr. Kern hopefully went to Heidelberg with six other supporting persons and expected the same number of discussing partners. But he was very surprised when there were 160 professors present and a great number of journalists of every important journal of the medical and the “yellow“ press. The agreement that both sides should alternate the presidency of the meeting was ignored: Prof. Wollheim, also a sharp opponent of Dr. Kern, governed alone and blocked the arguments pro ouabain and expanded all, even marginal aspects against Dr. Kern. Dr. Kern who was adressed as “accused Kern“, for the most part spoke alone, but the other side was alternating with prepared speech and dia shows. A main part of the discussion did not concearn the ouabain therapy but the pathogenesis of myocardial infarction (see above). Dr. Kern had substantial criticism in this point of view. The old positions of the “coronary theory“ were really quite contradictory and open to attack - the vulnerable plaques weren´t explored in that days. But the medical establishment insisted on its positions, and at the end of this event that lasted seven hours, the exhausted Dr. Kern was shouted down collectively. Prof. Rilling (Stuttgart / Tübingen), one of the supporting team of Dr. Kern, told the author, that Prof. Schettler who knew Prof. Rilling from older student days, said to him: “What do you do here ? Be careful - this will not have a good end. Dr. Kern is just condemned !“ In the whole press Dr. Kern was denoted as a medical quack and after this execution which the insiders know as “Tribunal of Heidelberg“, only very few doctors and professors dared to support the ouabain therapy in public.  The scepticism of many doctors in testing a substance which is classified as a cardiac glycoside, in angina pectoris, especially when in all textbooks is written that there is 0 % or 1-2 % absorption, is huge. For example there is a doctor, who has seen the excellent success in every of his 150 Angina pectoris-patients, but his collegues are laughing and even don't want to hear his story to the end. (I hope you are still reading...) There are doctors who have Strodival® in their drawer, and in case of emergency (severe angina attack, suspected AMI) they quickly applicate the capsule, but they don´t inform the hospital, what they have done, because they fear to make themselves ridiculous. A real tragical story... The author of this script had also written a scientific book about this theme (see below) with the preface of Prof. Hans Schaefer from Heidelberg, a worldfamous physiologist. Unthinkable that 20 german medical journals don´t want to publish an article, even not a recension, after a telephone call to a responsible editor and mailing the book and texts - only 2 had given notice, the others showes no reaction at all, althoug  It is an urgent challenge to save the real possibility to solve one of the biggest medical problems (really: Oubain could be in Coronary Heart Disease something like insulin is in Diabetes.) and to preserve a blessed medicine that helps so many patients. But there is an acute danger that oral ouabain could die: It is expected that there is no prolongation of the licence for Strodival®, the last orally administered ouabain preparation, because the big and cost-intensive clinical double-blind study is missing. Even a big multinational company would not pay a study for a substance without a protection by patent. The orally ouabain therapy may die in 2005, although the existing studies and reports are overwhelmingly convincing. The producer counts on the imminent end of ouabain production to 99,9 percent. A real tragedy...  A recent event (December 2005): For the first time in history the ministry of health as the competent supervisory authority issued an instruction to the federal office that is responsible for the license of medicinal products, namely that the license of Strodival(R) has to be prolonged because of an extraordinary public interest regarding the immense potential of this substance. In november 2005 the author participated at an intern meeting in Bonn between the two parties (ministry: 5 persons, federal office: 3 persons), additionally with two physicians who reported about their experiences with two hundred respectively several thousands of patients. Also 40 letters of patients were presented who reported their great fear about the time when Strodival no longer is available. Nonetheless the unimpressionable federal office was furthermore against Strodival(R) and protested against the instruction. There is a close relationship of the federal office with the pharmaceutical industry who is financing the office for the most part.  In 1996 the old producer “Herbert Pharma“ in Wiesbaden/ Germany was adopted by “BRAHMS Arzneimittel GmbH“ in Wiesbaden (the new name was “Herbert Arzneimittel GmbH“). In 2003 “Herbert“ was selled by “BRAHMS“ to “MEDA“, a Swedish combine. By the way, the director of the mother company BRAHMS AG, Dr. Bernd Wegener, is the first chairman of the organisation of pharmaceutic manufacturers in Germany ! (“Bund Deutscher Pharmazeutischer Industrie“) While the old, small producer was very busy in fighting for the ouabain therapy, the new producer is quite inactive. For example information about ouabain (g-strophanthin) was never found on the homepage of “BRAHMS“ or “MEDA“ (...)  Without doubt ouabain (g-strophanthin) could be the solution of the problem cardiac infarction to a large extent and especially the therapy with orally administered ouabain and the knowledge about this drug has to be brought forward because of medical, ethical and economic aspects.  Rolf-Jürgen Petry - 8. Aug, 18:14  [**...**](http://ouabain.twoday.net/stories/886258/)  **Appendix: More unknown pathogenetic aspects of acute myocardial infarction**  Because the effect of ouabain is nowadays explainable in both theoretical settings, compatible with the following “new cardiac infarction hypothesis“ as well as with the accepted theory of cardiac infarction, the following controversial standpoints are in fact very interesting, but in comparison to the concrete clinical success of ouabain only a matter of secondary interest, especially if they should provoke disaccord. Dr.med. Berthold Kern, the explorer of the oral ouabain therapy, and the International Society of Infarct Prevention (in the 1960ies up to the 1980ies, see above - the chapter “The solution of the problem is not wanted“) always closely associated the topic “ouabain“ with the “new cardiac infarction hypothesis“ and presented the latter often in a sometimes too unilateral manner, and so the resistance of the official medicine regarding new aspects in the pathogenesis of cardiac infarction was perhaps carried over to the topic of ouabain. Perhaps the “truth“ is a complementary one. In this topic I am not as competent as in the topic of ouabain, and the references are far from beeing complete. (I wish I had the time to read some weeks or months about this fascinating issue.) It is only an attempt to create a new viewpoint in a domain where in the last years many new insights could be won. I hope it is helpful. If you have criticism, please dont “transfuse“ it to the topic of the ouabain medication but rather please inform me ...  A point that has got too little attention is the existance of a coronary artery net inside the heart muscle which is present in every man and woman from birth and is not visible in common angiography. The coronary arteries outside the myocardium, however, are visably constructed like end arteries, with only few collaterals. The intramyocardial coronary artery net consists of countless collaterals and anastomoses. Prof. Baroldi (Washington / Milan) used a special synthetic liquid to perfuse the hearts of human corpses since 1967. After solidification of the liquid he removed all tissue by acid. In that way he made 5000 threedimensional models which revealed the true nature of coronary anatomy (57, 61). Prof. Doerr, the president of the German Society of Pathology at that time, repeated and confirmed the research of Prof. Baroldi in 1974 (65).  The intramyocardial coronary artery net is able to adjust to a stenosis in an extramyocardial coronary artery. In experiments with dogs (180-181, see also 182-183) an immediate and complete ligature of a big coronary branch led to a myocardial infarction in only 50 %. If the coronary ligature was gradually completed over a period of four days, no myocardial infarction was noticed any more, not even an impairment of cardiac output or the ECG. Because the development of coronary arteriosclerosis take place over a much more prolonged period, the significance of a coronary stenosis seen in angiography is put into question by these findings. Autopsy findings from patients with mortal myocardial infarction revealed that the collateral coronary net was always adequately adepted to compensate the stenoses and occlusions of the outer coronary arteries (60-61). The constitution of the intramural coronary net was the same as in patients with comparable outer stenoses and occlusions who had other causes of death (184). A maximal coronary stenosis of > or = 80 % is present in 70 % in coronary ischemic patients and in 38 % in control persons without any clinical sign of ischemia (185). The existance of this artery net should not entice us to overidealise it concerning its function, having in mind for example the possibility of paradox reaction to ischemia (see above, 39-40). There are many studies concerning the endothelial dysfunction, for example due to a reduced nitric oxid (NO). Citation of Schachinger and Zeiher 2000 (186), abstract: “Endothelium-dependent vasodilation is impaired ... mainly due to increased oxidative stress produced by superoxide anions, which rapidly inactivate nitric oxide. Experimentally, an imbalance between nitric oxide and superoxide anions towards reduced nitric oxide bioavailability enhances migration of monocytes into the vessel wall and proliferation of smooth muscle cells.  Citation from Baroldi & Giuliano 1986 (187), abstract: “The high frequency of severe and multivessel atherosclerotic stenosis in non cardiac patients and healthy subjects dying accidentally questions the direct cause-effect relationship between stenosis and ischemic heart disease; supports the view the dramatically enlarged collaterals always found in this condition may have an adequate compensatory role; and suggests the ineffectiveness of occlusion at the site of severe stenosis already bypassed by collaterals. The degree and number of severe stenoses in ischemic heart disease do not predict onset, course, complications, infarct size or death.“ This could perhaps also explain the contradictory findings of Mikkelsson et al. 2004 (188), who reported that in 61 % of fatal myocardial infarctions - having in mind that myocardial necrosis is mostly found in the left ventricle - thrombi were identified in the right coronary artery, although in only 17 % of these cases there was a definite right ventricular infarction. The study discusses a role of right coronary occlusion as a supposed cause of brady-asystolic cardiac arrest, but not the question why these thrombi do not provoke right ventricular necrosis in the other 83 %.  The knowledge about the intramyocardial artery net explains the findings of Ambrose et al. 1988 (189), that myocardial infarction frequently develops from previously nonsevere lesions (remember the experiments with dogs above (180-181, see also 182-183). Citation of Ambrose et al. 1988 (189), abstract: “In this retrospective analysis, progression of coronary artery disease between two cardiac catheterization procedures is described in 38 patients: 23 patients (Group I) who had a myocardial infarction between the two studies and 15 patients (Group II) who presented with one or more new total occlusions at the second study without sustaining an intervening infarction. In Group I the median percent stenosis on the initial angiogram of the artery related to the infarct at restudy was significantly less than the median percent stenosis of lesions that subsequently were the site of a new total occlusion in Group II (48 versus 73.5%, p less than 0.05). In the infarct-related artery in Group I, only 5 (22%) of 23 lesions were initially greater than 70%, whereas in Group II, 11 (61%) of 18 lesions that progressed to total occlusion were initially greater than 70% (p less than 0.01). In Group I, patients who developed a Q wave infarction had less severe narrowing at initial angiography in the subsequent infarct-related artery (34%) than did patients who developed a non-Q wave infarction (80%) (p less than 0.05).“ This indicates that severe, over 70 % stenoses are generally well compensated by collaterals.   The above finding is confirmed by the study of Little et al. 1988 (190), which deals with 42 consecutive patients who had undergone coronary angiography both before and up to a month after suffering an acute myocardial infarction. Citation abstract: “Twenty-nine patients had a newly occluded coronary artery. Twenty-five of these 29 patients had at least one artery with a greater than 50% stenosis on the initial angiogram. However, in 19 of 29 (66%) patients, the artery that subsequently occluded had less than a 50% stenosis on the first angiogram, and in 28 of 29 (97%), the stenosis was less than 70%. ... In only 10 of the 29 (34%) did the infarction occur due to occlusion of the artery that previously contained the most severe stenosis. Furthermore, no correlation existed between the severity of the initial coronary stenosis and the time from the first catheterization until the infarction.“  Also Brown et al. 1986 (191) report about the same phenomenon in 32 patients with myocardial infarction: In 10 cases, this original lesion was less than a 50% stenosis, and in 21 cases less than 60%.  The relatively low incidence of coronary thrombi was just mentioned above (54-66). Citation from Murakami et al. 1998 (54), abstract: “Intracoronary thrombus contributes little to the pathogenesis of average AMI.“ The incidence of thrombi is especially lower in smaller infarcts, for example 8 % in Roberts & Buja 1972 (59) and 27 % in Silver et al. 1980 (56), than in bigger, transmural infarcts (56, 58-59). In addition the thrombi are time-dependent. The longer the period between myocardial infarction and death of the patient, the bigger the frequency of coronary thrombosis (57, 60-66). This could be a indication that the thrombus could be a secondary event. The Swedish cardiologist Erhardt (et al. 1973 and 1976) used an irresistible method: He injected a portion of radioactive labeled fibrinogen into patients after a myocardial infarction. Fibrinogen builds up the thrombus and after this formation there is no exchange of fibrinogen any more. When a patient had died and a thrombus was found, in most cases the radioactivity was present in the whole thrombus, even in the middle section (192-193). This implies that the thrombus was not the cause but the consequence of the myocardial infarction. Prof. Doerr, the president of the German Society of Pathology in the 1970ies, shared the same opinion.  These findings perhaps could be explained by a continuation of the hypothesis of “myocardial infarction by loss of erythrocyte flexibility“ described above (page 6): At first tissue acidification occurs, because of ischemia or myocardial metabolic causes generated by an overstimulated sympathicus (see the next chapter below) or both, which could start the vicious circle of inhibition of Na-K-ATPase and enhanced erythrocyte rigidity which aggravates ischemia, perhaps until a total stop of microcirculation or even developing of a necrosis, without primary occlusion of a coronary branch. This microcirculatory stasis could lead to a tailback of blood in the proximal coronary system which could facilitate the formation of a coronary thrombus at a location of a coronary artery which is narrowed formerly, especially when the infarcted heart cannot build up the normal pressure of blood flowing from the aorta into the coronary system.  A “live report“ of an accidental acute transmural myocardial infarction during angiography of a 45-year-old man with a history of unstable angina is reported by Baroldi 1995 (194): the occlusion of a coronary artery developed 20 minutes after the occurrance of myocardial ischemia in ECG. A longer citation from Baroldi 1995 (194), p. S 4 “Following the fourth left anterior descending injection, the first ischemic electrocardiographic alteration (downsloped ST) occured. At this time there were no subjective or other clinical signs. Since the ECG abnormality persisted, four successive left anterior descending injections were performed without evidence of any change in the angiographic imagings of the coronary lesions. At the last injection the left anterior descending became fainter and disappeared. Again, this change did not result in any subjective, hemodynamic or clinical modifications. Immediate intracoronary vasodilator followed by calcium-antagonists and urokinase failed to restore the flow. ...At this time (approx. 90 min from the first ischemic ECG) the patient felt mild chest discomfort. Percutaneous transluminal angioplasty was then successfully done with re-establishment of a normal left anterior descending lumen. Paradoxically the clinical pattern deteriorated (increased chest pain and marked ST-elevation). Repeated contrast injections in the left anterior descending artery demonstrated ist progressive disappearance from the distal portion to ist origin from the left main trunk. Since another angioplastic attempt failed to restore flow, the patient underwent coronary artery bypass surgery. At that time, the whole left anterior descending artery was filled with coagulated blood (not thrombus) and the lumen was normal. When the clamp was released, both left anterior descending artery and the implanted vein graft distended but there was no flow indicated by the flow-meter. Repeated probings were unsuccessful. The patient recovered from a large antero-lateral-septal infarct.“  Citation Baroldi 1995 (194), p. S 6: “All the therapeutical procedures and clinical / pathological data apparently excluded the role of a spasm, or thrombus in the intramural system. The angiographic ´occlusion´ progressing from distal to left anterior descending origin (not at the site of previous stenoses) at the bifurcation of the main left trunk (unrestricted flow in the left circumflex branch) attested that hindrance of flow in the left anterior desending artery (and vein graft) was due to intramural blockage with secondary blood coagulation (not thrombosis). One case is one case. However, if the latter is the only case of acute transmural infarct in which the sequence of the events was documented, it raises some justified questions and comments. The first question is how many of the 87 % angiographic occlusions in vivo are pseudo-occlusions. Another question concerns the nature of the material removed at surgery or by atherectomy or seen by angioscopy: thrombus or coagulum ? The layered aspect of the different blood elements favors the latter diagnosis. Unfortunately, thrombus and coagulum (´red thrombus´) are often confused.“  Citation Baroldi 1995 (194), p. S 5: “As far I know, this is the only case in the literature in which several events were monitored. It may help in reviewing and understanding the sequence of physio-pathological mechanisms in the natural history of ischemic heart disease in general and acute coronary syndromes in particular.“ Citation p. S 7: “Two final comments regard: (a) the long period of time (90) min in the reported case, from the first ischemic ECG signs to manifest chest pain. This delay questions the correctness in timing the onset of an infarct in several clinical reports and trials; and (b) the angiographic imaging of thrombosis in atherosclerotic plaque of patients with unstable angina. The hypothesis of recurrent thrombosis plus embolization is contradicted by the previously reported case and, in general by the fact that these plaques may maintain for years their ´irregular´ aspects (195) without relation to clinical course. Several studies have shown that fibrinolytic therapy did not improve the prognosis of these patients (196). The concept of unstable, thrombogenic and emboligenic plaque, as the cause of acute coronary syndromes, still needs to be proven.“ Lange & Hillis 1998 (197) report in the “New England Journal of Medicine“ about four large studies with together more than 6400 patients with unstable angina or myocardial infarction, that investigated the use and overuse of angiography and revascularization for acute coronary syndromes in comparison with a control group that underwent a more conservative, medicinal management with revasularization surgery of only few selected patients. Citation p. 1838: “With remarkable clarity and consistency, all four studies show that routine angiography and revascularization do not reduce the incidence of nonfatal reinfarction or death as compared with the more conservative, ischemia-guided approach. In fact, in the VANQWISH study of patients with non-Q-wave infarction, the aggressive strategy (which those investigators call “invasive“) was associated with increased mortality during hospitalization, at one month, and at one year.“  Citation Baroldi 1995 (194) p. S 8: “Cause and pathogenesis of acute coronary syndromes, and ischemic heart disease are still hypothetical. Data may support an antagonist view according the following concepts (198-199): The coronary thrombus..., the frequency of which may have little, if any significance. In fact - and despite some unproved angiographic findings - the thrombus forms in severe stenosis already by-passed by functioning collaterals (199). Therefore, one may speculate that hemorrhage, rupture of the plaque and thrombosis (never shown in small plaques) are secondary events following an infarct. In the case previously reported the infarct was associated with blockage of intramural flow not due to embolization or ´no reflow´phenomenon, unlikely due to spasm of the intramural arterial vessels, and more probably due to extravascular compression by hyperdistension of atonic myocardium (worsening of preexisting hypokinesis) by intraventricular pressure. This intramural hindrance of flow determined a stasis in the infarct-related artery. When this occurs in a vessel with severe atheromathous and vascularized plaque bypassed by collaterals, hemorrhage and possible spasm leading to secondary fissuration and thrombus formation can be expected. (199). Clinical or experimental angioplasty does not result in thrombosis or severe embolization despite fracture of the wall. ...“ Baroldi 1995 (194) states that atherosclerosis may accelerate when distal intramural perfusion is impaired (increased stress forces on and neurogenic conrol of the arterial wall). Citation of Sroka 2004 (200), p.777: “...as a result of such an ischemia, secondary vascular lesions in the coronary-arterial system can occur. The sudden increase of the peripheral vascular resistance accompanying the onset of myocardial ischemia results in abrupt pressure increases within the supplying artery. In this case, tears in the intima and ruptures of plaques can occur, which then themselves can possibly trigger thromboltic-occlusive vascular processes.“  Baroldi 1998 (185) reports of another interesting finding: Adventitial lympho-plamacellular infiltrates around nerves adjacent to the tunica media at plaque site, may have a role both in the regional myocardial asynergy and / or coronary spasm and may be an important trigger of acute coronary sndrome. This process is only present in coronary ischemic patients.   An alternative generation of ischemia  That there is more than only one access to the complex of ischemia, i.e. the coronary stenosis and lack of oxygen, is documented by the follwoing finding: It is known that L-propionylcarnitine prevents ischemia-induced ventricular dysfunction and ST-segment depression in the ECG, not by affecting the myocardial oxygen supply-demand ratio but as a result of its intrinsic metabolic actions (201). As a (perhaps demagogic) parallel a lack of fuel is not the only possible cause of motor problems. This does not exclude the possibility of different mechanisms (i.e. sufficient or insufficient oxygen supply) existing simultaneously in different myocardial aereas.  Hypothetically (a secondary) ischemia could also be generated by the following cascade of events (which should not take place of the accepted hypothesis of ischemia pathogenesis, but could be a complementary cause of ischemia):  The overstimulation of sympathetic nervous system plays a causal role in cardiac infarction, angina pectoris (196, 202-203) and heart insufficiency (204). The hypersympathetic tone leads to massive glycogenolysis, glucose uptake, glucose oxidation and glycolysis, with only a minimal increase of fatty acid oxidation. The supply of pyruvate exceeding the mitochondrial capacity could lead to severe (areobic) lactate formation in the presence of sufficient amounts of oxygen, an aerobic glycolysis (205-207). The high pyruvate / lactate ratio in the coronary sinus blood of patients with angina pectoris, which are investigated predominantly only in the 1960ies, support this possibility (208-212). In animal models of ischemia due to coronary ligation there is a low pyruvate / lactate ratio (213). In patients with unstable angina pectoris myocardial glucose utilization is enhanced in spite of the absence of clinical, electrocardiographic, or detectable perfusion evidence of acute ischemia (214). In patients with coronary artery disease an acceleration in glucose utilization is visible also in myocardial areas supplied by normal coronary arteries (215).   In this situation of lactate production by aerobic glycolysis the decreased pH together with free radicals originating not only from leucocytes and endothelium but also from myocellular mitochondria (216-218) could inhibit the Na-K-ATPase of erythrocytes and could start the vicious circle described above. The tissue acidification could lead to a decrease in contractility (219-220) with subsequent stretching of the myocardial wall and increase of tissue pressure which also promotes ischemia and stasis in the coronary system (194, 221).  The myocardium, especially the inner, subendothelial layers of the left ventricle, can get supplied with oxygen and all other necessary substances only during the diastole, because during the systole the whole tissue is so compressed that all blood is driven back to more proximal sections. It is obvious that an increased heart rate due to a hyperactivity of the sympathetic nervous system contributes to ischemia not only because of increased demand but also because of diminished nutrition time periods of the myocardium. This leads also to a reduced lactate clearance and further tissue acidification.  In the presence of a functionating parasympathetic nervous system a strong sympathetic stimulation leads to an enhancement of acetylcholine production by about 20 times to counterbalance the sympathetic dominance. Simultaneously, afferent vagal fibers induce a reflex withdrawal of norepinephrine production (222, 223). Together with acetylcholine an effectual NO production leads to an enhancement of cGMP production in the myocardial cell to counterbalance the adrenergic cAMP production. In a healthy heart this measures are sufficient to to reestablish the adrenergic-cholinergic balancing process and have a causal anti-ischemic effect. But in the ischemic heart the sympathetic-vagal balance is badly defective.  The activity of the parasympathetic nervous system is markedly decreased in the minutes before ischemia, in part nearly to zero (200, 224-229, see also 230), as measured by heart rate variability (HRV). This leads in the presence of a preexisting increased sympathetic activity to a catapult-like, excessive overstimulation of sympathetic influence on the heart. The acute withdrawal of vagal drive preceding the onset of ischemia are not dependent on coronary artery disease (231-234).   Acute increases of sympathetic activity alone are mostly of no significance for the onset of ischemia (235).  Citation Sroka 2004 (200) p. 769: “A withdrawal of vagal heart activity previous to any manifestation of coronary artery disease proved to be an independent predictor for the onset of cardiac events in the following years (236)“. Citation p. 771: “The extent of vagal withdrawal in instable angina proved to be a prognostic marker in a study continous vagal withdrawals came along with persistent recurrent ischemic events, and increases of tonic vagal activity along with improvements (237).“ Citation p. 772: “As a result of numerous examinations, the extent of vagal withdrawal within the early post-infarction phase proved to be the strongest predictor for the risk of cardiac death within the following years (238-245).“  Citation Sroka 2004 (200), p. 772: “Until around 30 years ago, the medical profession worked on the principle that vagal innervation of the mammal heart is limited to the atrium. This view has since then been revised. ...The density of the cholinergic innervation of the ventricle is assumed to be approximately one fifth in comparison to the atrium (246). A striking characteristic of the parasympathetic cardiac innervation lies in the neuroeffectoric junction between the cholinergic fiber and the myocardial cell. In this case, there are no typical synapses but the terminal cholinergic fibers form varicosities that release acetylcholine (ACh) into the interstice. ACh diffuses spontaneously over distances of up to many tens of micrometers and thus reaches effector cells within a relatively large area. These facts were described for the first time 1958 (247) and are now proven (246). Due to this special neuroeffectoric junction, the parasympathetic nervous system reaches, despite its low postganglionbic fiber density, all myocardial cells whose cholinergic receptors are randomly distributed over the entire cellular surface (246)."  In the case of a transplanted heart all nerval connections are lacking. The influence of the parasympathetic nervous system is abolished, the blood catecholamines can act without control: there is a massive lactate production, despite excellent perfusion and oxygen supply (248-250).  Citation Sroka 2004 (200) p. 771: “According to the present state of knowledge provided by HRV analysis, roughly three quarters of myocardil ischemic events are triggered by the autonomic nervous system.“  HRV is higher in females, especially before menopause, lower during winter and decreased by physical and mental strain, a sedentary lifestyle and smoking, whereas physical exercise increases tha vagal tone. Citation Sroka 2004 (200), p. 777: “Especially during childhood, HRV analyses have made it clear that a vivid emotional and relational life is of crucial importance for the development of tonic vagal activity. Permitted feelings, emotional expressiveness and the ability to relate strengthen the vagal tone. The suppression of feelings and affects as well as a lacking ability to relate weaken cardiac vagal activity already during childhood. ...Psychological processes apparently influence the central parasympathetic power to a large extent. By means of HRV analysis, it is proven today that the tonic vagal activity is an intregral part of the socio-emotional development of a human being (251). ...Chronic suppression of the expression of feelings weaken the vagal tone (252). .... Touch (253), sex (255) and love (255) stimulate cardiac vagal activity.“  The hypothesis of a noncoronaryly generated ischemia is paralleled by the paradigm shift regarding sepsis, which shows that lactate production by sceletal muscle is not caused by a lack of oxygen, in humans (88, 256-257) and animals (89-90, 99-102, 258-60 nor by a defect in energy production (259-261). The title of the study of Gore et al. 1996 (257) is: “Lactic acidosis during sepsis is related to increased pyruvate production, not deficits in tissue oxygen availability.“ The same mechanism was accepted by Prof. Joseph Keul already in 1967 regarding the skeletal muscle during exercise (261-262). Also Cerretelli & Samaja M2003 (263) speak about an aerobic glycolysis that generates sizeable amounts of lactate and H(+) by way of the excess of glycolytic pyruvate supply.  Only a short notice regarding two points which are widely ignored: Vitamin B1 is a neurotransmitter of the parasympathetic nervous system (synonym: “Aneurin“ !). Furthermore the acetycholine synthesis is dependent of Vit. B1, also the degradation of glucose: Vit. B1 is part of the alpha-carboxylase I, which is necessary for the degradation of pyruvate and the following oxidative steps. Without Vit. B1 only anaerobic glycolysis is possible. It is approximated that the average population in the western world with its generally deficicency of vital substances in the fabrical food has a deficicency of vit. B1 because of the consumation of isolated carbohydrates (white flour and fabrical sugar in all variations).  The other one is the point of “hyperproteinism“, which has been intensively investigated by Prof. Lothar Wendt (Frankfurt on the Main). Too much protein because of a high consumation of meat results in a protein storage in the capillaries and later in the bigger arteries. The basal membran directly behind the endothel cell layer thickenes up to tenfold, and also the pores of this membrane get narrowed. Also the interstice is a target for the protein deposition. The effect is a hindrance of the passage of important substances, for example Vit. B1, a relatively large molecule, and ouabain and carnitine. (Oxygen is a very small molecule !) Also the evacuation of metabolic end products is complicated. According to Prof. Wendt this phenomenon is the cause of essential hypertension, because the organism augments the blood pressure to enforce the hampered passage through the smaller pores of the thickened endothel membrane. Furthermore it triggers atherosclerosis, because this protein deposition boosts the inflammatory processes known to be involved in atherosclerosis.  I think his elaborated books are only available in german language, but I found a reference in Pubmed (264), unfortunately without abstract, and a lot of pages at google about his work, for example: <http://www.healingcancernaturally.com/stored-protein-diseases.html>  <http://www.dr-schnitzer.de/hypertension-medication-side-effects.html>    **\* About the author**  After Rolf-Jürgen Petry had finished his schooling as an alternative practitioner in 1997, he became a permanent visitor of the medical libraries, where he had copied about 20.000 pages in the last years about ouabain and myocardial infarction. He has read many original studies and found that the orthodox positions with which ouabain is rejected exhibit serious faults. It's really a severe miscarriage of medical justice, as you could see with the proofs above.  He has written the first extensive and detailled book on this theme with 1380 references and the preface of Prof. Hans Schaefer from Heidelberg, who was a world-famous physiologist for some decades. The sharp attacks against the oral ouabain therapy by eminently respectable exponents of the medical establishment are described clearly but always objective and without polemics. The book came out in 2003 and the second edition is in process.   Rolf-Jürgen Petry: Die Lösung des Herzinfarkt-Problems durch Strophanthin (The solution for the problem of myocardial infarction), 320 pages text + 40 pages references, 24,90 € ISBN 3000195874 Verlag Florilegium, Pf 1305, D 27442 Gnarrenburg, Germany Tel. 0049 - 421 - 59 707 92 Fax 0049 - 1212 - 55 14 09 321 e-mail: strophanthin@web.de  The book is on a high scientific level, but at the same time the author had taken great care that it remains understandable even for a person without previous medical knowledge. This book is available only in German language until now. 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