

## May Strophanthin be a valuable cardiac drug ?

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### ABSTRACT

There are cardiac glycosides obtained from various plants. One is the group of digitalis drugs and the other is Strophanthin (= ouabaine). They all have a positive inotropic effect, i.e. they strengthen the heart muscle, lower the heart rate and have an anti-arrhythmic effect. All glycosides are potentially toxic in overdoses, but digitalis is more so than Strophanthin. We have never experienced a toxic effect with Strophanthin. In contrast, we have found that Strophanthin in the form of gastric juice-resistant capsules containing 3 mg has excellent effects in heart failure. The usual cardiological agents can thus be replaced by Strophanthin in many cases.

**KeyWords:** Strophanthin, Ouabaine, Heart failure therapy, Glycosides, Digitalis.

### Introduction

**G-Strophanthin**, also known Ouabaine, is a substance of plant origin on the one hand and a human hormone on the other hand. It is toxic in high doses. It is extracted from the seeds of *Strophanthus gratus* and the wood of *Acokanthera ouabaio*, which are widespread in Africa. Strophanthin is a cardiac glycoside; at low doses it is used to treat certain types of arrhythmias, atrial fibrillation and heart failure. It expresses its action by inhibiting the Na<sup>+</sup>/K<sup>+</sup> ATPase pump, also known as the sodium-potassium pump.(1,2)

### History

David Livingstone was a Victorian-era Scottish physician, missionary and explorer. In the journal of the Zambezi expedition, Dr. Livingstone upon arriving at the Shirè River wrote: "The poison used here, called kombi, is obtained from a species of Strophanthus and is very virulent. Dr. Kirk discovered this by an accidental experiment, which involved him personally, when he found that the poison works by lowering the pulse rate. Although it was in small quantities, the substance had immediately shown its power by lowering his pulse rate, which had

previously been increased by a cold, and the next day he was perfectly recovered. Not much can be deduced from a single case, but it is possible that kombi may prove to be a valuable drug."(3)

### Derivation

The glabrous strophanthus (*Strophanthus gratus*), has flowers with the laciniae of the corolla without appendages, yellow-brown or ochre seeds, glabrous. The drug consists of the seeds stripped of the remains and pappus; the seeds are odorless and have an extremely bitter taste. The active ingredients are glycosides with activity similar to that of digitalic glycosides but with rapid and short-lasting effect; they should be administered by injection because they are poorly absorbable when administered orally. Present in the seeds of *S. gratus* is G-Strophanthin, also known as Ouabaine.(4)

### Chemical structure

Ouabaine, being a cardiac glycoside, has a basic structure characterized by a cyclopentanoperhydrophenanthrene core consisting of 3 cyclohexane rings fused in nonlinear arrangement to a cyclopentane ring. This structure (Figure 1) is responsible for the pharmacological action.(4,5)

The steroid core, lactonic ring, and sugar constitute the typical structure of Ouabaine that allow interaction between the molecule and the sodium-potassium pump binding site.(6,7) Specifically, the nonpolar components of the sodium-potassium pump help to direct Ouabaine by establishing Van der Waals forces while the polar residues of glutamine, aspartic acid and threonine, along with the amide bond of an alanine, form hydrogen bonds

with the hydroxyl groups of the ligand.

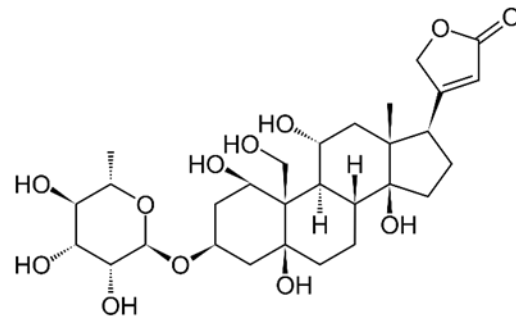


Fig. 1, The structure of the Strophanthin molecule

### Mechanism of action

Ouabagenin is a cardiac glycoside that inhibits the  $\text{Na}^+/\text{K}^+$ -ATPase pump. This transporter allows the active passage of potassium from the extracellular space to the interior of the cell and sodium from the interior of the cell to the extracellular space. Its inhibition causes a change in intracellular ionic composition, causing different effects depending on the cell involved and the dosage.(7)

The binding of Ouabaine to this pump prevents the conformational change necessary for the pump to perform its function, and this inhibition causes indirect effects on the contractile force, or inotropism of cardiac muscle cells. Ouabaine has a positive inotropic effect because inhibition of the  $\text{Na}^+/\text{K}^+$ -ATPase pump causes an increase in plasma sodium concentration since this cation can no longer be transported into the extracellular space. The increased sodium concentration, in turn, allows inactivation of the sodium-calcium exchanger and thus will increase the amount of intracellular calcium that can be accumulated in the sarcoplasmic reticulum. Calcium performs the function of a second messenger in many cellular signaling and regulatory pathways; its release within the cytoplasm of cardiac muscle

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cells increases the force of contraction, thus causing a positive inotropic effect.(7,8)

The positive inotropic action exerted by Ouabaine has also been studied in isolated myocardial tissue. In one study, the activity of Ouabaine on contractile force was shown at a concentration of  $10^{-7}$  mol/L while toxic effects were found at higher concentrations.(9)

Regarding pharmacological action, it was found that the action of Ouabaine at therapeutic concentrations results in a slight shortening of the action potential, a marked increase in intracellular free calcium concentration and contractile force. In addition, the light emitted by equorin, a calcium-activated protein, has also been recorded, and it can be seen that it is directly proportional to the concentration of intracellular free calcium, so it increases in the presence of Ouabaine compared with control. (9)

In conclusion, in these preparations it can be seen that force development and cardiac relaxation phase are both increased, with little or no change in the time required to reach peak force. This effect occurs in both healthy and compromised myocardium.

### **Toxicity**

It is classified as a toxic substance. A likely lethal oral dose is 5 mg/kg in the human species.(10) However, the applied therapeutic dose is usually 3 mg/person. To reach the toxic range, a normal person (60 kg) has to take 300 mg = 100 capsules. Ouabaine exerts its action in all excitable tissues, including smooth muscle tissue and the central ner-

### **Pregnant Women**

Ouabaine crosses the placenta, but the concentration in fetal and amniotic fluid is lower after a single dose than the concentration detected in maternal plasma.(11)

### **Elderly**

Maintenance dosages should be adjusted according to renal function.(11)

### **Side effects**

Possible adverse effects of exaggerated-doses of Ouabaine are: vomiting, headaches, pulse irregularity, heart block.(12)

### **Metabolism and pharmacokinetics**

Ouabaine is not extensively bound to plasma albumin and is mainly excreted unchanged.(13)

### **Absorption, distribution and excretion**

It is poorly absorbed by the gastrointestinal tract, where most of the orally administered dose appears to be metabolized.(14) So oral use as tincture or in normal capsules is not considered safe precisely because of the slow and irregular absorption of the substance by the gastrointestinal tract.(15) The effect of intravenously administered Ouabaine is seen immediately after injection, peaks after 5 minutes, lasts for about 5 to 7 hours and then declines rapidly.(16)

### **Half-life**

It is eliminated almost completely by renal excretion; its half-life is about 21 hours in healthy adults;

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however, it is longer in the elderly and even longer in renal insufficiency.(15)

### **Effect on catecholamine secretion**

In several studies, Ouabaine was seen to increase catecholamine secretion induced by acetylcholine (10-5 M), pilocarpine (10-3 M) and nicotine (3x10-6 M) during perfusion with Locke's solution. The adrenaline/noradrenaline ratio did not change from the use of Ouabaine. Furthermore, in the absence of extracellular calcium, acetylcholine and pilocarpine (but not nicotine) cause a small increase in catecholamine secretions, which were previously increased by treatment with Ouabaine (10-5 M) and calcium (2.2 mM) for 25 min.(17,18)

### **Endogenous Ouabaine**

The fact that there is a receptor for cardiac glycosides on the sodium-potassium pump has led some researchers to hypothesize the existence of an endogenous digitalic steroid-like, possibly Ouabaine or marinobufagenine.(9)

In fact, four biologically active inhibitors of the sodium-potassium pump have been detected in the human circulation that appear to be endogenous in mammals. Of these, one has been purified, and by various analyses, has been identified as a steroidal isomer of Ouabaine; in which the position and orientation of two or more steroidal hydroxyl groups differ. This isomer would be secreted by the adrenal cortical and play a role on cardiovascular function.(19)

Human endogenous Ouabaine would cause reversible inhibition on the sodium-potassium pump to

give inotropic and vasopressor activity.(19) Levels of circulating endogenous Ouabaine would depend on the adrenal cortical and the metabolic events that precede and follow pregnenolone formation. Within the adrenal cortical, the mechanisms of stimulation and secretion of endogenous Ouabaine would be distinct from those for aldosterone, thus indicating different regulations.(19)

### **Digitalis**

One should compare Strophantin with digitalis glycosides, e.g. Digitalis purpurea. Indeed, the leaves of this plant contain some pharmacologically active glycosides (e.g. digitoxin and digoxin) that have a powerful effect on the heart: they increase the contractile force of the heart muscle (positive inotropic effect) and have antiarrhythmic properties. They are mainly indicated for the treatment of heart failure. However, these same substances, when taken in excessive doses, can cause serious problems such as cardiac arrhythmias and heart block, sometimes fatal.(20)

Digitalis is a classic example of a plant-derived drug that has been used as a remedy in folk medicine. Its use has since been abandoned in herbal medicine due to its low therapeutic index and difficulty in determining the active dose. When properly dosed, digitalis toxin can increase cardiac ejection fraction. However, it is known that digitoxin and digoxin can lead to steep dose-response curves, i.e., a slight increase in the dosage of these substances can make the difference between a harmless and a lethal dose. It also has a vagal effect on the parasympathetic nervous system and is therefore used for recurrent arrhythmias and to slow ventricular

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velocity in atrial fibrillation.

The therapeutic concentration range in the blood is narrow with digitalis, and the toxic range is already reached with only several overdoses. Nevertheless, digitalis preparations were and are used, whereas Strophanthin was and is demonized as toxic. «Honi soit qui mal y pense».

A new publication on the subject of heart failure lists the currently indicated five agents: «ACE inhibitors, beta blockers, mineralocorticoid receptor antagonist, dapagliflozin, loop diuretics». These are all used in combination when possible.(21,22) Side effects are inevitable. What if Strophanthin could replace these expensive agents?

### Our experience

We have had the best experience with Strophanthin, and use - to avoid poor absorption in the stomach - 3mg enteric coated capsules. In mild cases 1 capsule per day, up to a maximum of 6 capsules in severe heart failure. We have always had success, even with the frequent arrhythmias with atrial fibrillation (esp. taking place since the mRNA vaccinations). No patient treated in this way suffered a heart attack or stroke. In cases with oedema, additional spironolactone/aldactone has proven successful.

### Conclusion

The author himself experienced how around the year 1970 in cardiology the non-patentable and proven Strophanthin was replaced by digitalis drugs (e.g. beta acetyldigoxine), which were patentable. The problem of overdoses and possible deaths was dealt with by determining the concentrations of digoxin in the blood. Troublesome. This procedure was

justified by the toxicity of Strophanthin and the low absorption in the stomach. What can be said about this? On the one hand, digitalis is much more toxic; in the case of strophanthin, the danger to life is only reached when approximately 100 capsules of 3 mg each are taken at once. On the other hand, absorption can easily be optimized by means of gastric juice-resistant capsules. We have been using this preparation for several years with excellent success. In Germany there is an association that tries to spread the truth about Strophanthin.(23) Many satisfied patients join the association.

### References

1. Faktenblatt zu Strofantine-G , auf sigmaaldrich.com , Sigma Aldrich.
2. A. Benedicenti, OUABAINA , in Enciclopedia Italiana , Rome, Istituto dell'Enciclopedia Italiana, 1935.
3. Wie ich Livingstone-Reisen, Abenteuer und Entdeckungen in Zentralafrika fand von Henry M. Stanley, 1872; zitiert in Marcello Nicoletti, Pharmazeutische Botanik: Geschichte, Aktivitäten und Verwendung von Heilpflanzen , EdiSES, 2007, S. 279, ISBN 978-88-7959-377-9 , OCLC 849072004 .
4. F. Senatore, Pharmazeutische Biologie und Botanik , 2. ed, PICCIN, ISBN 978-88-299-2126-3 .
5. F. Capasso and Rita De Pasquale, Pharmakognosie: Botanik, Chemie und Pharmakologie von Heilpflanzen , Springer Verlag, 2011, pp. 233–241, DOI : 10.1007/978-88-470-1652-1\_16 , ISBN 978-88-470-1651-4
6. Natrium-Kalium-ATPase – Proteopedia, Leben in 3D , in: proteopedia.org
7. Ouabain – Proteopedia, Leben in 3D , in: proteopedia.org
8. OUABAIN | CAMEO-Chemikalien | NOAA , in: cameochemicals.noaa.gov .

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9. B. G. Katzung and T. W. Vanderah, *Basic & Clinical Pharmacology* , 15. ed, ISBN 978-1-260-45231-0 .
  10. OUABAIN , [www.cameochemicals.noaa.gov](http://www.cameochemicals.noaa.gov) , CAMEO Chemicals | NOAA.
  11. C. Dollery, *Therapeutic Drugs* , vol. 2, 2. ed., Churchill Livingstone, 1999.
  12. Ouabaina , [su.humanitas.it](http://su.humanitas.it)
  13. Goodman, L.S. and A. Gilman., *The Pharmacological Basis of Therapeutics* , 5. ed, New York, Macmillan Publishers, 1975, p. 673 .
  14. Gosselin, R. E., R. P. Smith und H. C. Hodge, *Clinical Toxicology of Commercial Products* , 5. ed, 1984, p. 842.
  15. A. Osol (ed.), *Remington's Pharmaceutical Sciences* , 16. ed, Easton, Pennsylvania, Mack Publishing Co., 1980, p. 798.
  16. Furstenwerth H., *International Journal of Clinical Practice* , vol. 64, 2010.
  17. American Medical Association, *AMA Drug Evaluations* , 5. ed, Chicago, 1983, p. 611.
  18. Ouabain unterscheidet zwischen Nikotin- und Muskarinrezeptor-vermittelten Katecholaminsekreten in durchbluteten Nebennieren von Katzen. , [www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)
  19. Beobachtungen zur Natur, Biosynthese, Sekretion und Bedeutung von endogenem Ouabain , in: [pubmed.ncbi.nlm.nih.gov](http://pubmed.ncbi.nlm.nih.gov)
  20. <https://de.wikipedia.org/wiki/Glycoside>
  21. Albrecht R., Christen S., Alt und herzinsuffizient – wie findet man die optimale Behandlung? *Der informierte Arzt* 08 (2023) p. 38 (Switzerland)
  22. <https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/CVD-Prevention-Guidelines>
  23. <https://strophantus.de/>