

# THOUGHTS AND QUESTIONS ARISING UPON THE RECOGNITION OF THE BROADLY BIOACTIVE AND VERY WELL TOLERATED ANTISEPTIC N-CHLOROTAURINE AS A HIGHLY USEFUL MEDICANT FOR PROPHYLAXIS AND THERAPY

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## Мысли и вопросы, возникающие после признания широкой биологической активности и хорошей переносимости антисептика N-хлоротаурина как полезного лекарственного средства для терапии и профилактики

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This report emerged from the experiences and observations of the authors who explored fundamental features of NCT and accounted for production and essential understanding of its realm of welcome properties. N-chlorotaurine (NCT) is an endogenous mild active chlorine compound, which can be synthesized chemically and applied topically as an effective anti-infective and antiseptic to different body sites. Naturally, it is produced by activated human granulocytes and monocytes during the oxidative burst. Besides the typical broad-spectrum microbicidal activity of chloramines against all kinds of microorganisms, it has anti-inflammatory properties and is involved in termination of inflammation. Because of its high tolerability and absence of systemic adverse effects due to decay to ubiquitous taurine and chloride, it can be used in sensitive body regions, too, for instance the eye, body cavities and lower airways. The latter renders NCT inhalation a promising means for the prevention and treatment of viral pneumonia including SARS-CoV-2 (Covid-19), chronic bronchitis, and cystic fibrosis. Further clinical development is urgently needed to characterize the preventive and therapeutic effects in detail. Particularly the time of the present pandemic confirmed how difficult recognition and support of innovations frequently is.

**Keywords:** *N-chlorotaurine; antiseptic; anti-infective; Covid-19; nose spray; mouthwash; inhalation; tolerability; prophylaxis; public health*

Работа подготовлена на основе опыта и наблюдений авторов, которые изучали фундаментальные особенности N-хлоротаурина и учитывали возможности его производства и существенных его характеристик. N-хлоротаурин (NCT) является эндогенным «мягким» активным соединением хлора, которое может быть синтезировано химическим путем и применено местно в качестве эффективного антиинфекционного и антисептического средства на различных участках тела. Естественным образом он вырабатывается активированными гранулоцитами и моноцитами человека во время окислительного взрыва. Помимо типичной для хлораминов бактерицидной активности широкого спектра, он обладает противовоспалительными свойствами и участвует в прекращении воспаления. Благодаря высокой переносимости и отсутствию системных побочных эффектов, связанных с распадом на повсеместно распространенные таурин и хлорамин, его можно использовать и в чувствительных областях организма, например, в глазах, полостях тела и нижних дыхательных путях. Последнее делает ингаляции NCT перспективным средством для профилактики и лечения вирусной пневмонии, включая SARS-CoV-2 (Covid-19), хронического бронхита и муковисцидоза. Для детальной характеристики профилактических и терапевтических эффектов срочно необходимы дальнейшие клинические разработки. Время нынешней пандемии, к сожалению, подтверждает, как зачастую трудно бывает пройти путь признания важных инноваций, их поддержку и дальнейшую реализацию на практике.

**Ключевые слова:** *N-хлоротаурин; антисептик; антиинфекционное средство; Ковид-19; спрей для носа; ополаскиватель для рта; ингаляция; переносимость; профилактика; общественное здоровье*

### Historical background

**a) Gaining samples of novel naturally occurring agents.** A first information about the structure and specific properties of exemplary new agents needs their isolation from the natural environment, for instance cell culture or living tissue. It is evident that this involves a

rather tricky venture. Moreover, the yield will be rather low. Nevertheless, only using the pure active agent it is possible to establish the chemical structure and evaluate intrinsic chemical properties of a promising new agent.

**b) Who invented N-chlorotaurine (NCT)?** The first reference of NCT, molecular formula  $\text{Cl}(\text{NH})\text{CH}_2\text{CH}_2\text{SO}_3\text{Na}$ , in medical spheres also wrongly

named «taurine chloramine»<sup>1</sup>, dates back to the year 1971 when Polish researchers identified NCT as a natural active agent produced by activated human leukocytes and monocytes during inflammation with the purpose to kill the provoking microorganisms and to terminate the inflammation [1–2].

**c) Development of a pharmaceutic advantageous in medicine.** The next step in the evolution was the synthetic approach found by Gottardi, namely chlorination of taurine with chloramine T, which allows to provide it in unlimited quantities. The method was also applied for a patent. *Note:* Scrutinizing the patented NCT production, it came forth that the reaction product was contaminated with originally not detected impurities, which did not meet the requirements of pharmaceutical quality particularly for applications in delicate regions like the lower airways, the eye, body and abscess cavities. Consequently, it was necessary to modify the method, which finally succeeded furnishing NCT of almost 100% purity. Due to all these efforts, the laboratory guided by the authors of this publication can be estimated as the international reference regarding production of NCT in pharmaceutical quality, antimicrobial properties of NCT and its clinical development as antiseptic and anti-infective.

**d) NCT: a biocompatible drug.** Based on its mild oxidizing power it is — opposite to the very irritating HOCl — well tolerated by human tissue. A second consequence of its low reactivity is that it is not completely inactivated by reaction with reducing components of the tissue and part of the «long-lived» oxidants of innate immunity [3]. The source of this behaviour could be reduced to the lower oxidizing power of the N-Cl bond compared to the O-Cl bond derived from molecular constants published by Pauling [4]. NCT can be applied in high concentrations around 1% (55 mM), which enhances its sustainability, too [5]. These and other welcome features of NCT have already been summarized in review articles [6–9].

### What is the mode of action?

The active principle of NCT concerns the ability to oxidize and destroy vital components of the microorganisms causing infection. This very old insight was reported for the first time in the year 1831, when patients suffering from pulmonar tuberculosis were treated with inhalations of chlorine and iodine [10]. This kind of therapy, however, did not make its way and was not persecuted further, mainly caused by unexpected tissue-irritation and impossibility to reach the pathogens deep in the tissue. Interestingly, this instance reveals that in those times tolerability was no imperative category. Experience of following research indicated that this problem seemed to be solvable by using highly diluted oxidants (e.g. elements like chlorine and iodine,

hypochlorous acid and its alkali salts). It soon came out, however, that highly diluted strong oxidants in practice rapidly become ineffective because of inactivation by reducing tissue components [7, 11–12]. A satisfactory improvement is application of an agent revealing a low-strength oxidizing potency, which complies with the concurrent specifications adequate microbicidal power and tolerability. As an appropriate example, NCT was found finally, which perfectly fulfilled the claims of efficacy and tolerability at a concentration of 1% (55 mmol/L) [5, 6, 8, 13].

*Conclusion:* NCT protects from virulent microorganisms by killing them in an oxidative manner.

### Where is the location of microbicidal activity?

Since NCT is not compatible with blood (where it is immediately reduced), systemic application is not possible. Despite this drastic limitation valid for antiseptics in general, it has the odds of an intervention directly at the location of the inflammation, i. e. surfaces of organs like eyes, ears, skin, upper and lower airways.

*Conclusion:* The location of action resides right at the site of the inflamed tissue.

### Can NCT be suitable to control Covid-19?

This disease has several manifestations, from harmless to severe. Early administration of NCT and other antiseptics to the nose and throat in early stages can reduce the viral load and is highly suggestive to avoid progression to the lower airways and can be conceived to reduce the number of complications such as long Covid syndrome. Inhalation of NCT in patients with bronchitis and pneumonia may reduce the life-threatening syndrome and requirement of intensive care. Case series and hitherto studies with antiseptics confirm these intentions [14–20].

*Conclusion:* NCT may be to be a good means for combatting Covid-19 and its complications if administered in time. Controlled studies are urgently needed.

### Possible adverse effects of NCT

Since NCT is produced and released naturally (evolution controlled) by leukocytes and monocytes in case of an attack of noxious microorganisms and detoxifies HOCl upon its formation, therapeutic application of the completely identical synthetic agent per se is improbable to have severe adverse effects. This has turned out to be true in several clinical studies and many cases in topical application at different and sensitive body sites, where only transient and mild itching and burning may occur, and no systemic adverse effects.

<sup>1</sup> The name «taurine» already includes an amino-group (synonym of taurine is 2-amino-ethanesulfonic acid), why introducing a second amino-group with the apposition «chlor-amine» to taurine is misleading.

*Conclusion:* Presumed NCT is guided by professional personnel, considerable adverse effects can be excluded.

### Attempts to bypass patent protection

Referring to the development of NCT as a «well established» product, the intention of some companies to bypass the patent protection must be mentioned. Besides copying the underlying chemistry, they also tried to overcome the known reduced thermal stability, which necessitates to maintain a cooling chain for storage, which, however, means additional costs.

Encouraging results in view of «stabilization» were achieved by substituting the protons of the amino-function in NCT (2-amino-ethane sulfonic acid) by two methyl groups [21]. Though the resulting compound N-chloro-dimethyl-aurine and similarly textured ones revealed adequate stability [22–23], the desired compromise between bactericidal activity and tissue tolerability was not achieved, which is the main reason for NCT's pre-eminent properties [5, 6, 8, 13, 24, 25]. As a consequence, the idea to obviate a patent protection by applying a structural modification or even introducing a new compound was finally abandoned. This insight reveals the extraordinary trait of NCT representing an imitable and globally applicable pharmaceutical drug, which additionally is easily accessible, even in big dimensions and at a reasonable price.

*Conclusion:* Due to the insight that it seems impossible to obtain a different (other, second) compound featuring the same excellent properties, the plan to obviate a patent protection was finally abandoned.

### Can an antiseptic foster the eradication of Covid-19?

In view of the assiduous vaccinating measures, problems came forth due to the incidence of new mutants of Covid-19. At this situation, the application of an antiseptic like NCT appeared to be helpful, an assertion, which is based on experiments with NCT showing a killing efficacy against virtually all pathogens except spores of bacteria [6, 13, 26]. The comprehensive virucidal activity including SARS-CoV-2 has been shown, too [16, 18, 27–33]. Resistance development does not occur in active chlorine compounds as NCT, so that mutants of viruses will not play a role for therapeutic efficacy, which is similar to bacteria and fungi [26, 34].

## The utility of prophylactic activities

A reasonable application area concerns the prophylactic application of antiseptics to the upper airways after possible contacts with persons infected with Corona or other viruses, for instance upon meetings or crowding of people. Nose sprays and mouth rinses and gargling solutions to reduce the viral load rapidly and to prohibit the outbreak or to attenuate the course of infection are a logical approach and recommended, although definitely proving controlled clinical studies still need to be done [15, 16, 19, 35–36]. NCT appears to be a suitable candidate due to its high tolerability and broad-spectrum microbicidal activity typical for active halogen compounds [6, 17, 18, 37]. Even its inhalation is possible [38].

*Conclusion:* Hitherto evidence substantiates the high qualification of NCT for the cited options and confirms NCT as an efficient prophylactic agent.

### How reliably recognize persons involved in hygienic and public domains medical innovations released to the public?

A surprising and rather absurd, but possibly typical experience made a colleague and specialist in the field. Himself being very convinced of the beneficial potency of NCT, he sent written information on NCT to numerous (on the whole approximately 25) persons of sanitary and public relevance (hygienists, government officials, politicians, ministers of sanitary affairs, and others). It contained also a proposal how to comply with difficulties at combatting Covid-19. Unexpectedly, this action did not call forth interest as only scarce replies were sent back at all, which mainly contained the disappointing information of a non-existing interest.

The attitude of ignoring such a message by hygiene specialists could be comprehended as induced by a «not invented here» attitude or syndrome [39]. In case of public persons (e.g. politicians), who are rather responsible for the welfare of people, however, a form of ignorance is to fear. The missing recognition of the innovation contained in the dispatched NCT-information implicated a failure of the intended dissemination of a promising innovation with an impact on health and welfare.

*Conclusion:* To leave a realistic possibility to decrease the risk of patients suffering from a severe and potentially lethal disease unused, appears not justifiable for ethical reasons. Even more, viral spreading potentially could be reduced.

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