Going Beyond Antibiotics™

Scientific Backgrounder on Hypochlorous Acid (Neutrox™) and Dichlorodimethyltaurine (NVC-422), the Lead Aganocide® Compound

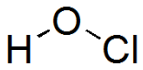
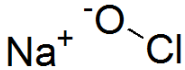
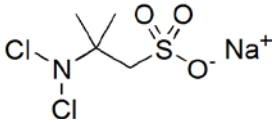
Hypochlorous Acid (HOCl) is Distinctly Different from NVC-422

NovaBay has developed two separate categories of anti-infective products, each with distinctive chemical structures, unique properties and target indications. The two categories have strong similarities, in that both are based on molecules produced by white blood cells as the first line of defense against invading microbes. Unlike antibiotics, neither class of product can give rise to resistant bacteria, because each uses oxidation of essential microbial proteins as its mechanism of action.

One category of products, which include i-Lid™ Cleanser, NeutroPhase™ and CelleRx,™ is based upon NovaBay's patented, proprietary formulation of pure hypochlorous acid (HOCl; see Figure 1A) in solution. HOCl is the most active anti-bacterial, anti-fungal and virucidal compound produced by a type of human white blood cells called neutrophils. HOCl is a charge neutral, small, short-lived inorganic compound that has the ability to rapidly inactive bacteria and fungi[1], bacterial toxins[2], and viruses[3]. Due to its small size and lack of ionic charge, HOCl can penetrate into bacterial biofilm and spores. In addition, HOCl exhibits anti-inflammatory activity by neutralizing inflammatory mediators in the body and those exuded from pathogens.

A number of commercial products, such as Dakin's solution contain HOCl. However, all other allegedly HOCl-based products also contain sodium hypochlorite (NaOCl; Figure 1B), the primary ingredient in household bleach. Because it is a charged species which cannot easily penetrate into bacteria, sodium hypochlorite is less effective at killing bacteria than HOCl. It is also substantially more toxic to healthy cells.[4]

Figure 1. The chemical structures of HOCl, sodium hypochlorite and NVC-422

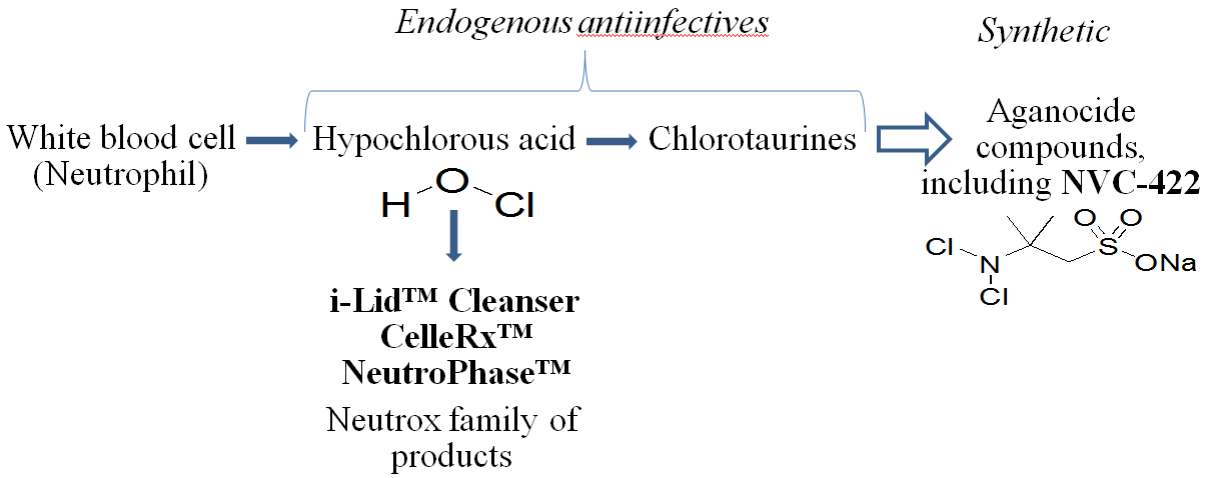
A	**B**	**C**
		
Hypochlorous acid	**Sodium Hypochlorite**	**NVC-422**
HOCl	NaOCl	Dichlorodimethyltaurine
Uncharged	Charged	Charged

NovaBay Pharmaceuticals, Inc., has developed an essentially pure solution of HOCl in a formulation that is made via a proprietary manufacturing process.[5] The company calls this formulation Neutrox™. i-Lid™ Cleanser, NeutroPhase™ and CelleRx™ are all members of the

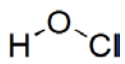
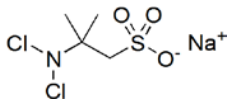
Neutrox family of FDA-cleared products currently marketed by NovaBay. Each of these products has been carefully formulated for the management of targeted medical conditions. Each is free from bleach-like impurities due to NovaBay's proprietary, patented manufacturing process. In contrast, other manufacturing processes for making HOCl yield significant amount of sodium hypochlorite (common bleach). Bleach-like impurities have the potential to be toxic to healthy tissues.[4]

The other category of NovaBay anti-infective products are Aganocides® such as NVC-422 (Figure 1C).[6] Aganocides are synthetic organic analogs of naturally occurring chlorotaurines, which are metabolites of hypochlorous acid (see Figure 2). When human white blood cells detect invading pathogens, they undergo an 'oxidative burst' and produce potent anti-microbial chemicals to destroy and inactive the microbes; those chemicals include both HOCl and the chlorotaurines. NovaBay has developed composition-of-matter patent-protected, rapidly acting molecules based on chlorotaurine – the Aganocides. In contrast to HOCl, they do not penetrate readily into cells and primarily affect surface/extracellular targets on bacteria, fungi and viruses. As a result, they have different medical uses than does HOCl, or Neutrox.

Figure 2. The relationship of HOCl to Aganocide compounds such as NVC-422



There are distinct medical uses for the two product families. Neutrox-based products are designed to cleanse skin (including eye lids), control bacteria and biofilms in wounds, and help heal delicate skin after surgical or laser procedures. Physicians have reported success using NeutroPhase to help fight flesh-eating infections and i-Lid Cleanser to control often-painful conditions like blepharitis. In contrast, the Aganocides are design to be used in conditions in which more sustained action against microbes is needed, such as irrigation of urinary catheters or skin infections such as impetigo. They work more slowly than HOCl, but last longer. The key differences between the two product groups can be summarized as follows:

Property	 **HOCl** (in Neutrox)	 **NVC-422** (an Aganocide)
Endogenous	√	No
Bactericidal	√	√
Fungicidal	√	√
Virucidal	√	√
Speed of activity	Very fast	Fast
Duration of activity	Short	Longer
Formulatability	Good	Excellent
Cytotoxicity	Low	Very low
Regulatory status	FDA-cleared	Investigational – IND
Patent protected	√	√

In summary, NovaBay's family of Neutrox products is quite distinct from the Aganocide compounds which are being developed as drugs. Each group has its own unique chemical identity and targets distinctly different unmet medical needs. Since the human immune system works without creating bacterial resistance, NovaBay has based its anti-infective technology on the effective and rapidly acting molecules that function within our own bodies by creating pure or stable analogs of these compounds.

References

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Contact:

Keith Bley, Ph.D.
Senior Vice President, Product Development
NovaBay Pharmaceuticals
www.novabay.com
(NYSE-MKT: NBY)
write to me by going to our website: http://novabay.com/contact-scientific-inquiries
(510) 899-8852