Virucidal agents in the eve of manorapid synergy®

Virusinaktivierende Substanzen aus der Zeit vor MANORAPID® SYNERGY

Abstract

Virucidal agents are chemical substances that attack and inactivate viral particles outside the cell (virions). In general this is accomplished by damaging their protein shells (capsid) or the substance penetrates the core itself, where it destroys the genetic material. Damage to the virion structure is also possible. These agents are used not only for traditional surface disinfection or sterilization of blood, blood products, and other medicinal products as well as in antiviral chemotherapy. They have also been used in recent times for inactivation of viruses in foodstuffs, detergents or cosmetics. Below is given an overview of the data currently available on the performance of these substances when used for the latter applications (cleaning and cosmetics). These include:
- hydrogen peroxide, hypochlorites, cupric and ferric ions, per-acids
- ethanol, parachlorometaxylenol in a sodium C14-16 olefin sulfonate, glutaraldehyde, quaternary ammonium salts, chlorhexidine and chlorhexidine gluconate, curdline sulphate, glycerol, lipids, azodicarbonamide, cicloxolone sodium, dichlorisocyanuric acid (sodium salt), benzalkonium salts, disulfate benzamides and benzisothiazolones, congo red, ascorbic acid, nonoxynol-9, para-aminobenzoic acid, bis(monosuccinamide) derivative of p,p'-bis(2-aminoethyl) diphenlyi-C60) (fullerene).
- merocyanine, benzoporphyrin derivative monoacid ring A, rose bengal, hypericin, hypocrellin A, anthraquinones extracted from plants, sulfonated anthraquinones and other anthraquinone derivatives
- gramicidine, gossypol, garlic (Allium sativum) extract and its components: ajoene, diallyl thiosulfinate (allicin), allyl methyl thioulfinate, methyl allyl thiosulfinate, extracts of ledium, motherworth, celandine, black currant, coaberry and bilberry, extract of Cordia salicifolia, steam distillate from Houttuynia cordata (Saururaceae) and its component, 5,6,7-trimethoxyflavone from Calicarpa japonica, isoscullarein (5,7,8,4'-tetrahydroxyflavone) from Scutellaria baikalensis and isoscutellarein-8-methylether, alkaloids and phytosteryl ester compounds.

Angel S. Galabov[1]

1 The Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences
Sofia, Bulgaria

Zusammenfassung

Virusinaktivierende Stoffe sind chemische Substanzen, die Viruspartikel angreifen und inaktivieren, die sich außerhalb der Zelle befinden (Virione). Im Allgemeinen geschieht dies, indem deren Proteinhülle (Capsid) beschädigt wird oder die Substanz in den Kern selbst eindringt und dort das Erbgut zerstört. Möglich ist auch die Beschädigung der Virion - Struktur. Diese Agens werden nicht nur in der klassischen Flächendesinfektion oder der Sterilisation von Blut, Blutprodukten und anderen Arzneimitteln bzw. in der antiviralen Chemotherapie eingesetzt, sondern neuerdings auch zur Inaktivierung von Viren in Lebens- und Reinigungsmittel sowie Kosmetika. Es wird eine Zusammenstellung über die aktuell bekannte Leistungsfähigkeit dieser Wirkstoffe im letzten Anwendungsbereich (Reinigung und Kosmetik) gegeben.

Introduction

Virucidal agents represent chemical substances (individual compounds or compositions) attacking and inactivating (decreasing the infectivity of) the extracellular viral particles (virions). Principally, virucidals damage the virion protein capsid or supercapsidal membrane, or penetrating into the virion destroy the viral genome. The viral particle integrity could also be affected.
Four major application fields of the virucidal agents could be distinguished, namely:

1. Disinfection of the environment - historically this is the oldest and still widely developing field.
2. Sterilization of biological products for parenteral administration: blood, blood products, medicinals.
3. Antiviral chemotherapy - some antiviral agents could exert virucidal mode of action as a specific or secondary effect.
4. Elimination of viruses from food, sanitary products and cosmetics. This is the newest and most prospective field of application.

The following literary update involves substances manifesting distinct virucidal properties making them potentially suitable to be used in sanitation and cosmetics. Some of them have been already registered as disinfectants or blood products sterilyzing agents.

Inorganic compound

Peroxide

Hydrogen peroxide (known as a disinfectant) in solution (3%-6%) showed a very low virucidal effect towards enteroviral virions (1 min treatment in the surface test vs. poliovirus 1 dried suspension) or lack of effect (1 min in the suspension test) [1].

Hypochlorites

High concentrations (9200 ppm avCl2) were effective (a >4 lg reduction) against a dried enterovirus (poliovirus 1) suspension (in the surface test) in 1 min. Lower hypochlorite concentrations (1000 ppm avCl2) were less effective [1].

Cupric and ferric ions

These metal ions were able to inactivate a comparatively wide spectrum of enveloped or nonenveloped, ss- or ds RNA or DNA viruses, e.g. Junin (arenavirus), herpes simplex viruses 1 and 2, and different phages (X174, T7, 6). The virucidal effect of these metals was enhanced by the addition of peroxide, particularly for copper (II). The combinations mentioned above should be able to inactivate most, if not all, viruses that have been found contaminating medical devices [2].

Per-acids

Per-acid based disinfectants are known as powerful virucides. Some commercial preparatives (e.g. “Peral-S” disinfectant) revealed a strong virucidal activity on enterovirus (Coxsackie B6 virus) and herpesvirus (herpes simplex virus 1) at 0.1% concentration within 30 seconds only. The so-called “floating technique” was applied in this study [3].

Organic compounds

Ethanol

At 70% this compound showed variable results in a virucidal testing (surface test) vs. the enterovirus polio 1, while in the suspension test was ineffective in 1 min [1].

Parachlorometaxylenol in a sodium C14-16 olefin sulfonate

At 0.5% this composition proposed as soap (for a health care personnel hand wash) demonstrated a strong virucidal effect against HIV1 in the presence of 50% whole human blood within 30-60 sec. More than 99.9% of the virus was inactivated at 1:5 - 1:30 dilutions [4].

Glutaraldehyde

At 2% this compound was effective in the surface test on poliovirus 1 (> 4 lg reduction) for 1 min [5]. A 2% alkaline glutaraldehyde was efficient as a virucidal and bactericidal agent against a mixture of some picornaviruses (hepatitis A and poliovirus 1) and some bacteria (Pseudomonas aeruginosa, Mycobacterium bovis and Mycobacterium gordonae) in the so called carrier test (with a contact time 10 min at 20°C). The criterion of efficacy was a minimum of 3-log reduction in the infectivity titers of the oreganisms tested. In this case the use of the compound was endoscopes disinfection via baths [6].

Quaternary ammonium salts

A newer generation of quaternary ammonium compounds showed a distinct virucidal effect against calici-, parvo- and herpesviruses (causative agents of diseases in domestic cats and dogs) for à 10-min contact at room temperature [7].

Chlorhexidine and chlorhexidine gluconate

Chlorhexidine could be considered as efficient vaginal virucidals preventing heterosexual transmission of HIV [8]. The gluconate derivative at 0.12% concentration (proposed for a mouthrinse preparative) was effective on a unusually wide spectrum of viruses: influenza A, parainfluenza, HSV, CMV and HBV. The poliovirus was unsensitive. The contact time was 30 sec [9]. The probable mode of action is an interaction with the virion envelope, and the deferences in the virucidal effects are based on differences in the physical/chemical structures of the virus envelopes [9].

Curdline sulfate

This newly synthesized sulfated polysaccharide preventing the binding of HIV to the surface of H9 cells exhibited a weak virucidal activity [10].

Glycerol

This substance known as a viral preservation medium in tissue samples at a 50% concentration for a short period of time, applied at higher concentrations showed a strong virucidal activity at different temperatures (4, 20 and 37°C) against HIV, HSV1 and polioviruses. Both a dehydrating action and an influence on the enzymatic processes of nucleic acid breakdown are discussed as the possible base of the glycerol action. Otherwise, glycerol is known to dehydrate the skin, the extracted water being replaced by glycerol, preserving the original structure [11].

Lipids

Purified lipids can inactivate enveloped viruses, bacteria, fungi, and protozoa. This activity is atributed to certain monoglycerides and fatty acids that are released from triglycerides by lipolytic activity. Medium chain length antiviral lipids can be added to human blood products that contain HIV-1 and HIV-2 and redice the cell-free virus concentration by as much as 11 lg $TCID_{50}$/ml. Antimicrobial lipids can disrupt cell membranes and subsequently lyse leukocytes which potentially carry virus [12]. Preliminary studies indicate that lipids decrease sperm motility and viability suggesting that lipids may potentially be used as combination spermicidal and virucidal agents [12].

Azodicarbonamide

This compound is a nucluocapsid inhibitor efficient against HIV-1 and other retroviruses, and its virucidal effect is based on the prevention of reverse transcription initiation and a block of infectious virion formation from cells [13].

Cicloxolone sodium

This compound manifested a wide-spectrum virucidal effect: towards HSV-1, HSV-2, VSV, adenoviruses (type 5). A relocation of assembled virus is presumed. Besides, a very well pronounced inhibitory effect on the replication of different virus families (picorna-, reo-, toga-, bunya- and adenoviruses) was established [14].

Dichlorisocyanuric acid (sodium salt)

The compound revealed a marked virucidal activity against ectromelia virus (poxvirus family). It is proposed for use as a water disinfectant [15].

Benzalkonium salts

This group of positively charged surface active alkylamine biocides interacts with guanine nucleotide triphosphate-binding proteins. Benzalkonium salts have antiproliferative effects on a variety of cells, affect cytokine gene expression, and are also effective virucidal, bactericidal and fungicidal agents. Virucidal actiivity was found against HIV, papillomaviruses and herpesviruses [16].

Disulfate benzamides and benzisothiazolones

A group of 4 derivatives possesses anti-HIV virucidal activity based on an ejection of zinc from the virus nucleocapside protein [17].

Congo red

This membrane-binding dye inactivates HIV in the presence of magnesium dichloride (Mg^{++} ions) only. This effect was found to be revesible as validated by washing of the cells by Hanks' solution + MgCl2 following capture of the virions from cell-free HIV-Congo red inactivation mixture [18].

Ascorbic acid

Vitamine C demonstrated a virucidal effect on HIV in the presence of Mg^{++} ions. Its virucidal properties are closed to those of Congo red [18].

Nonoxynol-9

This a virucidal and spermicidal agent used for vaginal treatment preventing heteroxual transmission of HIV or for impregnation of surgical gloves serving as a barrier for HIV infection [8], [19], [20].

Para-aminobenzoic acid

This compound showed a marked anti-herpesvirus (HSV-1) activity both in vitro and in vivo, and virucidal mode of action was presumed [21], [22].

Bis(monosuccinamide) derivative of p,p'-bis(2-aminoethyl) diphenyl-C60 (Fullerene)

This substance showed activity against HIV-1 and HIV-2. Its virucidal properties were confirmed by the contact (virus-inactivating) test. In cell-free system fullerene manifested comparable activity against HIV-1 reverse transcriptase and DNA polymerase (alpha), and a selective activity towards HIV-1 protease [23].

Photosensitizing virucidal agents

Merocyanine

This pyrimidinone derivative, a lipophilic dye, is a photosensitizing virucidal agent efficient vs. lipid-containing, enveloped, viruses, e.g. HSV. Its activity was proved initially on bacteriophages as surrogate for animal viruses [5].

Benzoporphyrin derivative monoacid ring A

This compound destroyed enveloped viruses (HIV) in blood and blood products when activated by light. Its eliminates the virus but did not damage blood cells or blood components [24].

Rose bengal

Virucidal spectrum of this compound envolves various groups of enveloped viruses: orthomyxo- (influenza A), paramyxo (Sendai), rhabdo- (VSV) and retroviruses (HIV, Friend leukemia virus) [25], [26], [27]. HIV and VSV were photodynamically inactivated by this dye at nanomolar concentrations [25]. The non-enveloped viruses are unsusceptible. The compound inactivated influenza virus upon exposure to light. It was established that the virucidal activity of photodynamic agents against enveloped viruses may be generally due to inactivation of their fusion protein(s). Concentrations required for inactivation were found to depend upon the ratio of rose bengal to virus, rather than on nominal aqueous concentration. The HA2 portion of influenza fusion protein HA underwent two different apparently mutually exclusive modifications upon illumination with rose bengal. Inactivation of the viral fusion was inhibited by oxygen removal or addition of azide or beta-carotene, and was enhanced by D2O, consistent with partial involvement of singlet oxygen. A direct interaction between the viral fusion protein and the photoactivated dye is also possible [26].

Hypericin

This natural polycyclic anthrone, first isolated from the plant St. Johnswort manifested is a strong photosensitizing lipophilic virucidal agent. Its effectivity was found upon influenza A virus, Sendai virus, VSV, HIV and other retroviruses (murine Friend leukemia virus, radiation leukemia virus and Moloney mouse leukemia virus, equine infectious anemia virus), HSV-1, HSV-2 and vaccinia virus [25], [27], [28], [29], [30], [31], [32]. The compound photodynamic virucidal efficiency vs. HIV and VSV was found at nanomolar coincentration [25]. Hyperacin did not showed selective antiviral activity against HSV, influenza A, adeno- or poliovirus. When virus was incubated hypericin before infecting cells, the drug was virucidal to all enveloped viruses tested (influenza A, Moloney mouse leukemia virus, HSV). The compound was not virucidal to the none-enveloped viruses (polio, human rhinovirus, adeno) tested. Evidently, the mechanism of viral inactivation for hypericin is dependent upon the presence of a viral lipid envelope [28]. The chemiluminescent oxidation of luciferin by a plant luciferase was found to generate sufficiently intense and long- lived emission to induce virucidal activity of hypericin [29]. Hypericin bind cellmembranes (and by inference, virus membranes) and crosslinks virus capsid proteins. Its anti-retrovirus action results in a loss of infectivity and an inability to retrieve the reverse transcriptase enzymatic activity from the virion [30]. Hypericin is convinient for use as virucidal (vs. HIV) treatment of blood products [30]. Addition of small amounts of Tween-80 to solutions containing hypericin enhanced by up to 2.6 lg hypericin's virucidal activity [32].

Hypocrellin A

This compound displays photoinduced virucidal activity, in particular against HIV. Hypocrellin A like hypericin executes an excited-state intramolecular proton transfer, and defferes from hypericin in two important ways: a. hypocrellin A absolutely requires oxigen for its virucidal activity; b. hypocrellin A does not acidify its surrounding medium in the presence of light [30].

Anthraquinones extracted from plants

Several virucidal compounds from this class were isolated from different plants (*Rheum officinale , Aloe barbadensis, Rhamnus frangula, Rhamnus purshuanus, Cassia angustifolia*), namely emodin, aloe-emodin, emodin anthrone and emodin bianthrone. Hypericin is also a member of this class. Their virucidal spectrum envolves a large scope of enveloped viruses: influenza, parainfluenza, VSV, herpesviruses HSV-1, HSV-2, VZV and PsRV [32], [33]. The compound effective concentrations were less than 1 mcg/ml in the so-called contact (direct pre-infection incubation) test. The activity of these substances

were lower than that of hypericin, By their virucidal effects the compounds could be arranged as follows: emodin bianthrone > emodin anthrone > emodin [32]. Aloe-emodin inactivated all of the viruses mentioned above; adenovirus and rhinovirus were insensitive [33].

Sulfonated anthraquinones and other anthraquinone derivatives

Anthraquinone derivatives acid blue 40 and 129, acid black 48, alizarin violet R and reactive blue 2 manifested a marked virucidal activity upon human CMV strains [34].

Natural products

Gramicidine

This polypeptide antibiotic derived from Bacillus brevis is a weak anti-HIV virucidal (thousand-fold less active than nonoxyol-9 and gossypol [20].

Gossypol

This substance, a polyphenolic aldehyde extracted from cotton seed, demonstrated several biological effects: a pronounced interferon-inducing activity, a contraceptive (spermicide) and an anti-HIV virucidal effects [20], [35]. The latter was proved in cell-free reverse transcriptase system.

Garlic (Allium sativum) extract and its components: ajoene, diallyl thiosulfinate (allicin), allyl methyl thioulfinate, methyl allyl thiosulfinate

Garlic has been shown to have antiviral activity. In the contact test the fresh garlic extract and several garlic associated compounds as mentioned above demonstrated a strong virucidal activity against wide spectrum of viruses - enveloped (parainfluenza virus type 3, VSV, HSV-1, HSV-2), non-enveloped (human rhinovirus type 2) and vaccinia virus as well. The order for virucidal activity of the garlic extract compounds was: ajoene > allicin > allyl methyl thiosulfinate > methyl allyl thiosulfinate. Ajoene was found in oil-macerates of garlic but not in fresh garlic extracts. No activity was found for the garlic polar fraction, alliin, deoxyalliin, diallyl disulfate, and diallyl trisulfate. Fresh garlic extract, ijn which thiosulfinates appeared to be the active components, was virucidal to each virus mentioned above. Experimental data demonstrated that virucidal activity and cytotoxicity may have dependedupon the viral envelope and cell membrane, respectively [36].

Extracts of ledium, motherworth, celandine, black currant, coaberry and billberry

The aqueous extracts of these plants manifested a virucidal effect towards tick-born encephalitis virus and induced resistance in mice infected with this virus [37].

Extract of Cordia salicifolia

A partially purified extract of this plant nas been shown to have a direct virucidal activity against HSV-1, to which could be attributed the inhibitory effect of this extract on viral replication [38].

Steam distillate from Houttuynia cordata (Saururaceae) and its component

The steam distillate prepared from fresh plants was found to have virucidal activity against several enveloped viruses: influenza A virus, HIV and HSV-1. Three major componenets of the distillate, methyl-n-nonyl ketone, lauryl aldehyde, and capryl aldehyde, also inactivated these viruses. Ithe data obtained demonstrate that the essential oils provide virucidal activity against enveloped viruses by interfering with the function of the virus envelope [39].

5,6,7-Trimethoxyflavone from Calicarpa japonica

This naturally occuring flavone exibited relatively high inhibitory effect on replication of poliovirus 1 and herpesviruses HSV-1 and CMV. The anti-HSV-1 action is not due to the inhibition of virus adsorption, entry, and viral protein synthesis, but might involve, at least in part, a virucidal activity, which results in a suppression of viral binding to host cells at an early replication stage [40].

Isoscullarein (5,7,8,4'-tetrahydroxyflavone) from Scutellaria baikalensis and isoscutellarein-8-methylether

These substances isolated from the plant leaf demonstrated both an inhibitory effect on the influenza A virus neuraminidase and a potent virucidal activity against this virus in ovo and in vivo. The virus-inhibitory effect of flavone and methylether were identical, but the flavone's virucidal activity was stronger [41].

Alkaloids and phytosteryl ester compounds

These substances (marigenol-concentrates comprising taxol and/or taxan esters as active principles) manifested an anti-tumor and antiviral/virucidal activity [42].
This was in general lines the virucidal agents' spectrum before the appearance of the pioneer of a new generation rubs, Manorapid Synergy® [43], [44].

Abbreviations

Abbreviations used: CMV - cytomegalovirus; HA - hemaglutinine; HBV - hepatitis B virus; HIV - human immunodeficiency virus; HSV - herpes simplex virus; PsRV - pseudorabies (Aujesky's disease) virus; TCID50 - 50% tissue culture infectious dosis; VSV - vesicular stomatitis virus; VZV - varicella zoster virus.

Curriculum Vitae

Angel S. Galabov, Ph.D., D.Sc.

Figure 1

Figure 1: Angel S. Galabov

Professor of Virology, Head of Department of Virology, Institute of Microbiology, Bulgarian Academy of Sciences, Sofia.
Angel S. Galabov reads medicine at the University in Sofia, where he takes his doctorate in 1962. He habilitates in 1968 at the Institute for Microbiology of the Bulgarian Academy of Science and afterwards moves - in the context of a scholarship - to the Louis Pasteur Institute in Paris to the winner of the Nobel Price, Andre Lwoff. Back in Sofia he manages from 1972 on the „Viral Inhibitors and Interferon Laboratory", Department of Virology, Institute of Infectious and Parasitic Diseases, Medical Academy, Sofia and at the same time is Associate Professor of Virology, at the Department of Virology, Institute of Infectious and Parasitic Diseases, Medical Academy, Sofia.
In between he moves to the National University of Moscow. Back in Sofia he is appointed Head of the Department of Virology, Institute of Microbiology, Bulgarian Academy of Sciences, Sofia. Professor Galabov is an internationally outstanding personality among the virologists: he has an extraordinary expertise in this demanding subject, almost 160 publications and 39 patents are proving it. His special interest is in the development of virus inactivating agents and therefore infection abatement. He researches the biological reactions of Interferon, interferon inducers, antioxidants, virucidal agents (disinfectants, sanitation agents), replication cycle of picorna, toga-, flavi-, orthomyxo-(influenza), paramyxo-, adeno- and herpes viruses, influenzavirus proteins, viruses – diabetes, viral role in the Balkan endemic nephropathy.
Prof. Galabov is a highly acknowledged member not only of nationally but also of internationally essential organizations, founder e.g. of the Balkan Society for Microbiology (BSM) or the first European International Symposia chain on Antiviral Substances.

References

1. Tyler R, Ayliffe GA, Bradley C. Virucidal activity of disinfectants: studies with the poliovirus. J Hosp Infect. 1990;15(4):339-45.
2. Sagripanti JL, Routson LB, Lytle CD. Virus inactivation by copper or iron ions alone and in the presence of peroxide. Appl Environ Microbiol. 1993;59(12):4374-6.
3. Durisic S, Milosevic V, Visacki M, Luka G. Med Pregl. Study of viral sensitivity to the disinfectant Peral-S using the "floating technique". 1990;43(7-8):293-4.
4. Lavelle GC, Gubbe SL, Neveaux JL, Bowden BJ. Evaluation of an antimicrobial soap formula for virucidal efficacy in vitro against human immunodeficiency virus in a blood-virus mixture. Antimicrob Agents Chemother. 1989;33(12):2034-6.
5. Lytle CD, Budacz AP, Keville E, Miller SA, Prodouz KN. Differential inactivation of surrogate viruses with merocyanine 540. Photochem Photobiol. 1991;54(3):489-93.
6. Mbithi JN, Springthorpe VS, Sattar SA, Pacquette M. Bactericidal, virucidal, and mycobactericidal activities of reused alkaline glutaraldehyde in an endoscopy unit. J Clin Microbiol. 1993;31(11):2988-95.
7. Kennedy MA, Mellon VS, Caldwell G, Potgieter LN. Virucidal efficacy of the newer quaternary ammonium compounds. J Am Anim Hosp Assoc. 1995;31(3):254-8.
8. Pauwels R, De Clercq E. Development of vaginal microbicides for the prevention of heterosexual transmission of HIV. Acquir Immune Defic Syndr Hum Retrovirol. 1996;11(3):211-21.
9. Bernstein D, Schiff G, Echler G, Prince A, Feller M, Briner W. In vitro virucidal effectiveness of a 0.12%-chlorhexidine gluconate mouthrinse. J Dent Res. 1990;69(3):874-6.
10. Aoki T, Kaneko Y, Nguyen T, Stefanski MS, Ting RC, Manak MM. Curdlan sulfate and HIV-1: II. In vitro long-term treatment of HIV-1 infection with curdlan sulfate. AIDS Res Hum Retroviruses. 1992;8(5):605-12.
11. van Baare J, Buitenwerf J, Hoekstra MJ, du Pont JS. Virucidal effect of glycerol as used in donor skin preservation. Burns. 1994;20 Suppl 1:S77-80.

12. Isaacs CE, Kim KS, Thormar H. Inactivation of enveloped viruses in human bodily fluids by purified lipids. Ann NY Acad Sci. 1994;724:457-64.

13. Rice WG, Turpin JA, Huang M, Clanton D, Buckheit RW Jr, Covell DG, Wallqvist A, McDonnell NB, DeGuzman RN, Summers MF, Zalkow L, Bader JP, Haugwitz RD, Sausville EA. Azodicarbonamide inhibits HIV-1 replication by targeting the nucleocapsid protein. Nat Med. 1997;3(3):341-5.

14. Dargan DJ, Galt CB, Subak-Sharpe JH. The effect of cicloxolone sodium on the replication in cultured cells of adenovirus type 5, reovirus type 3, poliovirus type 1, two bunyaviruses and Semliki Forest virus. J Gen Virol. 1992;73(Pt2):407-11.

15. Bogush TA, Mal'tsev MV. The virucidal properties of neoaquasept. Eksp Klin Farmakol. 1993;56(4):44-6.

16. Patarca R, Fletcher MA. Effects of benzalkonium salts on eukaryotic and microbial G-protein-mediated processes and surface membranes. Crit Rev Oncog. 1995;6(3-6):327-56.

17. Tummino PJ, Harvey PJ, McQuade T, Domagala J, Gogliotti R, Sanchez J, Song Y, Hupe D. The human immunodeficiency virus type 1 (HIV-1) nucleocapsid protein zinc ejection activity of disulfide benzamides and benzisothiazolones: correlation with anti-HIV and virucidal activities. Antimicrob Agents Chemother. 1997;41(2):394-400.

18. Rawal BD, Vyas GN. Magnesium-mediated reversal of the apparent virucidal effect of ascorbic acid or congo red reacted in vitro with the human immunodeficiency virus. Biologicals. 1996;24(2):113-6.

19. Johnson GK, Nolan T, Wuh HC, Robinson WS. Efficacy of glove combinations in reducing cell culture infection after glove puncture with needles contaminated with human immunodeficiency virus type 1. Infect Control Hosp Epidemiol. 1991;12(7):435-8.

20. Bourinbaiar AS, Lee-Huang S. Comparative in vitro study of contraceptive agents with anti-HIV activity: gramicidin, nonoxynol-9, and gossypol. Contraception. 1994;49(2):131-7.

21. Akberova SI, Leont'eva NA, Stroeva OG, Galegov GA. Action of para-aminobenzoic acid and its combination with acyclovir in herpetic infection. Antibiot Khimioter. 1995;40(10):25-9.

22. Akberova SI, Leont'eva NA, Stroeva OG, Galegov GA. Para-aminobenzoic acid in therapy of experimental keratitis caused by herpes simplex virus in rabbits: the therapeutic effect and decrease of infectious titer. Vestn Oftalmol. 1996;112(4):23-6.

23. Schinazi RF, Sijbesma R, Srdanov G, Hill CL, Wudl F. Synthesis and virucidal activity of a water-soluble, configurationally stable, derivatized C60 fullerene. Antimicrob Agents Chemother. 1993;37(8):1707-10.

24. North J, Neyndorff H, Levy JG. Photosensitizers as virucidal agents. J Photochem Photobiol B. 1993;17(2):99-108.

25. Lenard J, Rabson A, Vanderoef R. Photodynamic inactivation of infectivity of human immunodeficiency virus and other enveloped viruses using hypericin and rose bengal: inhibition of fusion and syncytia formation. Proc Natl Acad Sci U S A. 1993;90(1):158-62.

26. Lenard J, Vanderoef R. Photoinactivation of influenza virus fusion and infectivity by rose bengal. Photochem Photobiol. 1993;58(4):527-31.

27. Stevenson NR, Lenard J. Antiretroviral activities of hypericin and rose bengal: photodynamic effects on Friend leukemia virus infection of mice. Antiviral Res. 1993;21(2):119-27.

28. Tang J, Colacino JM, Larsen SH, Spitzer W. Virucidal activity of hypericin against enveloped and non-enveloped DNA and RNA viruses. Antiviral Res. 1990;13(6):313-25.

29. Carpenter S, Fehr MJ, Kraus GA, Petrich JW. Chemiluminescent activation of the antiviral activity of hypericin: a molecular flashlight. Proc Natl Acad Sci USA. 1994;91(25):12273-7.

30. Fehr MJ, Carpenter SL, Wannemuehler Y, Petrich JW. Roles of oxygen and photoinduced acidification in the light-dependent antiviral activity of hypocrellin A. Biochemistry. 1995;34(48):15845-8.

31. Lavie G, Mazur Y, Lavie D, Prince AM, Pascual D, Liebes L, Levin B, Meruelo D. Hypericin as an inactivator of infectious viruses in blood components. Transfusion. 1995;35(5):392-400.

32. Andersen DO, Weber ND, Wood SG, Hughes BG, Murray BK, North JA. In vitro virucidal activity of selected anthraquinones and anthraquinone derivatives. Antiviral Res. 1991;16(2):185-96.

33. Sydiskis RJ, Owen DG, Lohr JL, Rosler KH, Blomster RN. Inactivation of enveloped viruses by anthraquinones extracted from plants. Antimicrob Agents Chemother. 1991;35(12):2463-6.

34. Barnard DL, Fairbairn DW, O'Neill KL, Gage TL, Sidwell RW. Anti-human cytomegalovirus activity and toxicity of sulfonated anthraquinones and anthraquinone derivatives. Antiviral Res. 1995;28(4):317-29.

35. Polsky B, Segal SJ, Baron PA, Gold JW, Ueno H, Armstrong D.Inactivation of human immunodeficiency virus in vitro by gossypol. Contraception. 1989;39(6):579-87.

36. Weber ND, Andersen DO, North JA, Murray BK, Lawson LD, Hughes BG. In vitro virucidal effects of Allium sativum (garlic) extract and compounds. Planta Med. 1992;58(5):417-23.

37. Fokina GI, Frolova TV, Roikhel' VM, Pogodina VV. Experimental phytotherapy of tick-borne encephalitis. Vopr Virusol. 1991;36(1):18-21.

38. Hayashi K, Hayashi T, Morita N, Niwayama S. Antiviral activity of an extract of Cordia salicifolia on herpes simplex virus type 1. Planta Med. 1990;56(5):439-43.

39. Hayashi K, Kamiya M, Hayashi T. Virucidal effects of the steam distillate from Houttuynia cordata and its components on HSV-1, influenza virus, and HIV. Planta Med. 1995;61(3):237-41.

40. Hayashi K, Hayashi T, Otsuka H, Takeda Y. Antiviral activity of 5,6,7-trimethoxyflavone and its potentiation of the antiherpes activity of acyclovir. J Antimicrob Chemother. 1997;39(6):821-4.

41. Nagai T, Miyaichi Y, Tomimori T, Suzuki Y, Yamada H. In vivo anti-influenza virus activity of plant flavonoids possessing inhibitory activity for influenza virus sialidase. Antiviral Res. 1992;19(3):207-17.

42. Eugster C, Rivara G, Forni G, Vai S. Marigenol-concentrates comprising Taxol and/or Taxan esters as active substances. Panminerva med. 1996;38(4):234-42.

43. Kramer A, Doehner L. Hand disinfectant. US Patent 6,080,417. 2000

44. Kramer A, Galabov AS, Sattar SA, Dohner L, Pivert A, Payan C, Wolff MH, Yilmaz A, Steinmann J. Virucidal activity of a new hand disinfectant with reduced ethanol content: comparison with other alcohol-based formulations. J Hosp Infect. 2006;62(1):98-106.

Corresponding author:

Angel S. Galabov

The Stephan Angeloff Institute of Microbiology, 26 Acad. Georgi Bonchev Street, BG-1113 Sofia, Bulgaria

galabov@microbio.bas.bg

Please cite as
Galabov AS. Virucidal agents in the eve of manorapid synergy®. GMS Krankenhaushyg Interdiszip. 2007;2(1):Doc18.

This article is freely available from
http://www.egms.de/en/journals/dgkh/2007-2/dgkh000051.shtml

Copyright
©2007 Galabov This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by-nc-nd/3.0/deed.en). You are free: to Share — to copy, distribute and transmit the work, provided the original author and source are credited.