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An update on natural preservatives

SUMMARY

Natural preservation is one of the most popular topics in the industry and attracts the attention of even the most traditional of formulating chemists. This article looks at the theoretical development of a natural preservative system. The traditional methods of preservation, many taken from the food industry are summarised and the latest raw materials on offer within the industry are evaluated.

There was a time when the mention of natural preservation would have been greeted with scepticism. However, today the views of many scientists have changed and the use of plant materials and natural molecules is seen as a distinct possibility in their formulations. The author has been writing and updating the benefits of natural preservatives for over a decade (Dweck, 1994; Dweck, 1995; Dweck, 2003; Dweck, 2005). Costs for these new materials is high, but more than compensated for by the additional marketing claims such as "preservative free" or "contains no synthetic preservatives". The article reviews the most commonly used methods of preservation that are available to the formulator. The food and beverage industry may be called on for many of these examples.

Legal position

No preservative may be used which does not appear in Annex VI Part 1 or 2 of the EEC Cosmetic Directive 76/768/EEC – including the 7th amending Commission Directive 94/32/EC.

However, these natural materials are not legislated as preservatives, and when used for their beneficial effect on the skin, may coincidentally have a positive effect on the total preservative requirement of the formulation. Of course, no material appearing in Annex II may be considered.

The food industry often uses a preservation technique known as the "hurdle approach", where a number of different materials and factors that might eliminate organisms on their own if used at a high level are used in combination, but at significantly lower levels. This gives rise to a series of hurdles over which most organisms are unable to cross. The idea of using a whole variety of these "hurdles" to slowly weaken each organism, but at individual levels that would be ineffective, is an almost alien concept to the cosmetic and toiletry industry.

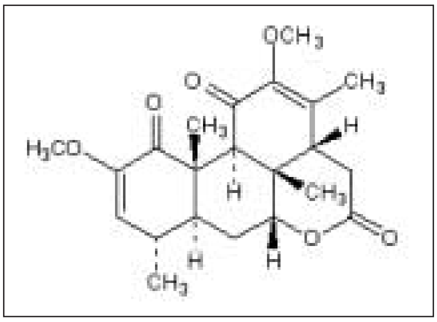

Figure 1: *Quassin.*

Sugar

High levels of sugar can preserve against spoilage organisms. This is a technique used in home-made jams, preserves, sweet pickles and marmalades. It is also an important factor in the preservation of boiled sweets and chocolates etc. Increasingly, it will be noticed that many products now have to be kept in the refrigerator or freezer once opened, because sugar has been replaced by an artificial sweetener which may be cheaper and healthier to eat, but has no preserving qualities at all.

Honey

Honey in its undiluted form is also a natural preservative and, indeed, there are many learned papers citing honey as a viscous barrier to bacteria and infection.

Alcohol

Not all organisms are detrimental. The production of alcohol from sugar by yeast is an industry in its own right. A wine that is carefully produced using sterile equipment and fermented to 13% by volume will just about resist further infection from external organisms, once that fermentation has completed. The time during the fermentation of the must is when the must is most vulnerable to infection. The naturally produced fermentation grade alcohol may be concentrated by distillation and used as a natural preservative in toners, aftershaves and colognes. Alcohol at a level of 15% is effective, but 20% is more assured.

The denaturant present in the alcohol is not "natural" and there is a need to return to Quassin (Fig. 1), the bitter substance present in Quassia (*Picraena excelsa*), which used to be acceptable as a denaturant.

Sadly, Customs & Excise might not view your antique solution to denaturing with quite the same enthusiasm, especially as we as an industry lobbied so strongly to be able to use Bitrex (Fig. 2). (INCI: Denatonium benzoate or N-(2-((2,6-dimethylphenyl) amino)-2-oxoethyl)-N,N-diethyl-, benzoate).

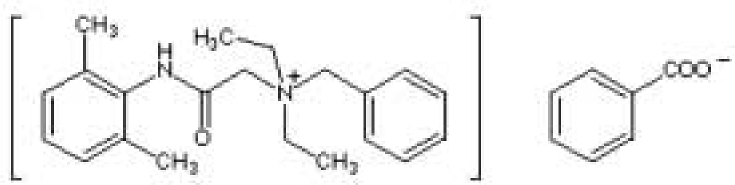

Figure 2: *Bitrex or Denatonium benzoate.*

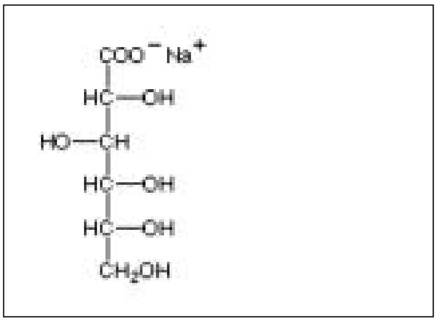

Figure 3: *Sodium gluconate.*

Heat
Heating, cooking, steaming and pasteurisation are another natural form of preservation that will sterilise products, especially where that product is designed as a one-shot use product – for example, a phial or a sachet. Alternatively, once opened, the product can be stored in the fridge or freezer to prevent microbiological degradation.

Cold
Placing a product in the cold merely "stops the clock" on microbiological growth and this is perfectly fine, provided the product was fairly "clean" microbiologically when it was placed in the cold. The discovery of prehistoric animals and mummified people in various frozen wastes shows that this method of preservation is effective.

Dessication
Removing water from a product or making it totally dehydrated will greatly reduce the possibility of spoilage. However, it must be recognised that the presence of spore-bearing organisms could become active once that water is reintroduced.

Anhydrous
In a similar vein, one could make products with materials that do not contain any traces of water and deliberately design and formulate a totally anhydrous product. However, creams that can be finished by the consumer, by introducing water to the blend of oils, fats and waxes are prone to the same restrictions as the desiccated products.

Salt
The use of extreme levels of salt – as used by the ancient mariners to preserve their meat, is effective and it is very likely that the preservation of the Egyptian mummies was in part achieved with the 40-day treatment in *natron* (a local salt that osmotically drained the tissues of water).

Acid pH
The preservative activity can be boosted by operating at as low a pH as possible. Natural acidity could be obtained from one of the many alpha hydroxy acids (AHAs) which are obtained from citrus species, where the major components are citric and malic acids.

Alkaline pH
High pH values also inhibit the growth of organisms and it is not necessary to preserve bar soaps, although it might be necessary to put a fungicide in the cardboard carton that surrounds a naked soap, as the moisture that leaves the soap can be the cause of mould and fungal growth in the card.

Chelating agents
In addition to formulating at low pH, chelating agents such as phytic acid extracted from rice bran could be added to enhance the activity of the natural preservative. There are a number of suppliers for this material.

Another option is to use a naturally produced material like sodium gluconate (Fig. 3). Sodium gluconate is the sodium salt of gluconic acid, produced by the fermentation of glucose. It is a white crystalline powder, very soluble in water. Non-corrosive, non-toxic and readily biodegradable (98% after two days), sodium gluconate is an effective chelating agent especially in alkaline and concentrated alkaline solutions.

It forms stable chelates with calcium, iron, copper, aluminium and other heavy metals. It is as effective as other chelating agents, such as EDTA and related salts. Aqueous solutions of sodium gluconate are resistant to oxidation and reduction, even at high temperatures. However, it is easily degraded biologically, and thus presents no wastewater problem. It is used in the food industry.

Chelating agents interfere with the cellular membranes that surround all organisms and weaken them by depriving them of the trace elements that they need for cellular function. Extremely high levels of chelating agent have been used as preservatives on their own.

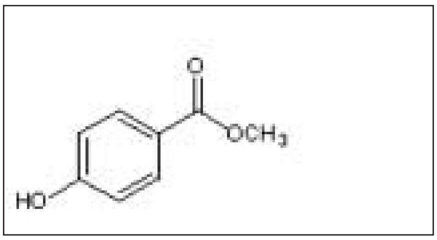

Figure 4: *Methylparaben.*

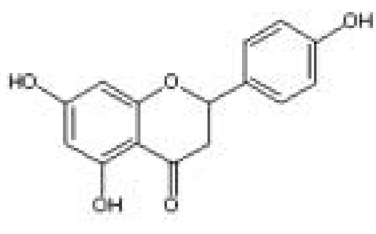

Figure 5: *Naringenin.*

Antioxidants
Antioxidants, such as natural tocopherol and ascorbic acid will further aid preservation, as well as reducing the potential rancidity. It has to be remembered that ascorbic acid is extremely unstable in water and is particularly sensitive to copper, iron or nickel and will brown quite quickly in aqueous systems.

Glycerine
High levels of vegetable glycerin, up to 15-20%, will also have a preservative effect, similar to that effect obtained by the use of high levels of sugar. There is a downside to these high levels which is increased stickiness.

Emulsion form
It has been argued that the formula comprised of a water-in-oil emulsion, where the oil is the continuous phase is far less likely to be subject of attack by spoilage organisms. This might be true, but it certainly does not exclude the use of a preservative system. It does, however, form another link in the hurdle approach to preservation.

Emulsifier type
A material was marketed many years ago called Lauricidin, which was Glyceryl Laurate and was said to mimic the sterile and protective action found in a mother's milk. It had been found that the properties that determine the anti-infective action of lipids are related to their structure: e.g. free fatty acids and monoglycerides. The monoglycerides are active; diglycerides and triglycerides are inactive. Of the saturated fatty acids, lauric acid has greater antiviral activity than either caprylic acid (C_8), capric acid (C_{10}), or myristic acid (C_{14}). Lauric acid is one of the best "inactivating" fatty acids, and its monoglyceride is even more effective than the fatty acid alone.

The system has been shown to work, but the formulating is difficult and not always predictable. It might be a good solution perhaps for those with a large research department and plenty of human resources.

Dr. Straetmans makes a series of natural solutions, amongst the emulsifiers is Glyceryl Oleate Pyroglutamate (Dermosoft GMO P-30).

Plants self-preservation
Plants that are living and connected to their root systems remain vibrant and resistant to attack by yeast, mould and bacteria. This is because every plant contains its own preservative system that keeps it fresh and vibrant. Smell a rose and then cut it and smell the same rose after as short a time as one hour. The smell of the rose will have changed

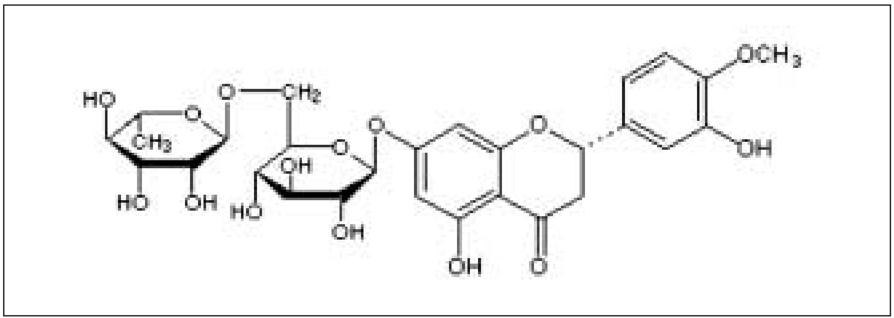

Figure 6: *Hesperidin.*

drastically as the chemical composition of the fragrant parts degrades with great rapidity.

In fruits, the seeds develop until maturity and then the fruit falls from the plant. Immediately the system that had protected the fleshy pulp surrounding the fruit from attack by yeasts, moulds and organisms ceases to function and now disintegrates. It is this breakdown of the fruit that provides nutrient for the seed to germinate and prosper.

If it were not for the failure of the natural preservation system we would be surrounded by plant material that would not rot. Plants that contain high levels of essential oil, like pine needles and firs are a classic example, where it takes a very long time for clippings to rot down – hence the advice that they should not be used for composting.

The chemicals present in all parts of the plant protect it from the environment. However, examples can be seen where tampering with the plant leads to a reduction in the efficacy of this natural mechanism.

It is concluded that the chemical constituents within each plant clearly differ in composition. Furthermore, that there may be in certain species a chemical or group of chemicals present in the plant that is capable of killing micro-organisms. This chemical composition varies according to whether the plant is alive or dead, and in certain/most plants will vary according to season.

In many cases, when these plants are extracted, it is found that the extracts are capable not only of resisting certain spoilage organisms, but in some cases can actively act to destroy them. The time and speed of extraction of the fresh plant is often critical if the preservative activity is to be retained.

Commercial products

There are a number of natural preservatives available on the market that are not, strictly speaking, legal since they have no entry in Annex VI as a permitted preservative. However, the use of a plant for its marketing claim, or for other functional benefits smudges the issue.

One may use a number of plant derivatives as fragrance components and coincidentally achieve a lower overall preservative requirement for the product in which they are used.

The debate over the safety of parabens (including the report that they cause breast cancer) shows the ignorance of phytochemistry, since parabens (Fig. 4) abound in nature. There are many cases where plants may contain paraben-type compounds in addition to other functional actives and the difficulty lies in deciding whether the botanical is being used as a preservative or for other legitimate and perfectly legal benefits.

A review of the solutions already present on the market

In days of old, wine and water was stored in silver vessels because it had been observed that the keeping time vastly improved when compared to earthernware jugs and pots. This is somewhat surprising, because one might have expected that the glazes (often rich in lead) on those pots might have further aided preservation.

Silver chloride

The modern preservative is comprised of silver chloride (20%) deposited on a substrate of titanium dioxide. It does appear in Annex VI, but is prohibited for use in children's products under three years of age. It is not allowed in oral products and those products intended for application around the eyes and lips. It is limited to 0.004% when calculated as silver chloride.

John Woodruff (Creative Developments Limited) wrote: "a silver chloride titanium dioxide composite is the basis of the JMAC range of antimicrobial products produced by Johnson Matthey in association with Microbial Systems International.

"JMAC is a silver chloride/titanium dioxide composite and JM ActiCare is a suspension of particles of a silver chloride/titanium dioxide composite in a water/sulfosuccinate gel which improves its activity against yeasts and moulds. Although recommended for most types of leave-on and rinse-off products JM ActiCare is particularly useful for preserving products containing finely dispersed particulates such as sunscreen preparations based on microfine inorganic oxides and makeup preparations.

When incorporating JM ActiCare into the formulation it is important not to add it to the oil phase as its activity is seriously affected if the particles become coated with oil. It is stable across the pH range 3-10 but it is affected by xanthan gum which binds the silver, and by some AHAs but not lactic and glycolic acids. Materials such as ascorbic acid and sodium metabisulfite which may reduce the silver chloride need careful evaluation and strong cationic materials may also be detrimental."

Nature identicals

There are a number of materials that are already allowed in the legislation and which occur naturally in nature. These include benzoic acid (limit 0.5% as the acid) and benzyl alcohol (limit 1%). They can be obtained naturally from natural sources such as balsamic resins, but extraction is expensive. Benzoic acid is moderately good against Gram+ve bacteria, yeast and moulds, but moderately poor against Gram-ve bacteria, while benzyl alcohol is good to very good against Gram+ve, moderately poor against Gram-ve, poor versus fungi and moderately poor against yeast.

Sorbic acid (and one supposes one could include its salt potassion sorbate) is found in nature (originally from *Sorbus aucuparia* or Rowanberry) but again purchase synthetically and can be used up to 0.6%. It is moderately effective against all bacteria and good against fungi and yeasts.

A two-pack system consisting of lactoperoxidase, glucose oxidase and glucose does not appear in Annex VI but has found a good following amongst green formulators. It is very fiddly to work with and has to be premixed just prior to addition to the finished batch. Its mechanism is said to mimic the conditions that keep a cow's udder free of infection whilst it is suckling its calf.

This material was formerly called Myavert C but is now renamed Biovert and available from Arch Chemicals.

The "illegal" preservatives

Citrus seed extracts

There are other dodges used by the "green" formulators in their quest to avoid the preservatives listed in Annex VI that do not occur in nature. Citrus fruits have always been a useful source of alpha hydroxy acids, of fragrant essential oils and useful astringents.

Everything in the fruit is useful, the juice for its vitamin C claims, the peel gives a fragrant essential oil and claims of "zest", the flowers yield an exquisite and very expensive essential oil called neroli, and the seeds yield an antibacterial, which is either naringenin (Fig. 5), hesperidin

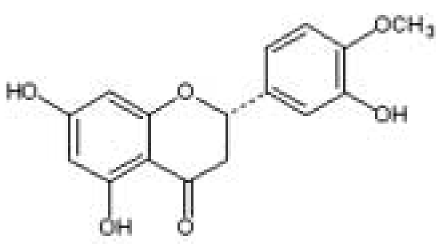

Figure 7: *Hesperitin.*

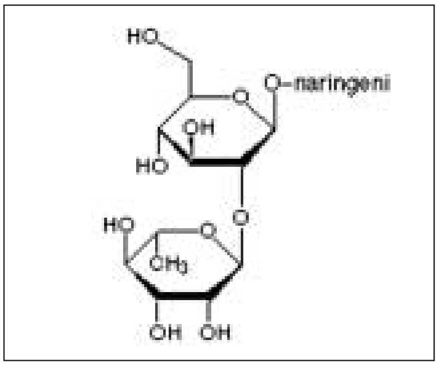

Figure 8: *Naringin.*

(Fig. 6), or hesperitin (Fig. 7) depending on the citrus species chosen.

This can be slipped in with other citrus components and is conveniently lost amongst the myriad of exotic ingredients. It is not simple to formulate with these types of materials and you have to do a lot of experiments, since not all systems are compatible, but success can be achieved.

The introduction of a natural preservative with the INCI name Citrus Grandis (Grapefruit) fruit extract called Citricidal which was available from a number of sources gave great hope for the future of natural preservation. However, reports started to circulate that the material had been contaminated with quaternary materials, and that it was this material that was giving the extract its preservative qualities. The original thoughts that it was the molecules above that were responsible for the action were dashed when a feature was found on the internet (the site has since disappeared):

"Grapefruit Extract (GSE) is made by first converting grapefruit seeds and pulp into a very acidic liquid. This liquid is loaded with polyphenolic compounds including quercetin, helperidin, campherol glyceride, neohelperedin, naringin (Fig. 8), rutinoside, poncirin, etc. The polyphenols themselves are unstable but are chemically converted into more stable substances that belong to a diverse class of products called quaternary ammonium compounds."

The web article then went on to say "Some quaternary compounds, benzethonium chloride and benzalkonium chloride, for example are used industrially as antimicrobials but are toxic to animal life…"

Clearly this material is no longer natural, but is best classified as a natural derivative and should not have the INCI name ascribed to it, since this is inaccurate.

Tree lichen extracts

The tree lichen (*Usnea barbata*) contains usnic acid (Fig. 9) which is a fairly powerful agent against yeast and moulds. It comes as no surprise therefore, that when this extract is used at a reasonable concentration that these spoilage organisms are not able to grow. The traditional use of this material for infections of the feet is well justified.

Usnic acid and its salts are available from a number of sources (e.g. A&E Connock) and as Deo-Usnate from Cosmetochem. As a word of caution, there are some individuals who are susceptible to irritation from this material and I feel that this is because it has some similarities to the potential allergens found in Oak Moss and Tree Moss which are now listed in the 26 potential allergens.

Japanese Honeysuckle extracts

A plant preservative that is based on the Japanese Honeysuckle (*Lonicera japonica*) is available that is described as being a complex mixture of esters of lonicerin and natural p-hydroxy benzoic acid (Fig. 10). The commercial material from Campo is called Plantservative WSr, WMr (INCI: Lonicera Caprifolium Extract).

Clearly this is a naturally occurring paraben, and we would expect this material to have antimicrobial properties.

Lonicerin is luteolin-7-O-galactoside (Fig. 11) (Chen *et al*). It has been reported (Lee *et al*) that *Lonicera japonica* has anti-inflammatory activity and though not as potent as the normal benchmark of prednisolone, it would nonetheless be effective in treating inflammatory disorders. This factor makes the preservative very attractive, since it has benefits for its soothing properties and also has antimicrobial activity. There are not many preservatives that would have this dual benefit. I have not searched the literature to see whether other luteolin derivatives have been found to have antimicrobial properties, but the flavonoids are certainly well respected for their anti-inflammatory activity wherever they are found in plant materials.

Formosan Hinoki Tree

Hinokitiol is a white crystalline acidic substance first isolated from the essential oil of Formosan Hinoki (*Chamaecyparis taiwanensis* Masamune et Suzuki) by Nozoe in 1936. This substance was also found in the essential oil of Aomori Hiba tree (*Thujopsis dolabrata* SIEB et ZUCC) at a later date.

Though the natural form of hinokitiol (Fig. 12) is no longer available, the nature identical form is still made. It may be a surprise to learn that this material is listed as a hair conditioning agent in the CTFA Ingredient Dictionary. It is one of those unfortunate events where a conditioning effect also had a preservation contribution. It is also unusual in that it has a 7-membered ring and is quite unlike any other preservative one normally encounters. It is available from S. Black, A&E Connock and Nikko with CTFA names Hinokitiol or Chamaecyparis Obtusa Powder or Oil (Ichimaru Pharcos), although I do not know if the last materials (presumably all natural) have preservative action.

The parfum (fragrance)

Another clever idea is to look at essential oils and then isolate one or two of the components that coincidentally have antimicrobial activity. Since these components came from an essential oil, they must be perfumery-based materials and so can be listed as parfum or fragrance.

One isolated material present in the Dr. Straetmans range of such preservatives was once revealed as being anisic acid (Fig. 13) which quite clearly is a paraben structure. Another material revealed was levulinic acid [CH3COCH2CH2COOH] or 4-oxopentanoic acid.

Anisic acid is found in Aniseed (Pimpinella anisum) amongst many sources, and levulinic acid has been found as a by-product in the production of diosgenin from Wild Yam (*Dioscorea villosa*).

There is a range of options from Dr. Straetmans called Dermosoft 688, Dermosoft 690, Dermosoft 700 and Dermosoft 710 all used at 0.5% to 1.5%. (INCI name: Parfum).

Another product from Sinerga called Naticide has also been shown to have excellent results at around 1% and despite

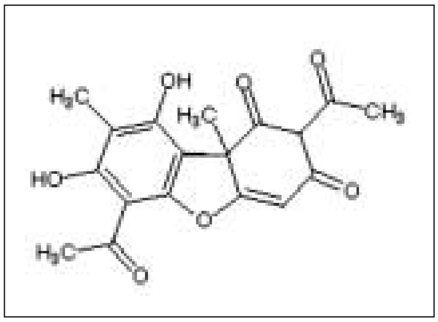

Figure 9: *Usnic acid.*

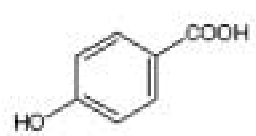

Figure 10: *p-hydroxy benzoic acid.*

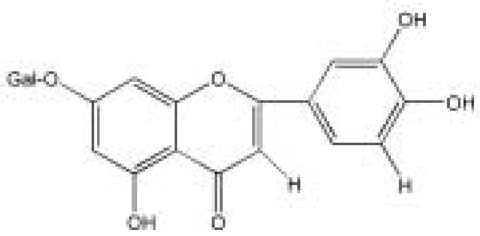

Figure 11: *Lonicerin.*

continual pestering have been unable to determine what plants have been used as the source of the active materials (INCI name: Parfum).

Bio-Botanica has two natural preservatives that are also extracted from plant actives, one called Neopein and the other Biopein which are composed of Origanum Leaf Extract, *Thymus Vulgaris* (Thyme) Extract, *Cinnamomum Zeylanicum* Bark Extract (Not present in the Biopein. I believe there is a new addition to this line that has just become available but have no data at the time of writing), *Rosmarinus Officinalis* (Rosemary) Leaf Extract, *Lavandula Angustifolia* (Lavender) Flower Extract and *Hydrastis Canadensi* (Golden Seal) Root Extract.

All of these materials are well-known for their antimicrobial activity and give rise to a host of active molecules: carvacrol, thymol, cinnamaldehyde, eugenol, cineole, camphore, α-pinene, rosmarinic acid, berberine, hydrastine, linalyl acetate and linalool. This area could be exploited far more, because there are many other essential oil components that have antibacterial properties.

Perillic acid

A material that was presumably first found in *Perilla frutescens* or the Japanese Shiso oil is perillic acid. The perillaldehyde present has already been found effective against *Acnes propionibacterium* and *Staphylococcus aureus* (Balacs).

This material is made commercially by the convertion from limonene using a biotechnology process. It has been found to have good activity against Gram+ve and Gram-ve bacteria. Perillic acid is available from Dr. André Rieks and Paroxite.

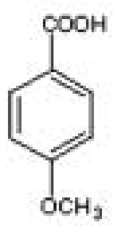

Figure 13: *Anisic acid.*

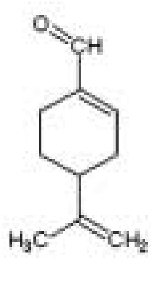

Figure 14: *Perillaldehyde.*

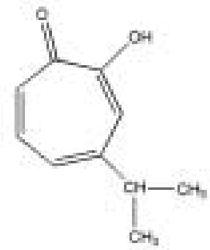

Figure 12: *Hinokitiol.*

Melaleucol

A refinement of *Melaleuca alternifolia* (Tea Tree) Oil, which contains 1,8-cineole, α-terpineol, α- and γ-terpinene, terpinen-4-ol and sesquiterpenes has been found to deliver good performance against a wide range of spoilage organisms. The smell is quite clearly the characteristic antiseptic smell of tea tree, but this might be acceptable when one considers that it has also been shown to have mosquito repelling effects as a bonus.

Wasabi (*Wasabia japonica*) or Japanese Horseradish

Active Concepts has a material called ACB Wasabi extract which is rich in allyl isothiocyanate. Used at 1-3% it is said to make a significant contribution to the antimicrobial activity and at the same time has antioxidant activity.

Packaging considerations

Considered have been the base and also the additives that one could introduce in order to reduce or eliminate spoilage organisms in products.

The last piece of the jigsaw is the packaging. Wide neck jars with shives (the plastic discs that cover the neck) are probably the worst news for the microbiological integrity of a product. Those covers allow water to condense on the surface and then enrich the organisms. The cardboard seal in the lid is another microbial sponge just waiting to act as a growth medium.

Tubes are far better (which is why they are more widely used in the pharmaceutical industry). The nozzle offers a smaller and more discrete surface for contamination. There are now tubes that have non-return valves, so that once pressed the tube cannot relax to permit the ingress of air. Notice how tubes for eye products have long tapering nozzles with a small pin hole for delivery of product. This makes good microbiological sense.

The new generation of pots does not allow the consumer to insert fingers that might be highly contaminated. There are pots with nozzles and sealed flat surfaces that have airless pistons that follow the product to completion. The product is offered to the consumer at a push and those days of scooping out are over, especially with the 7th amendment demanding a use after opening period to be declared.

It could be argued that in these sealed and hygienic environments, the need for a microbial challenge test is over, since the consumer and the air will never enter the product during its active life. The preservative requirement will be a fraction of that required for a wide-necked cream jar.

The most secure pack is a single application pack, the sachet, the blister pack and the single shot capsule. These are technologies that come to us from the fast food and pharmaceutical industry. You use it all or throw away the residue – it is the perfect preservative-free environment and the worst example of wastefulness.

Conclusion

There is a move towards "preservative-free", which is being achieved by many means. It is hoped that this overview has provided an insight into some of the techniques available. PC

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