Atmospheric Pressure Ionisation-Mass Spectrometry: A Tool for Food Security Policing and a Solution to Various Medicinal Problems

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Abstract:

Modern agriculture and animal husbandry increasingly require utilisation of advanced technology as exemplified by the large-scale use of veterinary drugs worldwide. Antibiotics in agriculture and veterinary medicine were introduced in the 1950s with oxytetracycline and chlortetracyclines being the first feed additives. Currently these drugs together with β-lactams, aminoglycosides, aminocyclitols chloramphenicols, peptides, ionophores, and macrolides are widely used for agricultural purposes. Anabolic steroids, anthelmintics and sulfonamides are also popular antibiotics in animal husbandry. Drug administration to animals is usually aimed at treating or preventing the outbreak of animal diseases or promoting growth. Unfortunately, these drugs or their metabolites have a tendency of appearing as residues in edible products such as milk, eggs, animal tissue obtained from treated animals. Some of the drugs have been implicated as carcinogenic with others having adverse effects to humans even at low levels. The knowledge of the type of drugs and their metabolites at residual level is essential for the safety of the consumer. In order to control and monitor the levels of these drugs in edible products, the development of sensitive, selective and accurate analytical methods is fundamental. The first part of this presentation will focus on atmospheric pressure ionisation mass spectrometry as powerful analytical tool for policing of abuse of veterinary drugs in animal husbandry.

The second part of the presentation will demonstrate the importance of API-MS with respect to various medicinal problems. Coupling liquid chromatography with API-MS/MS is ideal for biomarker discovery, metabolite identification and human health research and drug development. The future of medicinal development is through proteomic research. With the availability of genomic and protein databases, mass spectrometry is fast becoming the preferred method of protein identification. It is hoped that our understanding of diseases would be improved through our understanding of protein of the diseased and normal cells.

Introduction:

Natural and synthetic hormones, together with other veterinary drugs are used worldwide as growth promoting agents in animal breeding. There is increased concern about residue in foodstuffs of animal origin in many countries, particularly in the European Union (EU) and countries that export meat and meat products to the EU. Public health authorities and the Agrofood industries are challenged in satisfying consumers and exportation market demands regarding the quality of meat and the safety and control of different residues in food. The use of some of these compounds is completely forbidden within the European Union (EU) while as other substances have been permitted for which maximum residue levels (MRLs) have been set. In the case of banned compounds, this directs the analyst to develop methods with the lowest possible limits of detection, i.e. 'chasing zero', while in case of permitted ones, the analyst's concern might be better directed towards more rapid and definitive methods with limits of detection adequate to police the MRLs. The policing method may be direct, i.e., identification or quantification of residues of the parent compound or the metabolites in the muscle or tissue or edible organs give the measure of exposure of these compounds of interest. In most cases however, the monitoring method is indirect via derivatisation.

The use of forbidden compounds is evidenced by their detection in sample types, which are easily obtained or analyzed, such as injection sites, urine, faeces, and kidney fats. The detection for example of artificial anabolic agents illegally used as growth promoters in industrial farming is considered as a priority in the EU. Nowadays public concern is not confined to anabolic hormones but include other veterinary drugs. Several new groups of substances have received publicity, particularly, the sulfonamides, tetracyclines, anthelmintics, β-agonists, tranquilizers and genetically engineered bovine - and porcine – growth hormone (BST, PST).
Some of these drugs are allowed but the maximum residue limits (MRLs) are violated due to misuse of the drug or poor animal management. The EC directive 86/469 expanded the control to all veterinary drugs [1]. The criteria document 87/410 was extended in Commission Decision 89/610 to include all veterinary residues [2]. This latter document is now further revised to cover both screening and confirmatory methods of analysis. The commonly acceptable official techniques used until now for these controls have a number of limitations. As a consequence, positive results have to be validated by other, more reliable analytical methods.

The confirmatory analysis techniques most commonly used are thin-layer chromatography [3,4] and low resolution mass spectrometry coupled with gas chromatography (GC-MS) [5]. However, most compounds of interest are non-volatile or thermal stable and therefore require derivatisation prior to GC-MS. In addition, extensive sample preparation is required before the analytical determination. Rapid procedures for the detection of anabolic compounds for example, involves solid-phase extraction (SPE) on C_{18} empore discs and amino (NH_2)- bonded columns for sample pre-treatment of large volumes of sample material e.g. urine (30 ml), followed by GC-MS-MS determination [6].

Mass spectrometry is a technique that provides molecular mass and structural information of organic and/or inorganic compounds. In mass spectrometry, the sample in gaseous phase is ionised. The ions and/or charged particles formed are then separated according to mass per charge ratio (*m/z*). The most commonly used ionisation sources are electron ionisation (EI) and chemical ionisation methods (CI). The requirement that compounds to be analysed be volatile and thermal stable can lead to a limitation to usefulness of the technique. Therefore, a number of ionisation methods for the mass spectrometry have been developed to enable analyte that are non-volatile and/or unstable under electron ionisation (EI) and chemical ionisation methods (CI). Atmospheric pressure ionisation (API), mainly electrospray (ES) and atmospheric pressure chemical ionisation (APCI) is an example of such ionisation source that could be used for the analysis of compounds that are non-volatile and/or thermal unstable. The API source was originally developed as an interface for liquid chromatography-mass spectrometry (LC-MS) for macromolecules, such as protein and peptides by Fenn and co-workers [5]. Coupling LC to MS has several advantages over GC-MS, in particular in the multiresidue methods of monitoring veterinary drugs. In addition LC-MS has demonstrated great potential in medicinal related applications.

In this presentation the application of the atmospheric pressure ionisation-mass spectrometry to policing food security and medicinal application will be highlighted.

Experimental:

Materials and Reagents

i) Anabolic compounds used in this study included: 17α-trenbolone, 17β-trenbolone, 4-androstene-3,17-dione, 19-nortesterone, testosterone benzoate and, Testosterone enanthate, Epitestosterone, Nandrolone decanoate, Testosterone 17β-cypionate, Testosterone decanoate, Testosterone isocaproate, testosterone, all from Sigma (St. Louis, U.S.A).
ii) Sixteen sulfonamides; All the sixteen sulfonamides; 5-sulfaminouracil, sulfaguanidine, sulfadiazine, sulfamethizole, sulfamethoxazole, sulfathiazole, sulfabenzamide, sulfapyridine, sulfamerazine, sulfamonomethoxine, sulfamethazine, sulfamethoxypyridazine, sulfaquinoxaline, sulfadimethoxine, sulfasalazine used in this study were obtained from Sigma (St. Louis, USA)
iii) The benzimidazole anthelmintics (albendazole, fenbendazole, mebendazole, oxibendazole, and thiabendazole) were from Sigma (St. Louis, USA).

All organic solvents (e.g. methanol and acetonitrile) used in this work were filtered through a 0.45 μm organic membrane filter, type HVLP, Millipore (Dublin, Ireland) and were of HPLC grade and were from BDH Laboratory (Poole, England). Di-n-hexylether (99 %) was from Aldrich (Steinheim, German), sulphuric acid (99 %), sodium

hydroxide pellets (98 %), sodium bicarbonate (98 %), acetic acid were from Saarchem (Krugerdorp, South Africa). Tri-n-octylphosphine oxide (TOPO), n-undecane and ammonium hydroxide used were from Sigma (St. Louis, USA). Formic acid was purchased from N.T. Laboratory Supplies, (Johannesburg, South Africa). HPLC grade methanol and acetonitrile were from BDH Laboratory (Poole, England). Ultra high purity water was processed through a Millipore Quantum Ultrapure Ionex Gradient A10 purification system (Millipore, Molsheim-France). Aqueous solvents were further filtered through 0.45 μm pore size cellulose nitrate membrane.

Preparation of Standard Solutions:

One mg of each of the veterinary compounds was dissolved in 1 ml of methanol to make a stock solution of 1000 ppm. From this, diluents of different concentrations were prepared in (1:1) methanol and water.

HPLC separation of mixtures

Samples were separated using a Hewlett Packard Series 1100 consisting of; binary pump system, photodiode array detector (DAD) detector, thermostated column compartment, vacuum degasser, and controlled by HP ChemStation. A gradient mode was used to separate the mixtures using mobile phase; A = 100 % methanol; B = 85 % 25 mM acetic acid in water + 15 % methanol. 20 μl of sample were injected into a Waters XTerra microbore C_8 (150 mm x 2.1 mm x 3.5 μm) column. The separation was performed at a flow rate of 100 μl/min and monitored either by ES-MS or UV/Vis.

ES-MS of compounds of interest (anabolics, sulfonamides, etc)

The samples were introduced to the electrospray ionisation source by direct infusion using a Harvard Apparatus 22 syringe pump (South Natick, Massachusetts, USA). 50 μl of dissolved sample were mixed with 200 μl of buffer and the resulting solution infused at 3-5 μl/minute. The ionisation buffer used was (1:1) 25 mM acetic acid in water/methanol. The spectra were obtained using a ThermoQuest LCQ^{Deca} quadrupole ion trap mass spectrometer (San Jose, California, USA). The system used ThermoQuest Xcalibur software (San Jose, California, USA).

Preparation of bovine liver and kidney tissues samples of veterinary drugs mixtures

Finely sliced liver (after removal of the gall bladder) and kidney carcasses (~ 20 mg) from the local abattoir were minced and spiked with a known concentration of a mixture of anabolic androgenic compounds. The concentration of a mixture ranged from 1 ppt to 1 ppm. The spiked samples were homogenized by using a blender. The anabolic androgenic compounds were then solvolysed in 1 ml ethyl acetate containing 2 μl of 0.5 M H_2SO_4 at room temperature in a shaking incubator for 2 - 4 hours. The organic phase containing the androgenic compounds was washed with UHP H_2O and evaporated. The residues were dissolved in 1 ml of MeOH-H_2O (40:60, v/v) and then stored at 4 $^{\circ}$C until required for enrichment and/or clean-up with SLM and SPE.

Preparation of milk and urine samples of veterinary drugs mixtures

A 10.0 ml aliquot of milk or urine was transferred into 25 ml centrifuge tubes and then spiked with similar concentrations of anabolic compounds as was for liver and kidney tissues. The mixtures were then subjected to solvolysis in a similar manner as was for liver and kidney tissues.

Results and Discussion

The use of prohibited substances with or without political and ethical considerations will have an effect on the consumer of the products from treated animals. In case where administration of these compounds is prohibited,

there are many ways attempted to disguise their application by the producers. Hence, almost all parts of the animal are eligible for injection and thus certain edible tissues, such as tail base and neck muscle. Consumption of contaminated meat by athletes for example would result in unequivocal identification of banned substances in urine, such that an acute dose of hormone or drugs from contaminated meat constitute a serious liability to the consumer, in this case the athlete.

Steroid hormones are poorly soluble in aqueous media, and are not stored in gland cells. Instead, they are released directly into the blood stream after their synthesis therefore blood sera may be used as the sample from which to detect the presence of anabolic hormones. Steroid hormones and their metabolic products are ultimately disposed of via the excretory system, usually the kidneys hence it is possible to detect them in the urine of the consumer. Mammals are known to be unable to degrade the steroid backbone. Steroids are therefore ultimately excreted with the urine and to some extent with the bile. Methods for the detection of steroids in the urine can also be used to investigate the hormone metabolism.

An infringement of the hormonal substances for sportsmen is normally evident when these substances or metabolites appear in the urine or other body fluids. In some cases athletes could test positive due to consumption of contaminated meat or meat product Analysis of injected site of veterinary animals is suitable for determining the hormones that are illegally injected because the analysis of other biological matrices like faeces, kidney fat or urine may not be obtained owing to metabolization and selective excretion and/or deposition of these compounds.

The challenges, therefore to the analyst is to develop methods that can be utilised in monitoring of a variety of veterinary compounds in different biological matrices simultaneously. Traditionally a great majority of compounds had been monitored indirectly by GC-MS [10,11]. The advert of API interfaces has enabled the coupling of LC to MS with tremendous advantages over GC-MS. The use of LC as a multiresidue monitoring tool is more attractive than the GC. LC is not only limited to volatility or thermal stability of the analyte. In addition LC can utilise all the four modes of chromatography in the separation of the analyte. The addition of the mass spectrometry, with selected ion monitoring (SIM) capability not only enhances the selectivity but also sensitivity. It should be noted however, that MS as a detector for GC and LC is the same. In comparison with GC, the LC methods have a number of advantages over the GC methods such as: i) no need to derivatize the compounds and ii) can analyze the samples in the same matrix as the sample without the need to evaporate.

Monitoring of Anabolic Compounds by LC-MS

This group of compounds is non-volatile, that is, it is and non-GC active therefore cannot be separated under direct GC or GC-MS. Gas chromatographic methods via derivatisation have been normally used for determination of these compounds by either performing silylation, benzylation and methylation derivatisation. Mass spectrometry as a detector for GC was found to be more sensitive and selective than the conventional GC detectors. However, methods based on gas chromatography had limitation in quantification of these compounds due to the possibility of thermal decomposition. In addition the technique also displayed non-reproducible ionization in the ionization source of the mass spectrometer. Atmospheric pressure ionisation interface, in ES or APCI modes has the capability of ionising or transporting ions of the parent anabolic compounds directly from the biological matrices. Therefore, the API-LC-MS used in monitoring anabolic compounds completely eliminates the need for derivatisation. In our research group we have successfully used LC-API-MS in monitoring anabolic compounds in a variety of biological matrices [12]. Figure 1 shows a typical example of a chromatogram of five anabolic compounds under APCI-LC-MS conditions. A 150 mm x 1.0 3.5µm XTerra RP18 column was used for this gradient separation.

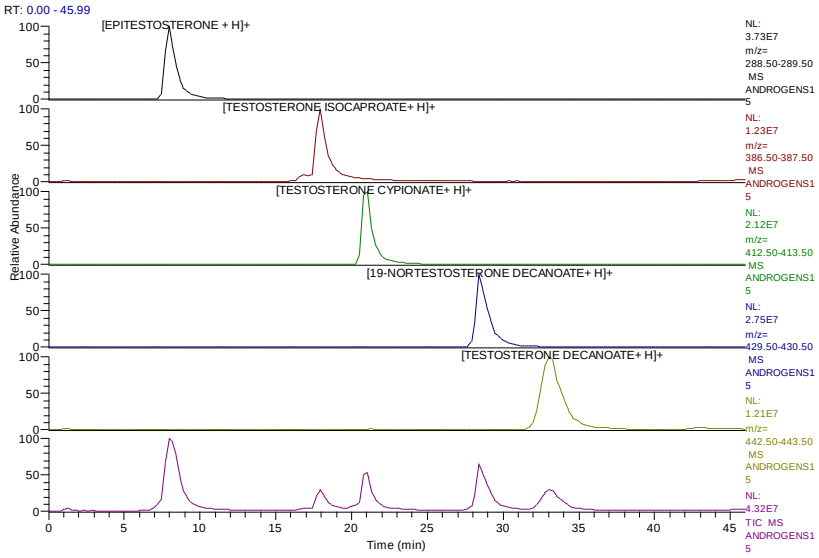

Figure 1 LC-APCI-SIM-MS chromatograms of testosterone and its methyl ester derivatives: Conc = 0.1 mg/L

Monitoring of Sulfonamides Compounds by LC-MS

Sulfonamides are a group of antibacterial agents commonly used in veterinary practice to prevent infections in livestock, to treat diseases, and to promote growth [14]. The presence of sulfonamide residue in food is of concern because some of the compounds are known to be carcinogenic [15] and they generally enhance the risk of developing antibiotic resistance [16], which makes the therapeutic use of similar medicine inefficient [17]. Recent evidence has implicated sulfamethazine as a possible thyroid carcinogenic agent [18]. Sulfonamide residue in food and animal tissues may be present in minute concentrations but may pose a health threat to consumers [19]. Therefore, monitoring of these compounds has attracted interest to the scientific communities.

Recently we have developed ES-LC-MS method of monitoring sixteen sulfonamides in variety of biological matrices [20]. Incorporation of sample supported liquid membrane (SLM) pre-treatment technique to ES-LC-MS allowed us to determine these compounds in concentrations below sub parts per billon (ppb). A typical ES-LC-MS chromatogram of sixteen sulfonamides drugs is shown in Figure 2a & b.

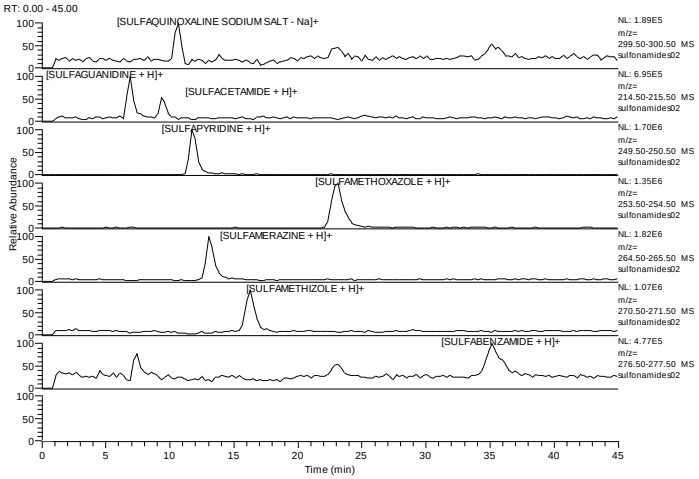

Figure 2a LC-ES-SIM-MS chromatograms of 1 mg/L of sulfonamides in UHP water

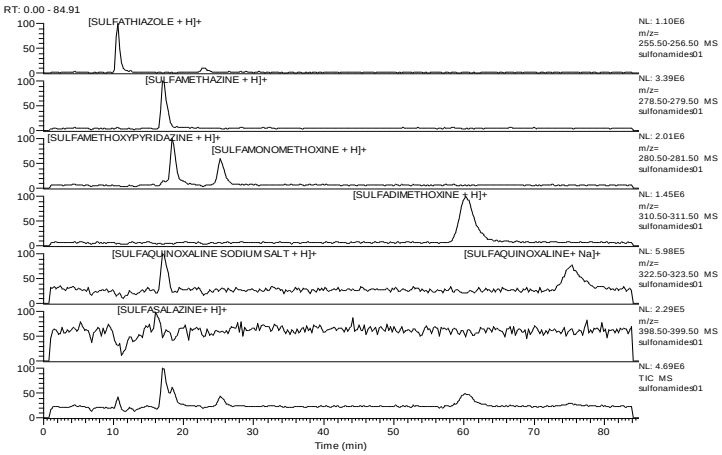

Figure 2 b LC-ES-SIM-MS chromatograms of 1 mg/L of sulfonamides in UHP water

Monitoring of Anthelmintics Compounds by LC-MS

Benzimidazole anthelmintic drugs are commonly used in the veterinary practices to treat gastro-intestinal infections and also for animal fattening purposes [21-23]. Generally, the presence of drug residues can be detected in various target organs/tissues, for example, liver, kidney, fat, skin, milk, eggs and blood; or in the metabolic by-products, such as, urine, feaces, bile and sweat [21]. The European Union (EU) has regulated the maximum residue limits (MRLs) for some of these compounds, ranging from 0.010 ppb to 1.00 ppb depending on the compound of interest and the type of food (type of tissue) [21-23]. Recently we demonstrated the use of LC and LC-ES-MS to monitor these compounds in various biological matrices [24, 25]. Figure 3 shows the separation of benzimidazole anthelmintics using a 150 mm x 2.1 mm x 3.5 μm XTerra column.

Medicinal Application of API-MS

Giant strides have been achieved in the field of medicine due to the use of API-MS as a tool especially when coupled to LC. In the area of traditional medicine LC-API-MS has been used in the monitoring of secondary metabolites [26,27]. Hyphenating liquid chromatography to mass spectrometry for many of the medicinal problems has several advantages. The combination of LC as a powerful separation technique to MS as a sensitive and selective detection technique makes an obvious marriage. The LC-API-MS/MS has in the developed world demonstrated its potential in the medicinal field through proteomics studies.

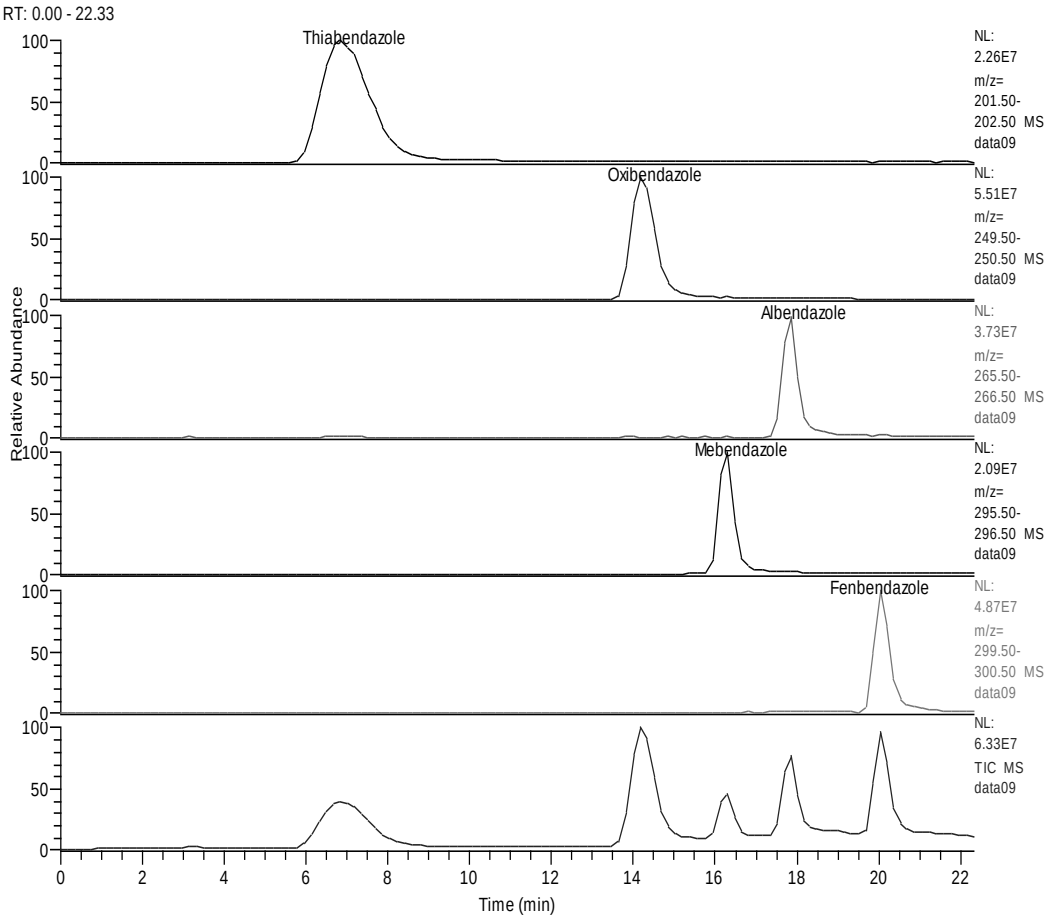

Figure 3

SLM/LC-ES-SIM-MS chromatograms of 1 mg/L mixture of benzimidazole anthelmintics in urine matrix

Proteomics is the study of protein composition of a cell, tissue, or organism. The primary objective in proteomics is to monitor changes in protein expression in response to changes or disturbance such as gene mutation or environmental stress. The focus to our understanding of the protein of diseases is that the possibility of development of disease specific drugs could be developed. This approach is totally different from the antibiotics type of approach treatment. In the developed world for example a great number of women are diagnosed with breast cancer each year, and hence breast cancer remains the major concern to public health. Proteomics using LC-API-MS/MS has to date contributed to our understanding of some forms of cancer [28]. In addition LC-API-MS/MS has also demonstrated great potential in the study and development biomakers and drugs for a variety of diseases [29,30]. We believe that Africa needs to invest into this technology so that it can start tackling some of its health related problems, which it does not share with the developed world.

Conclusions

The API-LC-MS technology has demonstrated its applicability as a monitoring tool to protect humans from abuse of restricted compounds targeted for veterinary use. This technology requires less time because the derivatisation step has been removed. The compounds of interest are monitored directly and in their environment. The potential of this technology with respect to medicinal application cannot be over estimated. Africa is a continent that is pledged with HIV/AIDS in addition to some diseases that mainly common to it.

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Anti-malarial Therapies in Africa. Preferred Dosing Combinations and New Potentials for Drug Development

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Keywordss

Abstract

The three mainstays in use for effective control of malaria are: anti-malarial drugs for the treatment of infection, pesticides to control the spread of the malarial vector, and pesticide-treated mosquito netting to prevent infection. Most recommended drug regimens for the treatment of malaria are based on artemisinin combination therapy (ACT). This presentation describes our work in West Africa and at Howard University to increase access to malaria drugs in Africa. The drugs halofantrine and lumefantrine (benflumetol) are addressed in this presentation. Halofantrine is a drug originally launched by Glaxo SmithKline that is very potent and possesses a convenient dosing schedule (two days of dosing at a one-week interval). Halofantrine is, however, essentially unavailable because of cost and poses a concern for cardiovascular toxicity. We will present new chemistry utilizing modest technology that greatly reduces the cost of this drug and points a way towards addressing concerns over potential cardiotoxicity. Lumefantrine is also a synthetic target for new chemistry to reduce the cost of the active pharmaceutical ingredient.

The Role of Intention in Technology Development

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Keywords: science of intangible, sustainable technology, chemical processing

Abstract:

If we follow the path of human intentions as a social form, how humans as individuals and collectives arrange their lives, we find that Intention is not a wish or an aspiration. Rather, it is a plan, a way to create a pathway. This paper posits that the overwhelmingly intention governing contemporary economic and social existence is the Establishment plan to control, contain, and sell off the whole world, again and again, and attempting to obliterate the natural world by transforming everything in it to products. This Intention has been imposed on all the peoples of the world. In this, the technology development has merely been a tool for sustaining status quo, which is aphenomenal in the context of nature, where everything is dynamic. This paper follows some of the dangerous pathways of contemporary attempts to control nature, and suggests another path for the world community.

1. Origin of Intention

For the last 200 years the role of intention in all social endeavors has been either ignored or carefully put aside. This includes practically all scientific analyses, and coincides with the commercialization of practically everything in our lives, including education [1] and charity [2]. The moment any action is judged against a commercial value, it is assumed that the intention of the action does not have any bearing on the action. This detachment from intention, which is actually the driver of all actions, is so embedded in all analyses that our research found no model that considers this factor in any model of the modern age.

Every action is preceded by intention. Every civilization, ranging from ancient Indian to European culture has recognized the role of intention. For instance, the relationship between 'Chetna' (inspiration) and 'Karma' (deed) was outlined in Mahabharat and in the scripts of Buddha. In Europe, the ancient criminal justice system was based on 'guilty mind' (*mens rea*). The most famous saying of Prophet Muhammad and the first one cited in the collection of Bukhari [3] is that any deed is based on the intention. A review of human history reveals that the perpetual conflict between good and evil has always been about opposing intentions. The good has always been characterized by the intention to serve a larger community while evil has been characterized as the intention to serve a self interest. Because nature itself is such that any act of serving others leads to serving the self in the long term, it is conceivable that all acts of serving others in fact amount to self interest in the long-term [2;4]. Some see this as the approach of obliquity. However, not many understand the value of this approach and the most dominant theme of the contemporary society is self-interest in the short-term is everything [5]. History also tells us that ruling entities have always covered up their intentions. From ancient Pharaohs to contemporary ruling elites, rulers have invariably maintained the façade of their good intentions. Whenever this covering up became exposed, the principle of "the King has been ill-advised" has been invoked. While the onset of the information age has begun to make it difficult to

cover up intentions, recent events in this new millennium show clearly that covering up intentions is bound to be very costly and will have short-term consequences. The US invasion and occupation of Iraq for trumped-up reasons is the most recent example, with tragic ramifications for humankind [6;7].

Few would dispute seeking peace is the loftiest goal of humans in society, yet human history is marred by war [8]. Since the beginning of the 20th century wars have given impetus to economic and technological breakthroughs as research and the development of better weapons of destruction, and their production create jobs and potential new products to be sold in the civilian economy. In the United States a war president is almost certain to be re-elected, and talking war is considered to be presidential. Ronald Reagan, the Star Wars president, was considered the most popular president ever, although the war (named for a popular science fiction television program) was to be about developing weapons systems to control outer space by the US against its perceived enemies. This scheme required such an enormous outlay of the collective wealth of the US that it was deemed, after long debate, unworkable. However, it has become a vastly successful commercial enterprise. Star Wars toys, stories, and movies are one of the most popular forms of entertainment even for adults. In the prevailing US culture, dominance is synonymous with weapons of mass destruction, which can be simultaneously morphed into consumer products engineered to becoming part of the human cultural space [9].

2. Nature for Sale

Energy

The sun shines 1.3 kW of energy per square meter on us, yet we burn some 50 million barrels of crude oil daily to have energy for our daily needs [10]. This crude oil is refined with numerous toxic additives that are particularly harmful when burned in all combustion engines. Natural gas is another form of energy on which we have become dependent. This gas is processed (to remove water, carbon dioxide, etc.) with toxic chemicals, such as, glycol, Diethylamine (DEA), and others. Even very small parts of these toxic chemicals are dangerous to humans, particularly when they too are burned, in every turbine and other type engines, and the gas stoves in our kitchens. Natural gas is also used to make fertilizers that can only be compared with drugs – the more taken the more needed. The ensuing dependency severely compromises inherent metabolic systems, and in the case of fertilizers, depleting the soil of its inherent nutrients. The cycle of poisoning does not stop here. Plastics are made from the toxic waste left after refining oil, 2.5 million tons of it every day. They are laid out on everything, from baby bottles (that emit dioxin when microwaved) and children's toys to carpets, wall paints, and pillow fillings. To make them user-friendly, more toxins are added. Meanwhile governmental agencies bombard the public is with slogans recommending, "Reduce, Reuse, and Recycle", knowing fully well that every cycle of re-use makes these plastics more toxic and oxidized, using very important oxygen molecules to produce even more harmful chemicals. This plastic is particularly poisonous when heated, yet they are marketed on non-stick™ cookware and recommend incineration as the ultimate fate of these plastics [11].

Air

Cigarettes (nicotine added tobacco) were introduced into the personal and public space less than 100 years ago, advertised as glamorous for women and masculine for men, who inhale toxic smoke directly into the lungs. Thus far, the only attempt to stop this human destruction, after years of research and law suits by the public, has been to put warnings on cigarette packs, and increase the price by value added taxes in the US and Canada. In the vast majority of developing countries, people who cannot afford food enough to sustain themselves, smoke billions of dollars of cigarettes daily, profiting only the entities that produce and sell these weapons of mass destruction. In addition many of these same countries are tobacco producers, whose economies to date are dependent on this crop [12], and although countries in Latin America and Africa have taken measures to prevent youthful smoking, Big Tobacco is leading an offensive against such measures in these areas of the world [13] .

Water

Nature offers free water through rainfall that, after passing through soil, becomes potable by picking up essential minerals. Every nation has access to this water, which is best consumed without any additive. Yet throughout the western world people have little option to drink this fresh water since the water supply system is infused with chlorine, possibly the most potent poison readily soluble in water. Chlorination of water was first introduced in England in 1908 and the US and Canada soon followed suit [14]. Products and services that result in 45% of the U.S. gross domestic product are rooted in chlorine chemistry. In addition to water disinfectants and pharmaceuticals, chlorine is critical to 25% of all medical plastics, 70% of all disposable medical applications, and 95% of crop protection chemicals; it also plays a significant role in the production of soaps and detergents, aluminum, and pulp and paper. The chlor-alkali sector is a solid job producer in the U.S., with a payroll of more than $360 million and

more than 37,000jobs [15].

In addition, many cities in the US and Canada have added fluoride to the water, as was recommended by the US Dental Association, the same Dental Association that once promoted the addition of fluoride in toothpaste, followed by the 'invention' of fluoride-free toothpaste. This form of corporate control is so intense, that there are now discussions about the efficacy of adding Aspirin™ and even Lipitor™ to drinking water [16]. Chlorinated water has become synonymous with some government/corporate definitions of health. Even the World Health Organization of the UN deems chlorinated water the only potable water. Human civilization has survived and indeed thrived for thousands of years, yet we are forced to believe today's civilization cannot survive without the addition of a toxic chlorine tablet. Countries that once had the most access to drinking water have become the most behind in accessing 'potable' water.

Food

Nature offers us free food in the form of plants and animals that feed on these plants. As infants, the best food is mother's milk, which is also free. However, every aspect of the food chain has been engineered, making each 'process' inherently toxic, so that now mother's milk contains traces of all the toxins the mother has ingested and the presence of plastic in umbilical cords [17;18]. The food we eat has a very high price tag because it has become a matter of public policy to throw away excess food to avoid 'price shock' [19;20].

Few doubt that processed and 'engineered' food is the cause of obesity (the second biggest killer in North America), yet the developed countries continue to flood Asia and Africa with processed food product technology. In the modern age, there is not a single famine that could not be averted by the West, yet it remains the imposed savior of the world, particularly the developing world. The developed countries have made a contribution to civilization in the form of the plastic bottle to carry water, yet people in Somalia have carried their water in clay containers since they learned to make pottery. Which water is less contaminated? Anyone capable of browsing the website would know the dangers of plastic bottles and with any knowledge of science would understand that leaching doesn't stop just because we cannot measure the amount leached with available technology [4].

3. The science of inefficiency

Historically, human efficiency has been synonymous with doing more with less – the essence of waste minimization. In the Western capitalist world, wasting is built in to the system. Canada, the only country that topped the UN-designated best place to live five years in a row is also the country that has the most energy consumption per capita [21]. If cold climate is an indicator of energy needs, Canada's per capita energy consumption is much higher than colder parts of the world, such as Alaska, Norway, Siberia, and others [22]. In the developing world, Kuwait spends 40% of its energy needs in burning fossil fuel so this tiny country can be cooled with air conditioning [4]. How could this type of absurdity be promoted? You keep repeating certain messages over and over and make sure that people are fascinated enough to stop thinking. This principle in modern age was promoted by Bernays [23].

In contemporary Western society, there is an all- pervasive perception that intentions don't count. Nobel Laureate Linus Pauling – prizewinner both for Chemistry and for peace, transmuted his work into the notion that humanity could live better with itself and with nature through the widest possible use and/or ingestion of chemicals, that chemicals are chemicals, i.e that knowledge of chemical structure discloses everything we need to know about physical matter- that all chemicals of the same structure are identical regardless of how differently they may actually have been generated or existed in their current form [24]. Paralleling this idea, the Nobel Laureate in Economics, Joseph Stiglitz, has redefined the entire field and science of economics along the line of the notion that information is destiny. Such dogmas have proven especially harmful for health and quality of life in the developed world and for basic economic welfare in the developing countries of Africa, Asia and Latin America [25]. Scientists need to be asking if the catchphrase 'chemicals are chemicals' is true, every nation that fell or was pushed into the trap of chemical fertilizer use by agribusiness, is now searching for ways to escape its myriad problems. If money, or investment, is "destiny" why do we see repeated economic collapse in developing countries proportional to the money invested from developed donor countries? Figure 1 illustrates this point. Following a term of service as the head of the World Bank, it was Prof. Stiglitz, in an August 2003 speech in Bangladesh, stated that "the World Bank and IMF only serve the interest of developed countries". From the time institutions in these countries overhauled their basic posture during the Kennedy Administration, guided by the theories of "economic takeoff" [26], and reoriented and realigned their policies in the closest possible collaboration with the United States' Agency for International Development (AID) programs, such an outcome could never have been in doubt.

According to the U.S. motivational guru Brian Tracy, “today the greatest single source of wealth is between your ears”. Human beings, by their labour, are the source of all wealth, yet modern civilization equates wealth with reducing the human population. With the exceptions of the U.S. and Canada, where population increases are now attributable entirely to immigration while the effective birth rate is zero and the natural rate of increase is below zero, population decline is the actual trend throughout the “developed” parts of the world. Yet, assistance from western industrial countries to countries of the developing world, whence the majority of immigrants originates, has been growing specifically in the form of aid to promote zero population growth – a hobby horse of George W Bush’s grandfather Prescott Bush and of his father George H.W. Bush [27] – as a solution to their underdevelopment. In these countries, an entire two generations of governments have routinely emulated the West, coming to consider population as their greatest impediment to prosperity. Countries rich with the resources of human population are considered to be the poorest [28].

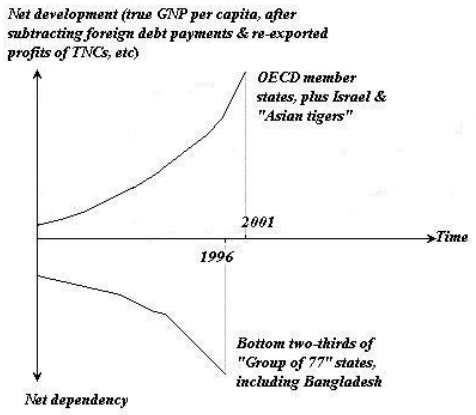
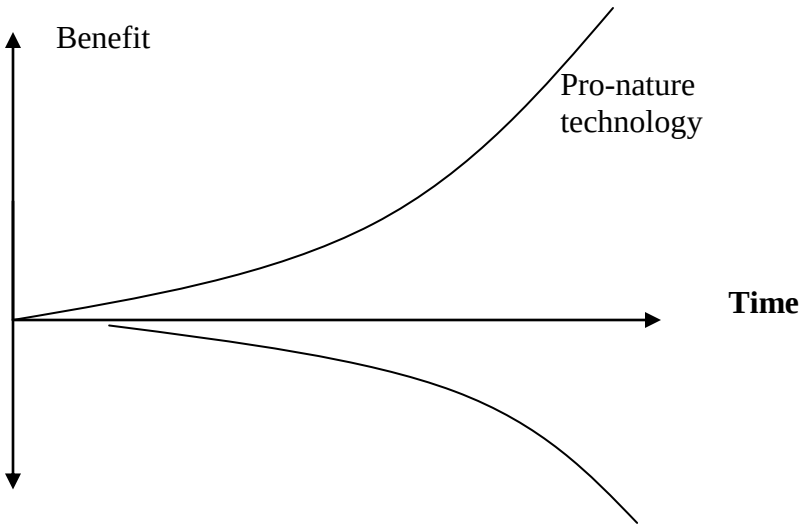


Figure 1. As a result of the overextension of credit and subsequent manipulation (by the creditors: Paris Club etc) of the increasingly desperate condition of those placed in their debt, nostrums about "development" remain a chimera and cruel illusion in the lives of literally billions of people in many parts of Africa, Asia and Latin America. (Here the curves are developed from the year 1960.)

4. Why is the current technology development mode anti-Nature?

As discussed earlier in this article, the current process is driven by an economic model that is wasteful and profit driven, along with the built-in inability to consider the long-term. Nature is infinite and operates at zero-waste, hence waste-based technology is anti-nature. By taking the short-term approach, mechanisms have been created that make the world environment continuously worse. (Figure 2 elaborates this aspect for technology development. However, it may be readily extrapolated to other aspects of social development, including politics and education. The absence of good intention can only bring long-term disaster.

Early civilizations considered themselves the guardians and caretakers of all living things on the lands they inhabited, and held themselves responsible for future generations. Indigenous American Nations considered themselves one with all around them. There was no special word for Nature, no separation: plants, animals, and humans were considered interdependent. In this world it was the coming of the European invader, funded by their own rulers at home, that led to the eventual corporatizing of the earth which all living things share in common, into a commodity to be broken up at will, through wars and land appropriation. The advent of property laws made “legal” after the fact, what had actually been acts of misappropriation. In nineteenth-century America, following the Civil War, specifically in order to to protect and encourage corporate property, this “right” to retain control or ownership of *any* form of property – especially property already accounted as a business asset (whether it originated as a natural resource or as a claim on someone else’s labour) but acquired without “colour of right” (*i.e.*, before there existed any law specifically defining or dealing with its legal existence as property [29]– was consciously elaborated as an exception to the Rule of Law. As the result of wars and other struggles waged to protect this corporatized form of property and the technological development that stemming from it – including associated long-term toxic effects – the world now finds itself in an environmental crisis [30].



Anti-nature
technology

Harm

Figure 3. Pro-nature and anti-nature development schema diverge in beneficial impacts. Only intention can account for this failure of greed-driven initiatives in bringing long-term good.

The deepening of this crisis is marked by a simultaneous extension of corporate abuse of Humanity's rights of access to fresh air, clean water and other absolute necessities, alongside a growing rebellion by the human productive forces sustaining these corporations as their market, against government accommodation of the abusers and their abuses. Today, water and air have become commodities. Governments and corporations now own access to water. Overuse by industry and agriculture have made it into a scarce commodity over which future wars will be waged [31;32]. Contaminated by industrial and agricultural runoff, the sale of bottled water, or home filters to the public who can afford it, is promoted as 'uncontaminated'. Pollution itself, created by chemical poisons released into the air by industry, agriculture, and the automobile, has become a money-making commodity – with the sale of pollution 'credits' from one polluter to another. Home filters to 'clean' the air in homes and public buildings, promote clean air, again for those who can afford it, autos in many places are required to have catalytic converters to filter out poisons emitted from the burning of fuel, to keep down air pollution. At the same time corporate activity, with its virtual immunity from prosecution, legal sanctions or legal responsibility in its home bases and main markets, is purchased and maintained by trying to dump unwanted wastes in various parts of Africa and Asia. This is arousing more and more people in the rest of the world against corporate fiat and dictate, energizing in its wake a rapidly widening discussion of alternative arrangements for Humanity's continued existence on this planet. Accordingly, the intention to control nature has become the last remaining pathway by which corporations hope to ensure a constant, n never-ending stream of profit – and a battleground on which the fate of Humanity for generations to come may be decided.

5. The myth of emulating Nature –The Aphenomenal Model

Few humans dispute that man is the most intelligent creation on this planet. No one disputes that nature is perfect (especially in the sense of complete). In fact, nature is so fully-formed and comprehensive that emulating nature has formed the basis for virtually all branches of knowledge, ranging from natural justice and dialectics of the social system to technology development. Unfortunately, however, no modern technology truly as yet emulates the *science* of nature. It has been quite the opposite: observations of nature have rarely been translated into pro-nature process development. Rather, it is the aphenomenal model [33] that which asserts relations between phenomena that do not exist, based on obscuring anything that contradicts a pre-determined outcome, followed by its justification through disinformation, that has taken the lead in all aspects of social life [2].

Even though it is widely accepted in the social framework that pro-nature arrangements such as would ensure natural justice and social equity, are absent – and not by accident but by design, few paid attention to the problem in so-called natural science. Today, some of the most important technological breakthroughs have been mere manifestations of the *linearization* of nature science: nature linearized by focusing only on its external features. Linearization forms the basis for the first line of disinformation involved [4].

Nature is non-linear and the claim of emulating nature with linear formulae is inherently untrue. Today, computers process information exactly opposite to how the human brain does. Turbines produce electrical energy while polluting the environment beyond repair even as electric eels produce much higher-intensity electricity while cleaning the environment [4]. Batteries store very little electricity while producing very toxic spent materials. Synthetic plastic materials look like natural plastic, yet their syntheses follow an exactly opposite path. Furthermore, synthetic plastics do not have a single positive impact on the environment, whereas natural plastic materials do not have a single negative impact. In medical science, every promise made at the onset of commercialization proven to be opposite what actually happened: witness Prozac™, Vioxx™, Viagra™, etc.

Nature did not allow a single product to impact the long-term negatively. Even the deadliest venom (e.g., cobra, poisoned arrow, tree frog) have numerous beneficial effects in the long-term. This catalogue carries on in all directions: microwave cooking, fluorescent lighting, nuclear energy, cellular phones, refrigeration cycles to

combustion cycles. In essence, nature continues to improve matters in its quality, as modern technologies continue to degrade the same into baser qualities. Table 1 shows how engineering is diametrically opposed to natural processes.

Table 1. Natural processes Vs. Engineered Processes

Natural Processes	**Engineered Processes/Synthetic**
1. Multiple/flexible	1. Exactness/rigid
2.Non linear	2. Linear
3. Heterogeneous	3. Homogenous/uniform
4. Has its own natural process	4.Breaks natural process
5. Recycles, life cycle	5.Disposable/one time use
6. Infinite	6.Finite
7.Non symmetric	7.Symmetric
8.Productive design	8. Reproductive design
9.Reversible	9.Irreversible
10. Knowledge	10.Ignorance or anti knowledge
11. Phenomenal and sustainable	11.Aphenomenal and unsustainable
12.Dynamic/chaotic	12. Static
13. No boundary	12. Based on boundary conditions

Nature thrives on diversity and flexibility, gaining strength from heterogeneity, whereas the quest for homogeneity seems to motivate much of modern engineering. In its non-linearity, Nature inherently promotes multiplicity of solutions. Modern applied science, however, continues to define problems as linearly as possible, promoting "single"-ness of solution, while particularly avoiding non-linear problems. Nature is inherently sustainable and promotes zero-waste, both in mass and energy. Engineering solutions today start with a "safety factor" while promoting an obsession with excess (hence, waste). Nature is truly transient, never showing any exact repeatability or steady state. Engineering today is obsessed with standards and replicability, always seeking "steady-state" solutions. Similar observation can be made for socio-economical development [2].

How could this happen? Our research shows that none of these technologies emerged from any good intention. 'Good', here, implies long-term good, or good for the general public. The promoters of these products are not incapable of developing 'good' products, they are rather incapable of seeing that 'doing good is good business'. In business development, self-interest in the short-term reigns supreme and promoters of these models are so focused in their short-term gains beyond the quarterly profit. They are quite aware that their motive of amassing profit at the expense of natural justice would offend any consumer, so they resort to hiding their motives right from the beginning. This kind of mendacity results, for example, leads to the corruption of scientific research. Recently two medical researchers, one in Norway and one in South Korea have admitted to faking their research data [34]. Research has become a race to patent potential money-making developments and Nobel prizes that lead to more money, in the name of assisting humanity. The offending research institutions attempt to single out individual researchers to blame, the one rotten apple, to obscure their own culpability and the future of funding of their projects. Researchers and scientists work in a pressure cooker culture of getting there first.

In this, the fault of the consumer lies with the lack of research. In fact, consumers have been so captivated by the short-term and external gains themselves, that they cannot read between the lines that the overwhelming corporate message is "Shut up and buy!". Often, they forget the reason behind buying a product other than the fact that it was on sale, or was seen on TV, or the neighbor has one [23].

6. False Promises

In 1960, when birth control pills were first introduced, each pill contained 10 times more male hormone than necessary to abort the egg. The promise behind this was the Liberation of women. Soon after, the anti-nausea drug thalidomide was introduced for pregnant women. The promise here was that women could have easy pregnancies by removing nausea. In reality, 20% of babies who mothers were on the drug became severely deformed. This drug was banned in 1962 but now it is making a comeback. Today, even a 12 year old can get prescribed for birth control pills (at least in Canada) and the same industry is busy producing 'correction pills' that would 'eliminate' the inherent injustice of woman's biology by stopping menstruation altogether [35].

In 1940's, baby disposable diapers were introduced. The inventor, Marion Donovan noticed that her babies would 'nearly instantaneously' wet their cloth diapers as soon as they were changed. In 1946, she introduced the 'breakthrough' technology of disposable waterproof diaper. Did the habit of 'nearly instantaneously' wetting the diaper go away? Of course not. In fact, the first name of these diapers was 'the boat', indicating it was meant to keep babies afloat on their own urine! However we are convinced that disposable diapers are synonymous with keeping the babies dry and civilized. Cotton nappies are expensive, and even considered germ carriers now [1].

Overall, modern development and social progress can be characterized by its driver, greed. Nature, on the other hand, operates on the basis of need and therefore there is no need to make false promises or to institute opacity if one wishes to introduce pro-nature development. The result of the greed-driven social development has led to the current 'technological disaster' (as stated by Robert Curl, a Nobel Laureate in Chemistry). This process has led to a sharp decline in a population that cares for nature, while the number of people focused on self interest and short-term gains has skyrocketed. During this time, the quality of human health has suffered tremendously. For instance, in last 50 years, there has been an increase of 50 times per capita in the use of sugar ('refined', externally processed, carbohydrate) plastic ('wrinkle free' leather or fabric, 'durable' wood, cheap water container), fertilizer ('refined' biomass), spirit ('refined' alcohol), cigarettes ('refined' tobacco), chemicals ('preservatives', Pasteurization, antibiotics), and 'remediative' surgery, while the 'life' expectancy has increased somewhat In the words of Albert Einstein, this 'life' isn't worth living. Unfortunately, this 'life' is being promoted as the only life human beings should live for. Figure 3 illustrates this point.

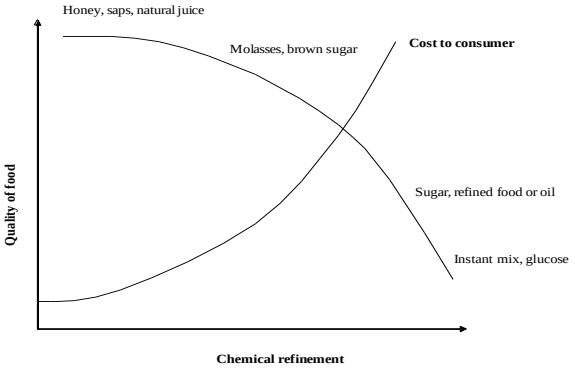


Figure 3. The outcome of greed-driven technology. The same applies to quality of human beings that have been 'refined' with the greed-driven education system or to the quality of human health of people who adopted this anti-Nature culture.

Table 2. Some "breakthrough" technologies

Product	***Promise***	***Truth***
Microwave oven	Instant cooking (bursting with nutrition)	97% of the nutrients destroyed; produces dioxin from baby bottles
Fluorescent light (white light)	Simulates the sunlight and can eliminate 'cabin fever'	Used for torturing people, causes severe depression
Prozac (the wonder drug)	80% effective in reducing depression	Increases suicidal behavior
Anti-oxidants	Reduces aging symptoms	Gives lung cancer
Vioxx	Best drug for arthritis pain, no side effect	Increases the chance of cancer
Coke	Refreshing, revitalizing	Dehydrates; used as a pesticide in India
Transfat	Should replace saturated fats, incl. high-fiber diets	Primary source of obesity and asthma
Simulated wood, plastic gloss	Improve the appearance of wood	Contains formaldehyde that causes Alzheimer
Cell phone	Empowers, keep connected	Gives brain cancer, decreases sperm count among men.
Chemical hair colors	Keeps young, gives appeal	Gives skin cancer
Chemical fertilizer	Increases crop yield, makes soil fertile	Harmful crop; soil damaged
Chocolate and 'refined' sweets	Increases human body volume, increasing appeal	Increases obesity epidemic and related diseases
Pesticides, MTBE	Improves performance	Damages the ecosystem
Desalination	Purifies water	Necessary minerals removed

Wood paint/varnish	Improves durability	Numerous toxic chemicals released
Leather technology	Add luster, color, wrinkle-free	Toxic coating, carcinogenic dyes
Freon, aerosol, etc.	Replaced ammonia that was 'corrosive'	Global harms immeasurable and should be discarded

7. The Science of Intention

Consider the transition highlighted in Table 2. Society started off with natural use products. Any alteration in these natural products ended up making these products toxic in the long term. The question becomes, why did we allow this transition? For the perpetrators, it is clearly greed. For the victims (consumers), it is ignorance. In a way, both of them suffer from the same focus on tangibles. None of these products would have a chance, if people were consciously making decisions before any of their actions [36]. This consciousness can come only with the awareness of intentions. In the past, this important intangible has been ignored.

Intention should essentially mean good intention and has to be guided by the conscience, which is unique to human beings and is the core of what sets humans apart from other animals. Other animals, fortunately, act uniquely on instinct and hence do not risk violating their natural traits. This is also true of every other entity, including, one could argue, the inanimate objects. Only human beings have the ability to intervene in order to alter the natural course of nature. If this intervention is motivated by greed or self interest in the short-term, this intervention will invariably lead to disasters.

If human beings do not succeed in reversing this pattern, nature will make adjustments in order to alleviate the long-term harm of greed-driven initiatives. Here, we include effects that result from man-made activities. For instance, the use of 'refined' oil in combustion engines has led to global warming that destabilized the entire climate system. The reaction of nature is not the 'wrath of God', it is rather the ongoing effort to revert the current trend. The emergence of numerous diseases among humans is not 'God's revenge', it is the reaction of human bodies (a very natural system) trying to resist the ill effect of viruses. Note that viruses do not have natural microstructures or forms, they are rather the product of anti-nature processes [37]. Similar statement can be made for all chemicals that have been introduced since the industrial revolution, ranging from DDT to Freon.

8. Conclusions

It would be easy to say we can solve all our human and environmental problems by resorting to some atavistic memory of living in some imagined past. Fortunately, all tangible features of nature are dynamic and unidimensional and there is no way we can revert to a former physical existence. Any claims that this is possible, surely falls into the category of the perpetrators of the aphenomenal model. Take for instance, the following transition: Sugar cane sap → molasses → sugar → saccharine → Asparteme

Modern science tells us this transition has been devastating. So, *where* do we revert? Some suggest going back to molasses or brown sugar. But current methods of producing molasses are unacceptable. Today, developing countries engaged in these processes embrace toxic chemistry such as arsenic use to bleach molasses, while wealthy countries wouldn't hesitate to collect toxic residues from sugar factories to sell as molasses or brown sugars (some would even paint it brown (add "food coloring" to increase profitability). Others propose, 'Organic' sugar, at an extra cost. And although organic sugar means the sugar cane was not tainted with toxic pesticides or the use of chemical fertilizers, it doesn't guarantee that the 'refining' process itself was free from toxic chemicals (in fact, no sugar mill uses organic bleach). Similar statements can be made for other exotic varieties of sugar products that are currently flooding the market (including 'fair trade', kosher, etc.) None of these 'alternatives' can be considered good because, all of them have the same intention behind their marketing, which is to increase the profitability of the product, using the cheapest available means.

A late 20th century view of the world has emerged in Western nations, led by the US, which posits the world, including nature, as a market. Here everything is for sale, includin how people think and feel. As theories of the world, market based approaches need not only to be evaluated in terms of their success or failure, but also in terms of the symbolic and cultural effects they make possible by placing a cash value on people's needs.

Unless intention is changed, the pathway that we have traveled cannot be changed. Intentions can only change with knowledge. Knowledge can only come with long-term vision, which is the essence of education that is not equated with training or learning of skills. It helps us to see how focusing on the short-term has made it possible that

whatever we long for eludes us. It is the kind of knowledge that allows us to see and plan for the long-term, mindful of where the path of our actions can take us. With this kind of knowledge, even in the short-term, doing good can be good business, for technology development as well as general social progress.

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