MedCrave
Step into the World of Research

Review

Michael W Popejoy
Royal Society for Public Health, Association for Middle Eastern Public Policy and Administration, USA

Bioterrorism and Biosecurity

September 23, 2016: The activities of several extremist groups worldwide have been focused on methods to inflict high mass casualty incidents. They seek weapons of mass destruction which they would not hesitate to deploy into densely populated regions in America or anywhere in the world. Fortunately, the level of security guarding nuclear arsenals is high and the required security clearances and ongoing government surveillance over key personnel working in the nuclear weapons industry is also high. The control over nuclear weapons and raw materials makes it difficult, but not impossible, for a group of determined extremists to acquire essential materials and technical skills to build a nuclear device or buy an operational one on the black market.

However, a far less secured and less government regulated industry with equal potential for high mass casualty incidents exist in virology laboratories throughout the world today. Advances in virology have far surpassed existing public policy controls and government regulatory safeguards that would serve to secure laboratories at reasonably the same level as the nuclear weapons industry. Laboratories are not closely regulated and key scientists have not been vetted and cleared by extensive background screening procedures or kept under the close surveillance protocols as they were during the Manhattan Project while developing the first atomic bomb during WWII.

To some readers this commentary may just be dismissed as alarmist. It is nonetheless important to understand that the technology to create deadly viruses is available; and, dangerous pathogens could be under development now in any of the many unregulated laboratories operated by unsupervised scientists. International public policy and global multinational government regulation have not kept pace with the advances in biological sciences. It is assumed that scientists regulate themselves; however, if any scientist who is also an extremist either religiously or politically engineers a novel virus or reanimates an extinct virus as scientists have been doing with the Spanish Flu virus that killed an estimated 100 million people worldwide in 1918, they will have a potential weapon of mass destruction in terms of mass casualties. Ask the U.S. CDC why they keep the deadly smallpox virus alive and on hand in their laboratories in Atlanta, Georgia? Further, what security clearance investigations have been conducted on the U.S. CDC scientists and what ongoing security surveillance protocols have been implemented to ensure their compliance with high level biohazard security risk procedures?

Scientists who are working in biosyn research are designing novel viruses in laboratories as small as a single car garage that have the potential for high infectious rates and high case fatality rates. CRSPR cas9 technology is available without regulatory restrictions and is capable of manipulating the genome of existing or bioengineered microscopic organisms altering them to become designer pathogens posing a dangerous public health risk. The laboratory equipment and technology are available for sale at reasonable cost without government regulation controlling the means for someone with the requisite skill and knowledge to create new viruses with the intention for release on populations. It is easier to buy this new technology than it is to buy a gun in America. Who is minding the store today?

The Science of the New Age of Terror: Bioterror or Biological Warfare

Some viruses and biological agents are potentially dangerous if not secured properly in high security laboratory conditions. This paper concerns the risks of bioterrorism or the intentional release of a dangerous biological organism; and, is increasingly necessary in view of global insecurity and the ongoing quest by some groups for means of causing mass casualties.

A critical appraisal of these potential new population health risk issues could help prevent international viral storm epidemics that could be intentionally inflicted on densely populated areas of the world. The Ebola virus, Marburg virus and Small Pox are devastatingly infectious viruses with exceedingly high case fatality rates. And, to date, attempts have been made to acquire them by groups with ulterior motives. Today, more than ever before in history, scientists have the technology and the requisite skill to engineer a dangerous novel virus or reanimate a formerly extinct virus into an even more infectious disease organism with an even higher case fatality rate than that which existed in nature. The cost of this new technology is within the means of trained biological scientists and can be procured without government oversight or regulation.

The Influenza virus is unique in its ability to recombine and evolve into highly pathogenic unique strains. Genetic engineering has selectively enhanced the transmissibility hence the need to be current with this virus and as well as many others. Since no broad spectrum vaccine exists for all viruses, it is important to consider the possibilities for the development of a bioweapon and enforce measures to prevent or mitigate any intentional release. Public health systems globally must prepare to detect a pandemic early and respond promptly. Developing countries need to prepare for a potential public health emergency as there is increased traffic across international borders resulting from high volume international travel. Potentially harmful viruses do not respect international boundaries and they travel at the speed of air travel; and early in the infection stage, they can be virtually undetected and carried by passengers on any airplane to a destination of intended impact.

Bioterrorism

Filoviruses and smallpox are dangerous viruses which are a major threat to any nation; indeed, the world swarms with viral zoonoses. Some genetically-engineered viral proteins that can be transfected exist and this reality underscores the need for governments globally to monitor the activities of laboratories with genetic engineering capabilities. Genetic fingerprinting forensic studies; and the use of genomics for manipulation of agents including viruses are critical [1]. The threat of emerging infections and bioterrorist attacks has heightened the need for a more sensitive, specific, and timely pandemic disease surveillance system [2,3]. Many countries in the developing world are not prepared even as they rely on the importation of biological and medical supplies. In the event of an intentional pandemic attack, the magnitude of human deaths in these unprepared areas would be significant.

The primary purpose of reporting diseases is to trigger appropriate public health response so casualty figures are reduced and public fears allayed [4]. Continual virus global movement has prevailed because of failure to identify early the vertebrate reservoir and effectively and quickly quarantine infected animals or humans [5]; and in part, because of the lack of ecological data supporting or refuting any alternative modes of transmission [6].

Recently, the U.S. Centers for Disease Control and Prevention has funded the development of electronic laboratory reporting (Jorgensen, 1997). A more thorough understanding of the pitfalls of such existing reporting systems can provide insights into the development and implementation of new methods in infectious disease surveillance. With recent funding for activities to defend public health against terrorism and naturally occurring diseases, development of automated reporting systems has accelerated [7].

Reverse Genetics

Michael W Popejoy
Royal Society for Public Health, Association for Middle Eastern Public Policy and Administration, USA

Artificial generation of influenza A [8], B [9], and C [10] viruses are now possible through dynamic systems that rely on intracellular synthesis of influenza viral RNAs by a cellular enzyme called RNA polymerase I that transcribes ribosomal RNA in the nucleus of eukaryotic cells. Influenza viral segments are encoded by cDNAs flanked by the RNA polymerase I promoter and the RNA polymerase I terminator or a ribozyme sequence. RNA polymerase I transcription in transfected cells results in the efficient synthesis of RNA transcripts with defined 5' ends whereas the integrity of the 3' ends is achieved using the nucleotide-specific RNA polymerase I terminator [11] or a self-cleaving ribozyme [8]. RNA polymerase I transcripts are neither capped nor polyadenylated therefore they exactly resemble influenza viral transcripts. Cells are transfected with eight plasmids to provide all eight viral RNAs, as well as four plasmids for the expression of the polymerase and NP proteins that are required to initiate viral replication.

Although this approach requires the co-transfection of cells with 12 plasmids, it is highly efficient and routinely yields 108 plaque-forming units of influenza A virus per mL of cell culture supernatant. In one modification, both the RNA polymerase I transcripts (for vRNA synthesis) and the RNA polymerase II transcripts (for mRNA synthesis) are derived from the same template [9], which reduces the number of plasmids required for virus generation to eight. In another modification, the eight RNA polymerase I transcription units for the eight viral RNAs were combined [11], allowing the generation of the entire viral genome from a single plasmid.

These dynamic biological systems revolutionized influenza virus research by allowing researchers to study the functions of viral proteins, their contributions to the viral life cycle, and role in pathogenesis and host range restriction. They are invaluable tools for the generation of influenza virus vaccines and vaccine vectors. In fact, reverse genetics has permitted the generation of inactivated and live vaccine strains for H5N1 viruses that could not have been produced by conventional approaches. Fouchier and other researchers from the Erasmus Medical Center Rotterdam, The Netherlands in September 2011 announced they had successfully engineered a mutant form of influenza H5N1 (avian influenza) that was transmissible by respiratory route between ferrets. Given that ferrets' immune response to influenza is considered to be similar to the response in humans, the studies suggest that the engineered H5N1 is likely to be transmissible from human-to-human.

The researchers suggested that the transmissible flu they had created remained as lethal as the original strain on which their work had been carried out. A strain estimated to be fatal in ~30-60% of cases in humans [12-14]. Several months later it became widely known that a second research group, led by University of Tokyo and University of Wisconsin Professor Yoshihiro Kawaoka similarly had engineered a mammal-to-mammal transmissible form of H5N1 [15,16].

Counter bioterrorism measures

Identification of viral sources, surveillance, disease reporting, early detection and management of a bioterrorism attack are means of preventing and mitigating mass casualties in bioterrorist epidemics. As the popular saying goes; to be forewarned is to be forearmed, giving advance notice of an impending virus outbreak. There is hope that the tools and the imaginations of molecular biology will find the means to prepare some effective biological defense [7]. There is also a possibility of linking rapid detection to rapid responses through vaccine and therapeutic antibody development in an attempt to abort epidemics caused by new viruses while as it rages [17].

Decisions about the treatment or prophylaxis of emerging infections must take into account the effect on patients' health and the potential risks such as a mother's health and that of the fetus. In preparation for bioterrorism emergencies, the U.S. government stockpiled medications and vaccines, rated by the FDA, as one of the categories B through X indicating they could pose risks to the fetus or that insufficient information exists to evaluate their potential fetal risk. Some are routine healthcare products like ciprofloxacin, gentamicin and doxycycline while others are reserved for emergency preparedness and response activities, and for deployed military personnel such as small pox and anthrax vaccines [18].

Some emergency response medications and vaccines fall outside of the FDA labeling system because they are not licensed by the FDA. Some are newly developed and still in pre-licensure clinical trials; others are no longer licensed and pre-date the classification system [18].

In an emergency with high risk of life-threatening exposure to an infectious pathogen, vaccinations and prophylaxis when available will be used for pregnant women despite unknown risks to the fetus. Other measures that can protect persons who are unable or choose not to receive vaccination or prophylactic medications include; selective or mass population quarantine for prevention of exposure to persons who may be infected, avoiding public gatherings and restricting travel to affected areas [18]. Since public health does not have the power to order any type of quarantine, it will be decisions made by public administration and the political will of government executives such as governors and the President and global heads of state to issue a mandated enforceable order for quarantine.

A plan by multi-national scientists to conduct research on enhancing mutating H7N9 avian flu to mimic person to person spread was greeted with controversy, following the backlash of similar research on H5N1 in 2011. In letters published in Science and Nature journal, Fouchier and colleagues from a dozen research centers in the US, Hong Kong and Britain outlined plans for what they called gain-of-function research to create potentially stronger strains, including ones that might easily spread through the air between laboratory animals. They opined it was promising research which could highlight the most important mutations for public health officials to watch and monitor the natural spread of the virus or determine how to manufacture vaccines.

The Obama Administration tightened oversight of research involving dangerous germs while the U.S. Department of Health and Human Services announced an extra step. It is expected that in addition to scientific review, researchers proposing to create easier-to-spread strains of the new H7N9 will have to pass special review by a panel of experts weighing risks and potential benefits [19]. However, since the technology is readily available cheaply without a security clearance or government license, could scientists globally engage in various dangerous genome altering experiments even while under the surveillance of international governments?

A complication of the new science of genetic engineering is that the cost of doing these risky procedures are much lower than the cost of developing other weapons of mass destruction; and, anyone with the requisite skill, and a reasonably small investment in laboratory equipment, could be engineering a novel virus that could be catastrophically dangerous if intentionally released into densely populated regions of the world; and, they could do it given the current existing weak to nonexistent governmental controls to prevent such dangerous experiments.

Public health priority

In the event of outbreaks, masses of people will fall ill and likely die, hence the need for improved public health community measures and deployment of adequate resources toward developing a local, regional, national, and global response plan. The second reason this should be considered a top public health priority is that such outbreaks overlap with preparedness for naturally occurring outbreaks of

Michael W Popejoy
Royal Society for Public Health, Association for Middle Eastern Public Policy and Administration, USA

other communicable diseases. The core functions of public health are assessment, policy development, and assurance; therefore, the public health system is tasked with providing ongoing surveillance of infectious diseases as well as ensuring that populations and communities have access to health services when necessary. The infrastructure to promptly identify and respond to naturally occurring infectious disease outbreaks if synchronized will help in this regard [20].

References

1. Lindler LE, Lebeda FJ, Korch GW, (2004) Book review and public biological weapons defense: Infectious Diseases and counterterrorism. Humana Press, Totowa, New Jerse, USA, pp. 597.
2. Henderson DA (1999) The looming threat of bioterrorism. Science 283(5406): 1279-1282.
3. Fine A, Layton M (2001) Lessons from West Nile encephalitis outbreak in New York City 1999: implications for bioterrorism preparedness. Clin Infect Dis 32(2): 277-282.
4. M'ikantha NM, Southwell B, Lautenbach E (2003) Automated laboratory reporting of infectious diseases in a climate of bioterrorism. Emerg Infect Dis 9(9): 1053-1057.
5. Monath TP (1986) Yellow Fever. In: Monath (Edr.), The arboviruses: Epidemiology and Ecology vol. V. Baco Raton (FL): CRC Press, USA, pp. 139-231.
6. Carrion R, Brasky K, Mansfield K, Johnson C, Gonzales M, et al. (2007) Lassa virus infection in experimentally infected marmosets: liver pathology and immunophenotypic alterations in target tissues. Journal of virology 81(12): 6482-6490.
7. Centers for Disease Control and Prevention (2001) Guidance for fiscal year 2001 supplemental funds for epidemiology and laboratory capacity for infectious diseases (ELC) cooperative agreement National electronic disease surveillance system NEDSS activities.
8. Fodor E, Devenish L, Engelhardt OG, Palese P, Brownlee GG, et al. (1999) Rescue of influenza A virus from recombinant DNA. J Virol 73(11): 9679-9682.
9. Hoffmann E, Mahmood K, Yang CF, Webster RG, Greenberg HB, et al. (2002) Rescue of influenza B virus from eight plasmids. Proc Natl Acad Sci U S A 99(17): 11411-11416.
10. Muraki Y, Hongo S (2010) The Molecular Virology and Reverse genetics study of influenza C virus. Jpn J Infect Dis 63(3): 157 165.
11. Neumann G, Fujii K, Kino Y, Kawaoka Y (2005) An improved reverse genetics system for influenza A virus generation and its implications for vaccine production. Proc Natl Acad Sci USA 102(46): 16825-16829.
12. Herfst S, Schrauwen EJA, Linster M, Chutinimitkul S, de Wit E, et al. (2012) Airborne Transmission of Influenza A/H5N1 Virus Between Ferrets. Public Health and Biosecurity. Science 336(6088): 1534-1541.
13. Fouchier RAM, Hersfts S, Osternaus ADME (2012) Public Health and Biosecurity. Restricted data on influenza H5N1 virus transmission. Science 335(6069): 662-663.
14. Murillo LN (2012) Ferret-transmissible influenza A(H5N1) virus: let us err on the side of caution. MBio 3(2): e00037-12.
15. Enserink M (2011) Infectious diseases. Controversial studies give a deadly flu virus wings. Science 334(6060): 1192-1193.
16. Kawaoka Y (2012) H5N1: flu transmission work is urgent. Nature 482(7384): 155.
17. Bryant J, Wang H, Cabezas C, Ramirez G, Watts D, et al. (2003) Enzootictransmission of yellow fever virus in Peru. Emerg Infect Dis 9(8): 926-933.
18. Anderson NG, Gerin JL, Anderson NL (2003) Global screening for human viral pathogens. Emerging Infect Dis **9**(7): 768-773.
19. NPR (2013) Controversy surrounds man-made bird flu plans. World Poultry.
20. Rebecca K (2001) Biological Weapons: A National Security Problem that Requires a Public Health Response. Working Paper 2001-04 Office of population Research Princeton University working paper series, p. 1-38.

Michael W Popejoy* and Bernard A Onoja
[1]*Royal Society for Public Health, USA*
[2]*Department of Virology, University of Ibadan, Nigeria*
Email: dr_popejoy@hotmail.com

Mohd Ismaeel Khan
Herboveda Healthcare Private Limited, India

October 08, 2016: This product is an innovative product strong enough to minimize the appearance of sagging, flabbing and bulging tummy. It helps to slim the flabby, slag & less taut Tummy and waistline area. It is a non greasy, fast to absorb, with a great active delivery system, quick and ease to apply. Smoothes and tightens the skin .Firms tissues and Restores the waist & tummy in shape. Waist & Tummy tend to suffer from ungainly flab, uneven skin texture and dimpled skin. And it is affected by the laxity of the tissues due to pregnancy, weight gain or age.

Skin is constantly replenishing itself. When we younger our skin's turnover rate is about every 15-18 days. When it starts approaching the mid-thirties the process slows down to as much as every 28 days. The upper most layers, the *epidermis*, is where we shed our skin cells and reveal the newer cells that are produced in the *basal* layer (the bottom). The next level down is the *dermis*. This level contains oil glands, nerves, capillaries, your body's melanin (the cells that are responsible for coloring and a tan) plus sweat glands that moderate your body's temperature. The dermis also contains natural *collagen* and *elastin* in addition to fat and water storage. Collagen and elastin are responsible for the springiness that gives your skin its youthful vitality. Without this, your skin would feel like crepe paper and would almost split down the middle when you were pregnant or had excess weight. We tend to lose a lot of our elastin and collagen as we age, hence the skin-thinning and laxity that we hate so much.

Many female bodies hold excess fat in our thighs, buttocks, hips and stomach. Men seem to hold it in their abdomen and general waist area. Men seem to also have *better* connective tissue as opposed to Women, which betray them and fails to keep superficial fat IN or unrestricted, creating cellulite. And as we age our metabolism slows. Resulting in stubborn pockets of fat in areas that we don't want it and fat loss in areas we'd like to keep it. It causes appearance of sagging, flabbing and bulging.

Prime reason for cellulite is adipose tissues. Adipose tissue, singularly a fat cell being an *adipocyte*, this layer is very important. One may hate it and despise its effects on his thighs and abdomen but we need it. There are primarily two types of fat... White Fat and brown fat. But we have to worry about the white fat because we have this only. Without a fat layer you would freeze to death, have no energy stores and have to eat constantly, your body would not function properly, you'd burn muscle tissue more often, and worse. But, we all have a little more than we'd like or need - so if you can't work it off, get it sucked out. Since cellulite is no ordinary fat, it needs special attention and will not disappear with just routine exercise or dieting.

Shape up Waist & Tummy Shaping Gel is the result of extensive research and ongoing R&D at VLCC. Based on ancient knowledge and goodness of Ayurveda this product made with herbal Extracts and Essential Oils. Shape up Waist & Tummy Shaping Gel has been specially formulated to slim the flabby, slag & less taut Tummy and waistline area and to reduce cellulite. It firms skin and increase skin elasticity. It's a hyderating, tightening, smoothing, silky texture, non greasy easy to apply and get absorbed quickly. It makes the skin smooth, taught and restores the body's youthful look with visible results.

Application method

For an optimal result, take the shaping gel crème and spread on the stomach and waist line area and massage for several minutes till get absorbed. On stomach with smooth strokes from the bottom to the top at an angle. On waist line, make circular massage movements from top to bottom. Repeat several times till the product absorbs completely.

Dosage & duration

Crème Gel: 5 - 10 gm, 04 Weeks, apply twice a day. VLCC Shape up is a highly effective combination of fat burning actives for a topical treatment of waistline and tummy area.

1. **The Active Substances are Mentioned below**
   a. Cyprus Pertinuis (Cyprus) Oil
   b. Ptychotis Ajowan (Ajowain) Oil
   c. Citrus aurantifolia (Lemon) Oil
   d. Foeniculum Vulgare (Black Pepper) Oil
   e. Punica Granatum Linn (Pomegranate) Oil
   f. Rosmarinus Officinalis (Rose Mary) Oil
   g. Geranium sylvaticum (Geranium) Oil
   h. Quercus infectoria (Majuphal) Extract
   i. Cynodon Dactylon (Doorva Grass) Extract
   j. Triticum Vulgare (Gehun Ankur) Extract
   k. Spirulina Platensis (Spirulina)
   l. Soy Isoflavones (Genistein)

The biologically actives form of soy isoflavones (Genistein) improves the collagen content in the skin and in doing so, strengthens the connective tissues. Furthermore Genistein. Inhibits the formation of new adipocytes and this in turn will lead to the breakdown of fat.

Consequently, this will result in:

a. An increase on skin firmness.
b. A reduction in adipose tissue.

These highly active compounds in combination were first used by VLCC, as a fat loss stimulant and to increase the metabolic rate. Ingredients activate the breakdown of lipids in fat cells of the adipose tissue. To enhance the penetration into deeper skin layers, ingredients are blended into active carriers and easily absorble crème gel system. A in-house human study with Shape up Waist & Tummy Shaping Gel showed (after 6 weeks treatment), an very effective Multiple targeted firming, anti-cellulite and slimming action

a. Cellulite reduced by 32%.
b. Abdominal girth reduced by 3.8%.
c. Firmness of skin improved by 60%.
d. Skin smoothness 23%.

Shape up Waist & Tummy Shaping Gel

Biochemistry of the fat breakdown

Neutral fat (triglycerides) is stored in fat layers, also called adipose tissue. The metabolism of fat is regulated by hormones. The hormone Epinephrine (adrenaline) is the initiator of the breakdown of neutral fat. It leads to the release of free fatty acids from the adipose tissue into the blood system.

Epinephrine binds to the adrenergic receptor on the surface of fat cells. Binding leads to the production of the second messenger cAMP inside

Mohd Ismaeel Khan
Herboveda Healthcare Private Limited, India

the fat cell. The messenger cAMP activates the enzyme lipase that leaves neutral fat into free fatty acids and glycerol. Free fatty acids are then transported into the blood system and used to generate energy.

The actives in VLCC Shape up Waist & Tummy Shaping Gel formulation are incorporated in such a manner that enhances the penetration and active delivery mechanism. So, it involves in all mechanisms of lipolysis: fatty acid liberation, transport and decomposition, supports sub-cutaneous fat diminishment & energizes the fat-liberated tissue cells. It is used to stimulate fat burning and therefore contouring the body. Also Smoothes and tightens the skin, thus

a. Optimizes your fitness efforts to reshape your body.

b. Restoring its youthful contours.

The ingredients of Shape up are very traditional and these ingredients stimulate fat breakdown. The actives inhibit the activity of phosphodiesterase, the enzyme that normally leads to the breakdown of the messenger cAMP. Thus it increases the half-life of cAMP, the activator of the lipase enzyme. And thus initiates the release of fatty acids and increases the breakdown of neutral lipids in the adipose tissue.

Study design

A Crème Gel formulated using the above mentioned ingredients and then tested over 04 Weeks by twenty five women at the age of 24 to 48. The product was applied twice daily on the stomach by massaging with both hands simultaneously in smooth strokes from the bottom to top at an angle. Repeat several times. And on Waist line & bottom area, massage one side after the other, by circular massage movements from the bottom to top. Repeat several times.

The test parameters were firmness and elasticity (measured with Cutometer MPA 580), Skin fold thickness and abdominal girth. Study results After 04 weeks treatment the condition of the skin was clearly improved. Skin texture (firmness & elasticity) is assessed after 14 days by 22.72% and after 28 days by 46.15%. Shape of Waist line area assessed as 15.9% after 14 days and 33.3% after 28 days. Skin Tightness assessed as 15.9% after 14 days and 46.15% after 28days.

Change in girth of the abdomen of the individual test persons. In 16 cases the abdominal girth was reduced after the treatment period. In 2 cases there was no change and for 7 test persons there was a slight increase in the girth. In average the girth of the abdomen was reduced by 2.5cm after 4 weeks.

Claims with shape up waist & tummy shaping gel

Ingredient claims: Shape up is a highly effective combination of fat burning ingredients for topical treatments of all body parts you feel concerned about. It interacts at an early stage with the lipid pathway and keeps the amount of stored lipid at a normal range by:

a. Reducing lipid uptake into the adipocytes.

b. Reducing lipid accumulation in the adipocytes.

c. Accelerating the cAMP pathway.

Reduces the size of the lipid droplets

a. Decreases the lipid amount in adipocytes.

b. Smoothes and ameliorate skin appearance.

c. Increases the cAMP, therefore it also helps to remove the lipids which are already present in the adipocytes.

d. Accelerates the breakdown of body lipids.

e. Refines body contours & Smoothes skin.

f. Firms and tones.

g. Exclusively designed to target the problem waist and tummy area.

h. Massaging effect makes the cream penetrate faster and deeper into the skin.

The thermogenic formula with Shape up prevents the appearance of body fat and by its firming properties helps restore the body's smooth contour. Shape up shapes, firms and contours while it leaves the skin with a silky touch. Reshaping Body with an immediate and efficient skin tightening effect for visible firmer skin.

Dermatological tolerance: The dermatological tolerance of Shape up Waist & Tummy Shaping Gel has been carefully watched in healthy volunteers (determinations of irritating effects to the skin – not seen, even a single case). In addition, it is well formulated from the ingredients that will decrease the irritation potential of many substances.

Manufacturing of the product

We manufacture the product by following the "Good Manufacturing Practice'' in accordance to the WHO-GMP & ISO 9001:2000 guidelines. Shape up is a highly effective combination of fat burning ingredients for topical treatment of thighs, buttocks, hips, waist, tummy and arms.

Shaping cream

Helps to reduce fat deposits and minimize skin's puffy appearance in problem areas. Thermogenic formula to tone and smooth the skin and to increase the metabolism and Hydrolysis by stimulating the action of messenger hormone cAMP. For optimum results, use in conjunction with your daily fitness program.

Shape up: is a combination of lypolytic substances for a topical treatment of problem zones such as waist, tummy areas.

It consists on following ingredient

A brief detail is given below separately about all the ingredients.

a. Spirulina Platensis (Spirulina)

b. Soy Isoflavones (Genistein)

c. Triticum Vulgare (Gehun Ankur) Extract

d. Cyprus Pertinuis (Cyprus) Oil

e. Citrus aurantifolia (Lemon) Oil

f. Camellia Sinensis (Green Tea) Extract

g. Quercus infectoria (Majuphala) Extract

h. Rosmarinus Officinalis (Rose Mary) Oil

i. Punica Granatum Linn (Pomegranate) Oil

j. Geranium sylvaticum (Geranium) Oil

k. Piper nigrum (Black Pepper) Oil

l. Ptychotis Ajowan (Ajowain) Oil

Spirulina platensis (Spirulina): Spirulina platensis is classified as a blue-green algae. It is a simple, single cell form of algae that lives in warm, alkaline fresh-waters. The word "spirulina" is derived from the Latin word for "helix" or "spiral". This denotes the physical configuration of the organism when it forms swirling, microscopic strands.

Mohd Ismaeel Khan
Herboveda Healthcare Private Limited, India

In Japan, Spirulina is a popular food supplement and is marketed as a nutritional supplement in many other countries. It has a very impressive ability to synthesize high-quality concentrated nutrients. Spirulina is a rich source of both proteins and rhamnose sugars (complex natural plant sugars). It also contains chlorophyll, carotenoids, minerals, gamma-linolenic acid (GLA) and some unique pigments. Spirulina is one of the few plant sources of vitamin B12 and is usually only found in animal tissues.

Soy Isoflavones (Genistein): It contains the soy isoflavone Genistein, will successfully fight cellulite in the following two ways:

a. Its skin thickening and strengthening activity will enhance the firmness of the skin.

b. Genistein is an inhibitor of phosphodiesterase and as such, it acts directly on the fat metabolism.

Phosphodiesterase is an enzyme that inactivates cyclic AMP (cAMP), which itself stimulates

The enzyme lipase that breaks down fat. Therefore, the overall reduction of fat is made possible and the amount of fatty tissue will decrease.

Triticum Vulgare (Gehun Ankur)

Constituents: Proteins 12.4, starch, 67.9, fat 1.4, fiber 2.5.

Action: Natural source of Vitamin E. Emollient, laxative. Wheat Germ is the "heart" of the wheat kernel, the embryo of the seed, and a concentrated source of several essential nutrients. It is the by-product of wheat milling, and offers an excellent source of protein and vitamins. It is the richest source of Tocopherol (vitamin E) of plant origin and is also rich in thiamine, riboflavin and niacin, Vitamin B1 and B3, dietary fibers and minerals (potassium, calcium, zinc, magnesium and iron). As a dietary management it is reported to be beneficial in hyperlipidamea in humans (13). Wheat germ oil contains the following fatty acids (Table 1).

Table 1: Components in Wheat germ oil.

Component	Amount
Linoleic acid (omega-6)	55%
Palmitic acid	16%
Oleic acid	14%
Linoleic acid (omega-3)	7%

Functions of important constituents of wheat germ oil (12) (13) (15)

Vitamin E is a very important antioxidant. It is helpful in preventing the body's aging process.

Vitamins B1 and B3 are very important to maintain energy levels and maintain healthy muscles, organs, hair and skin.

Wheat germ oil is particularly high in octacosanol - a 28 carbon long-chain saturated primary alcohol. Octacosanol has been studied as an exercise and physical performance-enhancing agent.

Linoleic Acid has anti-inflammatory and moisture retention properties.

Presences of Wheat Germ Oil along with other actives especially with Hydroxyprolisilane helps in facilitate the delaying of aging of the skin. Being a rich source of Vitamin E, B1 and B3, it is a strong antioxidant and healthy and beautiful looking skin, which is free of freckles and dead cells. Invariably it delivers more youthful looking skin.

Nagarmotha (Cyperus Pertenuis)

Constituents: Fat, sugar, gum, carbohydrates, essential oil, aluminous matter, starch, fiber and ash. There are traces of an alkaloid. β sitosterol , 4α, 5α- oxidoeudesm- 11- en- 3α- ol from (rhizomes); pinene, cineol, alcohol- isocyperol (essential oil from the tubers); linolenic, linolic, oleic, myristic and Stearic acids and glycerol (fatty oil); a sesquiterpeneketone- Mustakone and copaene, cyperotundone, sesquiterpenes- (+)- copadiene, (+)- epoxyguaine, (-)- rotundone and cyperolone; cyperenone designated as isopatchoul- 4(5)- en- 3- one and aureusidin (essential oil); two sesquiterpenic ketoalcohols, α-rotunol, β-rotunol, kobusone and isokobusone; oleanolic acid and its glycoside, oleanolicacid- 3-0- neohesperidoside alongwithsitosterol, sesquiterpenes- α- cyperone, cyperene, β-selinine and cyperenone (tubers); luteolin and aureusidin (leaves).

Cyperus (*Cyperus rotundus*): also known as Nut grass is a plentiful species occurring throughout the plains of India, especially South India. (12) Nut grass is an anti-inflammatory medicine, a general and nervine tonic.

Constituents: α-cyperene, β-selinene, cyperene, cyperotundone, patchoulenone, sugeonol, kobusone, and isokobusone. It is reported to be Analgesic; Antibacterial; Antibiotic; Antispasmodic; Antitussive; Aromatic; Astringent; Carminative; Contraceptive; Diaphoretic; Diuretic; Emmenagogue; Lithontripic; Sedative; Skin; Stimulant; Stomachic; Tonic; Vermifuge (19). An essential oil in the tubers has antibiotic activity and has been shown to arrest the growth of Micrococcus pyrogenes (19).

Action: Refrigerant, aromatic, stomachic and alterative. The tubers are bitter, astringent, cooling, anti- inflammatory, and smooth muscle relaxant, antimicrobial.

Therapeutic evaluation: In clinical trial oral administration of root powder of Cyperus rotundus, 1gm twice daily, in 64 patients of obesity produced significant reduction in their body weight. Blood pressure of hypertensive obese patients was also reduced significantly, whereas there was no change in the blood pressure of normotensive patients.

Lemon (Citrus Aurantifolia)

Constituents: lemon juice contains citric acid 7-10%, phosphoric and malic acids, also citrates of potassium and other bases, sugar, mucilage and ashes. Lemon peel contains a volatile oil, hesperidin 5 to 8%. (*Citrus aurantium*) is a popular fruit grown widely all over India. Flowers and Dried Peel of the fresh fruit contains a volatile oil called oil of neroli, a fragrant yellowish liquid of bitter aromatic taste. This Oil is aromatic, internally stomachic and externally stimulating, and tonic. This also has antispasmodic and anodyne properties. It is a source of anti-oxidants and chemical exfoliants. This essential oil is refrigerant, antifungal and antibacterial (19).

Green tea (Camellia Sinensis): Tea is widely cultivated around the whole world. Black tea, green tea & Oolong tea are known as three major kinds of manufactured teas and the green tea appears as the richest in flavonoid compounds. Generally fresh green tea leaves can contain about 20-35% of polyphenols in a dry weight and the composition of this plant varies with the age of leaves, season and climate .The major components of green tea extract are catechins – compounds displaying anti-radical and anti-inflammatory activity. Except for these compounds the tea contains, interestingly from the cellulite point of view, caffeine. Caffeine is a methylxanthine which stimulates lypolysis by acting through phosphodiesterase inhibition, which leads to the increase in the concentration necessary for triglyceride hydrolysis cAMP. Apart from it, the tea contains beta-adrenergic stimulators –theobromine and theophylline, which are methylxanthines. These properties make green tea extracts a usefull ingredient in lypolysis.

Mohd Ismaeel Khan
Herboveda Healthcare Private Limited, India

Pomegranate (Punica Granatum) oil

Constituents:- Bark and the rind of the fruit contain tannin 22 to 25% and the root bark contains punico- tannic acid 20 to 25% , mannite,sugar, gum, pectin, ash 15% an active liquid alkaloid pelletierine and oil liquid 'isopelletierine" and two inactive alkaloids me hyl- pelletierine and pseudo-pelletierine.

Action: Astringent, cooling & Refreshing.

Pomegranate oil: Pomegranate fruit extract, from the tree Punica granatum, contains several polyphenols and anthocyanidins (pigment that gives certain fruits their dark red colors), which are highly antioxidant, protecting hair and skin from environmental stress.

Majuphal (Quercus Infectoria)

Constituents: - The principal chemical constituent of galls is tannin or tannic acid (gallo-tannic acid) 50 to 60 or 70 % and about 3% of gallic acid. When strongly heated, Gallic acid is converted into meta-Gallic acid.

Action: Astringent and styptic. They are rich in tannins and are known for their ability to combat various viruses, while at the same time strengthening the tissues. They are one of the strongest natural astringent herbs available and also are antiseptic.

Rosemary (Rosmarinus Officinalis) oil: This crisp and clean smelling essential oil is great for stimulating the brain, improving memory and mental clarity, while helping with a variety of congested respiratory tract problems, stiff muscles, coldness as well as boosting the liver and gall bladder. It is also used for improving hair and scalp health.

Origin of rosemary oil: it is a shrubby evergreen bush that grows up to 1.5 meters (4 feet) high with green-gray needle-shaped leaves and pale blue/lilac flowers that bees just love and is originally from Asia, but is now cultivated in France, Tunisia and Yugoslavia. The name is derived from the Latin 'Rosmarinus' or 'sea dew', as it is rather fond of water. The Egyptians, Hebrews, Greeks and Romans considered the herb as sacred and even in the middle Ages it was used to ward off evils spirits and used as a protection against the plague. It was burnt in French hospitals during epidemics.

Extraction: Rosemary oil is extracted from the fresh flowering tops by steam distillation. It yields 1.0 - 2.0%.

Chemical composition: The main chemical components of rosemary oil are a-pinene, borneol, b-pinene, camphor, bornyl acetate, camphene, 1, 8-cineole and limonene.

Therapeutic properties: The therapeutic properties of rosemary oil are analgesic, antidepressant, astringent, carminative, cephalic, cholagogue, cordial, digestive, diuretic, emmenagogue, hepatic, hypertensive, nervine, rubefacient, stimulant, sudorific and tonic.

Uses: Rosemary oil has a pronounced action on the brain and the central nervous system and is wonderful for clearing the mind and mental awareness, while having excellent brain stimulant properties, as well as improving memory. It helps with headaches, migraines, neuralgia, mental fatigue and nervous exhaustion and the antiseptic action of rosemary oil is especially suitable for intestinal infections and diarrhea, easing colitis, dyspepsia, flatulence, hepatic disorders and jaundice and relieving pain associated with rheumatism, arthritis, muscular pain and gout. It also helps for arteriosclerosis, palpitations, poor circulation and varicose veins. The diuretic properties of rosemary oil are useful with reducing water retention during menstruation, and also with obesity and cellulite. On the respiratory system, it is effective for asthma, bronchitis, catarrh, sinus and whooping cough. Because of its astringent action, it is also effective for countering sagging skin. Its stimulating action benefits scalp disorders and encourage hair growth. On the skin, it helps to ease congestion, puffiness and swelling and can also be used for acne, dermatitis and eczema, but a very popular use of this oil is the use in hair care products, as it has a pronounced positive effect on the health of the hair and scalp. It increases the circulation to the scalp and is therefore also effective for promoting hair growth. Rosemary, in the dried form, is extremely high in iron, calcium, and Vitamin B6 .

Summary: Rosemary oil is effective for mental fatigue, circulation problems, pain relief for the muscular system, decongests the respiratory tract and is a skin and hair booster. The diuretic properties of rosemary oil are useful with reducing water retention during menstruation, and also with obesity and cellulite.

Geranium (Geranium sylvaticum) Oil: This fresh essential oil has a firm place in aromatherapy, as it helps to balance the mind and emotions, while stimulating the adrenal cortex and balancing the hormonal system and stimulating the lymphatic system. On the other hand, it balances the production of sebum in the skin, while keeping it supple and helping with the healing of wounds.

Origin of geranium oil: The plants originated from South Africa, as well as Reunion, Madagascar, Egypt and Morocco and were introduced to European countries such as Italy, Spain and France in the 17th century. There are about 700 different varieties of the plant, yet only 10 supply essential oil in viable quantities, as the normal garden geranium produce far too little oil for extraction. It is a hairy perennial shrub, often used in hedgerows, and stands up to about one meter high (3 feet) with pointed leaves, serrated at the edges and it has pinkish-white flowers. In early times geraniums were planted around the house to keep evil spirits at bay.

Extraction: The leaves and stalks are used for extraction, and the oil is obtained through steam distillation.

Chemical composition: The essential oil is composed of various chemical constituents and includes a-pinene, myrcene, limonene, menthone, linalool, geranyl acetate, citronellol, and geraniol and geranyl butyrate.

Therapeutic properties: The therapeutic properties of geranium oil are astringent, haemostatic, cicatrisant, cytophylactic, diuretic, deodorant, haemostatic, styptic, and tonic, vermifuge and vulnerary.

Uses: Geranium oil can be used to help in the treatment of acne, bruises, burns, cuts, dermatitis, eczema, hemorrhoids, lice, as a mosquito repellant, ringworm, ulcers, breast engorgement, edema, poor circulation, sore throat, tonsillitis, PMS, menopausal problems, stress and neuralgia.

Ajowan (Ajowan Ptychotis): Is native to and produced mainly in India but also cultivated in Iran, Egypt, Pakistan, and Afghanistan. The oil is steam distilled from the seed or herb of this tall graceful tree growing to 30 meters high with bright green heart-shaped leaves, and powerfully fragrant yellowy-white flowers. It is related to Cumin but tastes more like dried thyme. For flavoring purposes, use thyme as a substitute. Ajowan oil is spicy-medicinal and strongly odored; it is generally used as a cheap perfume in soaps. The seeds are often chewed on their own for medicinal value, tasting bitingly hot and bitter, leaving the tongue numb for a while. Cooking mellows it somewhat, when crushed; they have a strong and distinctive thyme-like fragrance. Ajowan seeds are used for indigestion and gas relief in Middle Eastern countries like Iran and Egypt. The seeds contain an essential oil which is about 50% thymol which is a strong germicide, anti-spasmodic and fungicide. Thymol is also used in toothpaste and perfumery.

Mohd Ismaeel Khan
Herboveda Healthcare Private Limited, India

Principal constituents: The alcoholic extract was found to contain a highly hygroscopic saponin, with a hemolytic index of 500. Yellow, crystalline flavones (m.p. 291-94°) and a steroidal substance (m.p.140-50°) have also been isolated from the fruits1. The principal constituents of the essential oil from the fruits are the phenols, mainly thymol and some carvacrol. The Indian Pharmacopoeia requires Ajowan oil to contain not less than 40 percent thymol. The remainder of the oil is called 'thymene'. Thymene, which constitutes c.45, per cent of the oil, has the following composition: p-cymene, 50-55; g-terpinene, 30-35; a- and ß-pinenes, 4-5; and dipentene, 4-6%. Presence of minute 'amounts of camphene, myrcene and D3-carene are also reported.

Pharmacology: Preliminary pharmacological studies of the oil indicated that it had a parasympathomimetic effect and produced contraction of the isolated ileum, tracheal chain and bronchial musculature in guinea pigs. It depressed the cardiac musculature in frogs and caused a marked fall in blood pressure in cats. On account of its low toxicity, further trials of the oil as a hypotensive agent are recommended. The drug also seems to possess some anti-diuretic effect 3.

Indications: Ajowan is much valued for its antispasmodic, stimulant, tonic and carminative properties. It is administered in flatulence, atonic dyspepsia and diarrhea, and often recommended for cholera. In the Unani system, Ajowan is used as a crude drug to enhance the body's resistance, and is prescribed in amebiasis. It is a potent antimicrobial agent. The seed powder showed hypocholesterolemic, hypotriglyceridemic and hypophospholipidemic effect whereas serum cholesterol binding reserve and HDL were increased (Agrewala and Pant, 1986).

Black pepper (Piper nigrum) Oil: Black pepper contains about 3% essential oil, whose aroma is dominated (max. 80%) by monoterpenes hydrocarbons: sabinene, β-pinene, limonene, furthermore terpinene, α-pinene, myrcene, Δ3-carene and monoterpene derivatives (borneol, carvone, carvacrol, 1,8-cineol, linalool). Sesquiterpenes make up about 20% of the essential oil: β-caryophyllene, humulene, β-bisabolone and caryophyllene oxide and ketone. Phenylether (eugenol, myristicin, safrole) are found in traces. Loss of monoterpenes due to bad storage conditions (especially for ground pepper) should be avoided. The most important odorants organoleptically in black pepper are linalool, α-phellandrene, limonene, myrcene and α-pinene; furthermore, branched-chain aldehydes were found (3-methylbutanal, methylpropanal). The musty flavour of old pepper is attributed to the formation of heterocyclic compounds (2-isopropyl-3-methoxypyrazine, 2,3-diethyl-5-methylpyrazine) in concentrations of about 1 ppb. (Eur. Food Res. Technol., 209, 16, 1999) The essential oil of white pepper has received less attention; the content of essential oil is lower (1%), and the most abundant compounds are monoterpene hydrocarbons: limonene, β-pinene, α-pinene and α-phellandrene. Organoleptically most important are linalool (although occurring as a minor component), limonene, α-pinene and phenylpropanoids (eugenol, piperonal); furthermore, short-chain aldehydes and carboxylic acids have been found important. In overstored white pepper, scatole is formed (2 ppm) and imparts an disagreeable, faecal flavour. (Eur. Food Res. Technol., 209, 27, 1999) The pungent principle in pepper is an alkaloid-analog compound, piperine; it is the amide of 5-(2,4-dioxymethylene-phenyl)-hexa-2,4-dienoic acid (piperinic acid) with azinane (piperidine); only the trans,trans conformer contributes to pepper's pungency. Several piperine-analogs have been isolated from black pepper where the acid carbon backbone is partially hydrogenated (piperanine) or two carbon atoms longer (piperettine); amides of piperinic acid with pyrrolidine (piperyline) or isobutylamine (piperlongumine) have also been isolated. Total content of piperine-analogs in black pepper is about 5%. Black pepper is native to Malabar, a region in the Western Coast of South India; today, this region belongs to the union state Kerala. Pepper is cultivated since millennia. The wild form has not yet been unambiguously identified, but there are closely related pepper species in South India and Burma. While black and white pepper were already known in antiquity, but green pepper (and even more, red pepper) is a recent invention. Pepper reached South East Asia more than two thousand years ago and is grown in Malaysia and Indonesia since about that time. In the last decades of the 20th century, pepper production increased dramatically as new plantations were founded in Thailand, Vietnam, China and Sri Lanka. In the New World, Brazil is the only important producer; pepper plantations there go back to the 1930s [1-7].

Actions: Warming, mental stimulant, physical energizer. *Culinary* spices have been used through the ages for their flavour appeal and stabilizing effects in foodstuffs, but only recently has their effectiveness as antioxidants in edible fats been clearly demonstrated. The Lypolytic activity of spices has received little scientific attention and it was therefore of interest to obtain some quantitative information on five spices used extensively in the baking industry. Lypolytic activity observed in samples of commercially available material.

References

1. Heath H (1963) Rep Prog App Chem 48: 512.
2. Aggarwal J, Sethi S (1950) Stabilization of edible fats by condiments or spices. Nature 166(4221): 518-519.
3. Chipault J (1952) Food Res 17: 46.
4. Yesair J, Williams O (1942) Spice contamination and its control. Food Res 7: 118.
5. Fabian F (1939) Food Res 4: 269.
6. Templeton W, Carpenter B (1953) Analyst 78: 726.
7. Martin H, Peers F (1953) Biochem J 55: 523.

Mohd Ismaeel Khan*
Herboveda Healthcare Private Limited, India
Email: mismaeelkhan@gmail.com

John Glynn
Ludwig Von Mises Institute, USA

November 30, 2016:

Big Pharma

Apart from the words President Trump, few other utterances possess the ability to make every man, woman and child tremble with genuine fear. Similar to The Donald, the term Big Pharma has come to connote something dishonest, malevolent, and thoroughly distasteful. An enigmatic entity consisting of corporations, regulators, politicians, and a growing number of physicians, Big Pharma has a vice like grip on western culture, shadowing us all like an ominous cloud.

From the world of academia to the world of politics, Big Pharma is a contentious, unavoidable topic of discussion. Sen. Bernie Sanders, Vermont's answer to Doc Brown, was one of the first mainstream politicians to single out Big Pharma for criticism. For well over a decade, in typical Sanders fashion, the 74 year-old has worked tirelessly to break down the barrier surrounding patent protection for new medication.

The disheveled looking renegade has spoken at length about radically slashing prescription drug spending. Unsurprisingly, the bold proposal has angered drug company lobbyists and high ranking officials, some of whom had, and continue to have, intimate connections with the Bush and Obama administrations. Up until quite recently, Sanders' warnings of a prescription fuelled America went largely ignored. Some labelled him a sensationalist, some labelled him a demagogue, and some labelled him a Communist. It appears he was and is neither of the three. Sanders' predictions were in fact as accurate as they were prescient.

In October of 2015, when asked to rank the most important issues of the 2016 presidential campaign, New Hampshire residents ranked drug abuse as the number one area that needed addressing. This, in their opinion, was a more pressing issue than job creation and economic growth. Politicians started voicing their concerns, with the prophetic Sanders labelling addiction "a disease, not a criminal activity."

More recently, cast your minds back to Super Bowl 50. Amid ads plugging savory snacks and sumptuous sports cars came an ad that was strange and striking. No, not the ad for Mountain Dew's 'Puppy Monkey Baby.' This ad, even more unexpected than a puppy, monkey, baby freak show, addressed OIC, or Opioid Induced Constipation. Considering a prime time, 30 second ad during the Super Bowl costs somewhere around $5 million, the condition must be very real and somewhat rampant.

Why, so many asked, was such a random advertisement airing during one of the most widely viewed sporting events in world history?

And the answer might have something to with the fact that many drug companies have an inalienable, financially lucrative interest in painkiller medication. Although the advertisement sought to address the issue of OIC, the far greater issue concerns Opioid use and Opioid addiction.

What exactly are opioids? They are a class of drugs that include the illegal drug heroin and the legal prescription pain reliever's oxycodone, hydrocodone, codeine, morphine and fentanyl [1]. Up until the last decade of the 20th century, opiates were either prescribed for the treatment of short-term pain or for chronic pain caused by terminal illnesses. However, in the 1990s, a dangerous myth swept across the medical community. Many doctors, manipulated by Big Pharma propaganda masquerading as medical literature, believed these drugs to be neither destructive nor addictive. The prescription of opiates became much more frequent and the self-serving desires of drug companies were assuaged.

Recent studies show that nearly 22 million Americans, ages 12 and up, struggle with substance abuse, with 2 million suffering from a disorder involving prescription pain relievers [2]. On May 11th of this year, shortly after meeting with presumptive Republican presidential nominee Donald Trump, House Speaker Paul Ryan drew attention to the work he and his associates were doing to address the nation's drug and opioid addiction crisis: "Right now, more Americans die every year from drug overdoses than car accidents. We are acting on 18 bills to deal with this. I hope that each and every one of you will be back here when we sign this bill." Indeed, prescription drug overdoses are crippling middle class America, and opioid addiction has enabled this epidemic to gain traction. Paul Ryan made a valid point, and that's a statement you seldom hear a liberal make.

In 2015, according to various road crash statistics, 32,675 people were killed in motor vehicle crashes, with prescription drug and heroin overdoses alone claiming more than 29,000 lives [3]. Overdose death rates are four times higher now than they were ten years' ago, and with 260 million prescriptions written for opioids on a yearly basis, the gap is widening [4]. And just to put that 260 million figure into perspective - The U.S. has a population of 319 million.

The Centers for Disease Control and Prevention, a leading national public health institute of the United States, recently published its guidelines for the prescription of opioids for chronic pain. As the nation's health protection agency, CDC stated that opioids should only be used when the benefits for pain relief clearly outweigh the risks, with avoidance of concurrent Opioid and benzodiazepine use if at all possible. The progressive move received widespread approval from academics, addiction treatment professionals, divisive politicians like Hilary Clinton and Jeb Bush, as well as President Obama. Everyone with a conscience, it seemed, was behind the CDC initiative, everyone except those who stood to make a financial loss.

After all, advisory guidelines could hamper pharmaceutical company profits, and heavyweights like Purdue Pharma, Johnson & Johnson, and Endo Pharmaceuticals rushed to combat the threat. They made weak claims that such actions would make it too difficult for patients to access necessary medication, and, unsurprisingly, the feigned cries of concern worked. To this day, their legal representatives have succeeded in keeping the CDC from implementing policies of a genuinely substantial nature.

After all, there's money in medicine, and no one understands money-driven medicine quite like Big Pharma.

Take the Sackler family, for example, the people behind Purdue Pharma. As one of the richest families in the U.S., the Sackler's reportedly made their billions - 14 to be precise - from providing doctors and hospitals with huge amounts of OxyContin, a synthetic analgesic drug that Peter Shumlin, Governor of Vermont, recently labelled "the match that ignited America's opiate and heroin crisis." (Vermont has one of the highest rates of opioid addiction in the country).

It's no coincidence that rising death tolls come at a time when the pharmaceutical industry is aggressively encouraging medical practitioners to prescribe highly addictive opioids. Primarily used for pain relief, opioids are now being prescribed for all manner of complaints, from persistent coughing to diarrhea. Acting on opioid receptors, the potent drug produces morphine-like effects, making the painkiller incredibly addictive and highly dangerous.

I had the opportunity to interview Alan Cassels, a University of Victoria researcher and the co-author of 'Selling Sickness: How the World's Biggest Pharmaceutical Companies are Turning us All into Patients' (co-written with Ray Moynihan). For two decades, Cassels, a former naval officer and diver, has immersed himself in very different waters, namely the murky ponds of pharmaceutical policy research.

Primarily focusing on three areas: prescription drug information, pharmaceutical industry persuasion tactics and medical media, the Canadian is one of Big Pharma's most vocal adversaries. When

John Glynn
Ludwig Von Mises Institute, USA

asked to describe Big Pharma's influence on the world of prescription medication, Alan had this to say:

"I think that pharma's influence on the act of prescribing is persuasive, pernicious, and very unhealthy for society and the health of the population. This is based on 20 years of observations of the industry and its bamboozlement of doctors and especially specialists who pretend to practice evidence-based medicine without realizing the 'evidence' it is basing prescribing decisions on has been thoroughly corrupted by, altered and misshapen by the company's marketing products."

Keen to discuss Big Pharma's underhanded tactics, Cassels continued, "The pharmaceutical industry funds the misleading and frequently deceitful courting of politicians and health policymakers, who end up making decisions that favor the industry's profit margins. It also funds unscrupulous marketing campaigns to consumers by buying patient and disease advocacy organizations or infiltrating those who cannot be bought."

Cassels concluded the interview with an ominous assertion, "What isn't transparent, and is the most egregious concern, is the permeation of almost every organ that has a hand in physician education and training, all under the banner of 'evidence-based' (medicine), blindly purveying and spreading the idea of a drug for every ill."

Because Big Pharma thrives on the notion that a drug exists for every ill, Cassel's final point is especially striking. With drug prices in the U.S. rising by 10% on an annual basis, suppressing the seemingly irrepressible greed of drug companies appears to be an improbable and unenviable task. Today, with prescription drugs becoming more expensive and legally allocated for a prescribed duration, heroin, once an outlier drug, has become a popular choice for upper-middle class Americans. With its ability to tranquilize the body and suppress pain, heroin often evokes temporary states of euphoria. In stark contrast to stimulants like cocaine, heroin is a depressant and is favored by users looking to self-medicate. After the euphoric effects wear off, however, a user may start to experience severe withdrawal symptoms, and it's common for long-term users to lose their teeth, experience respiratory illnesses, as well as manic depressive states, a loss of appetite, and chronic insomnia.

It's no secret that heroin has made the transition into middle class society. No longer just a big city drug, heroin use is rampant in the suburbs. The U.S. is a country that loves to self-medicate, and heroin offers a transient escape from varying levels of anxiety and despair. Many users are well educated twenty-something's. Scaremongering and lectures on the detrimental effects of heroin no longer work. Did they ever?

The sooner people realize that substance abuse, like cancer and diabetes, is a disease that requires close attention, the better. Labeling users criminals and dishing out prison sentences is an archaic, all too primitive response. A change is needed, however, tangible results are impossible to achieve if the pharmaceutical industry continues to manipulate and influence the treatment programs of patients across the nation. Arnold S. Relman, MD, who served as editor of The New England Journal of Medicine from 1977 to 1990, was one of the first to speak about the dangers posed by the "medical-industrial complex," the network of corporations which supply health care services and products for a profit.

Dr. Relman, just like the aforementioned Sanders, was chillingly accurate and largely ignored.

Today, with medical ghostwriting rampant in the world of academia, Relman's warnings seem more relevant than ever before. This dishonest practice often involves an anonymous author employed by the industry or its service agencies to produce seemingly independent manuscripts for peer-reviewed journals and conference presentations. Corporate-funded medical ghostwriting continues to capture public interest and continues to blur the lines between ethical and legal practices. Common logic tells us that reputable studies require a reputable author, and this is where things take an even more sinister turn. Physicians are approached and encouraged - often through financial incentives - to attach their names to manuscripts as though they had conducted actual research. As many of these published papers are inaccurate and misleading, there is a certain irony in a doctor lending his or her name to doctored information.

ProPublica, a non-profit newsroom that specializes in investigative journalism, famously ran a piece which disclosed payments from pharma companies to doctors and other health care providers. The report named and shamed more than 20 well established, U.S. based doctors. Generously compensated by various drugs manufacturers, each medical practitioner received more than $500,000 for speeches and consulting [5].

AstraZeneca, Johnson & Johnson and Eli Lilly, to name just three juggernauts of the pharmaceutical industry, have had to pay out sizeable sums in federal settlements over allegations that they approached doctors to promote drugs for unsanctioned uses. The major issue here has little to do with the fact that the physicians most probably violated both medical school policies and federal laws (the money they received was never reported to either their affiliated academic institutions or the IRS).

No, it's more worrying that these professionals promoted the 'findings' at national medical conferences and/or departmental meetings.

Seemingly undeterred by all of the negative publicity and bad press, the divide between medical practitioners and the pharmaceutical industry continues to erode, both domestically and globally.

China, with a population of 1.357 billion people, is struggling to provide healthcare for its vast and rapidly ageing population, and this challenge has presented Big Pharma with a new and lucrative opportunity. Although China harbors ambitions of developing and promoting its own pharmaceutical sector, the Middle Kingdom has little option but to reluctantly accept significant contributions from overseas. The U.S., unlike China, presents one major challenge for pharmaceutical companies - patent cliffs, a term which refers to the phenomenon of patent expiration dates and an abrupt drop in sales that follows for a group of products capturing high percentage of a market.

Eastern Asia, and especially China, on the other hand, is a relatively new market, thus presenting pharmaceutical companies with a relatively open field, and it's no secret that the communist nation's regulatory environment is - at best - questionable. Furthermore, the world's most populous nation offers a wealth of patients willing to participate in clinical trials.

How to stop big pharma?

Well, that's the multi-billion dollar question that offers little in the way of concrete solutions. Ever since the 1930's, when the Rockefellers privatized healthcare in the United States, a subculture of unethical behavior and profit driven medicine gradually became mainstream. Today, if you happen to study any list detailing the most powerful companies in the U.S, you will see a number of pharmaceutical corporations listed. Big Pharma's influence, from drug wholesalers and chain pharmacies to medical conferences and academic journals, is extremely powerful. The next president of the U.S. will have a major part to play in the demise or further ascension of Big Pharma, and if that president happens to be an orange haired, mini fingered baboon, don't bet on a rapid demise any time soon.

References

1. National Institute on Drug Abuse (2015) Drugs of Abuse: Opioids. Bethesda, MD: National Institute on Drug Abuse.
2. Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality (2015) Behavioral health trends in the United States: Results from the 2014 National Survey on Drug Use and Health. Rockville, MD: Substance Abuse and Mental Health Services Administration.
3. Center for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System, Mortality File (2015) Number and Age-Adjusted Rates of Drug-poisoning Deaths Involving Opioid Analgesics and Heroin: United States, 2000–2014. Atlanta, GA: Center for Disease Control and Prevention.
4. Centers for Disease Control and Prevention (2014) Opioid Painkiller Prescribing, Where You Live Makes a Difference. Atlanta, GA: Centers for Disease Control and Prevention, USA.
5. http://www.theguardian.com/society/2003/dec/07/health.businessofresearch

John Glynn*
Ludwig Von Mises Institute, USA
Email: dr_popejoy@hotmail.com