Conventional drugs are not silver bullets

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**Background**

Many people routinely take conventional drugs, whether for rapid relief of acute disorders such as headache, stomach upset or infection, or over the longer term for chronic ailments such as diabetes, hypertension, cancer or high cholesterol. The clinical benefit they obtain varies according to the type of drug used, the nature of the ailment being treated, and the person's temperament. There is, however, an important drawback to their use, and that is their inclination to cause side effects, or, more accurately, *adverse drug reactions*.

Conventional drugs are accepted, or *tolerated*, by the user to a greater or lesser degree; otherwise they would be withdrawn from the market. Their therapeutic benefits must exceed their drawbacks. However, no drug is free from side effects. Some, like over-the-counter medications, are generally well tolerated, and free from unwanted side effects when used properly. For these, the risks of side effects are far outweighed by the benefits the drug confers. Other drugs, such as those used in cancer chemotherapy, are, notoriously, certainly not so, and are associated with a myriad of serious side effects.

In fact, if a drug does not have side effects, it most likely does not work at all, and will be viewed with suspicion. So goes the conventional wisdom. Side effects can be minor, such as nausea or stomach irritation; or they can have a major impact on a person's quality of life, such as hair loss, fatigue and insomnia. In fact, many admissions to hospital can be laid at the door of conventional drug use, misuse or abuse.

The treatment of cancer illustrates the point well. This disease is now one of the leading causes of death in the developed world. In most cases it is treated by chemotherapy ("chemo"), radiation or surgery, or various combinations of the three. The aim of chemo is to eliminate cancerous cells by one pharmacological action or another. Unfortunately, healthy, normal cells are also killed, as "innocent bystanders!. The drugs employed create a plethora of side effects, due largely to their impact on healthy cells, nausea and vomiting, for example, which are perhaps the most feared side effects of chemo. Not
only that, but certain anti-cancer drugs can themselves cause cancer, which is a terrifying, unexpected consequence of chemo. Finally, the side effects brought about by chemo will themselves demand additional drug treatment in order to alleviate the symptoms troubling the patient, such as pain, ulcers, and nausea, and many others. These additional drugs in turn will trigger other side effects ... and so on.

This review examines some modern drug; some highly specific, others less so, for one type of receptor, which do have side effects – because the same receptor is involved in other, separate, metabolic functions or processes. These drugs are the cholesterol-lowering statins, anti-secretory proton pump inhibitors, anti-cancer drugs, and anti-retroviral drugs.

**How conventional drugs work**

Key-Lock analogy for drug action: 
A drug can be compared to a key, which must be the correct shape to open only one lock – the receptor. Otherwise, no effect.

Drugs generally act on natural microscopic structures called receptors which are located in cells of all living organs and tissues, and carry out regular functions. Normally they respond to natural internal substances such as hormones. Different types of cell have different mixes of receptors, depending on their role in the body. Whether a drug has an effect depends on the presence or absence of suitable receptors, and their 'population density' on the tissue cell surface.

Many drugs work by inhibiting certain enzymes. These are proteins which catalyse chemical reactions in different parts of the body, and are absolutely essential at all levels of life. Certain disorders are linked to abnormally active enzymes, so reducing their activity with drugs should, theoretically, lead to improvement in the condition.

A number of commonly used drugs which target enzymes are the ACE inhibitors (hypertension), statins (high cholesterol), and COX-2 inhibitors (rheumatic disorders).

Other drugs target channels in the cell membrane. These are gateway structures which allow or restrict the entry of substances into the cell, such as ions and small molecules. An example is a calcium channel blocker such as nifedipine, used to treat hypertension.

**The Tibb perspective on conventional drugs**

Although conventional drugs relieve the symptoms of diseases they are used for, they rarely bring about a cure. Many of their side effects and long term adverse reactions arise because of the broad effects most drugs have upon the body's metabolism and power of inner healing. In fact many drugs, especially the antibiotics and steroid-based agents, actually depress the immune system to a greater or lesser extent. This can have serious repercussions for present and future therapy.

Tibb, on the other hand, has a different approach to ailments. It regards good health as the outcome of a three-way harmonious balance between a person's nature, the environment, and his or her diet and lifestyle. This harmony, also termed homeostasis, is regulated by Physis, the body's vital force, or power of inner healing. This operates at all levels in the body, from individual cells, via general metabolism, up to integrated organ systems. Tibb regards disease as arising from a disturbance to this harmony, so treatment focuses on supporting the inner healing potential of Physis.

Unlike conventional drug therapy, the objective of traditional Tibb treatment is to support and enhance Physis; never to restrict or diminish it. The underlying disharmony which leads to the symptoms of an
Ailment is usually brought about by a faulty lifestyle, a depressed immune system, or an acute event like infection. This disharmony is rectified in Tibb by improving the person's lifestyle, herbal medicines, or by hands-on techniques, in order to boost and support Physis.

Why side effects occur with conventional drugs

In most cases, modern drugs are synthetic, new-to-nature chemicals, or semi-synthetic derivatives of biologically active herbal substances.

They cause unwanted reactions in our body for several reasons.

Drugs are usually artificial by nature, so they pose a real threat to the harmony of our body's metabolism. They are alien, and could be poisonous. Our body's Physis therefore takes precautions, by responding to them appropriately, and effectively, by rapidly expelling them. Very efficient detoxification mechanisms are part of our body's Physis, which exist to protect us from threats from the outside environment. The person will vomit or develop diarrhoea as a way of expelling the presumed toxin. For example, a whole range of detoxification mechanisms come into play to make the drug or other alien substance more water soluble and so easily excreted via the kidney.

- Drugs either stimulate or inhibit one or more type of receptor which is distributed in various tissues and organs. Depending on the nature of the drug, certain side effects will appear. For example, a beta blocker will inhibit adrenergic receptors, leading to a fall in blood pressure. It may also affect cholinergic receptors, resulting in a dry mouth, dizziness and blurred vision.

- Drugs can also interfere with the body's basic metabolism, upsetting internal harmony, and so provoking changes in the body, such as a rise in potassium levels or blood sugar. Furthermore, key enzymes may be damaged by the drug binding chemically, and irreversibly, to them, so they are no longer are effective.

- Drugs may have local toxic effects on living tissues. As they are largely synthetic, alien and new-to-nature substances, they can exert a serious toxic effect by direct contact with sensitive tissues in the digestive tract or on the skin, especially at high concentrations.

- Drugs may provoke allergic reactions. This complex mechanism is yet another aspect of Physis that exists to protect the body. If one occurs in response to the alien drug, then side effects like flushing, laboured breathing, sweating and difficulty in swallowing can occur.

Improving drug tolerance

Side effects are therefore a major problem for conventional drugs, and they often severely restrict their usage, especially for chronic or recurring disorders. The search for drugs which are less prone to side effects has been at the forefront of modern pharmaceutical research for decades. Better dose forms, improved dosage schedules and different routes have been successful in varying degrees.
Another route followed has been the design of drugs whose chemical structure is more selective or specific.

This means that if a particular receptor (on a tissue cell or enzyme) is not functioning properly, and this is linked to the underlying cause, or symptom, of the disorder, then stimulating (or inhibiting) this with a specific drug is surely the route to restoring health without triggering side effects.

However, if the drug interferes with other receptors in the body's tissues – in effect, innocent bystanders! – then this can result in undesirable, and inevitably unwanted, side effects. So the more specific a drug is for the target receptor, then the less likelihood of side effects. In other words, drugs should act as target pistols, not shotguns.

Unfortunately, this approach does not work in most cases for one simple reason. The target enzyme or receptor has more than one function in the body, so the drug will have numerous effects, often unrelated. The living body is far more complex than the mechanistic system projected in conventional medical model.

Another unintended consequence of drug action happens when the desired effect in one area carries over into another area, which can upset the local harmony. For example, lowering acid levels in the stomach may be the desired effect, but this can create problems in other areas of the body. The proton pump inhibitors are an example of this activity.

Yet another unintended consequence follows when the action of a drug reduces the level of a particular metabolite in the body. This may be the desired objective; however, this metabolite may also be critically important in other functions, and therefore have a 'knock-on' effect in these unrelated biological activities. The statins are an example of this activity.

Examples of drugs which affect either enzymes (such as the statins and the anti-retrovirals) or a receptor (such as the proton pump inhibitors) are provided below.

[A] Statins

Preamble. Statins such as Lipitor, Zocor, Crestor and their generic equivalents are the most widely prescribed class of drugs in many countries, including South Africa. As many as one in five adults is taking them, mainly for reduction in blood cholesterol and for the prevention of strokes and heart attacks.

The most common side effect is muscle pain and weakness, a condition called rhabdomyolysis, most likely due to the depletion of ubiquinone, a nutrient that supports muscle function. There are,
however, many others, which usually appear after several months of therapy\textsuperscript{10}.

Cholesterol is essential for many functions (see box), and comes in part from the food we eat, but much of it is produced in the liver. The process starts with acetate, which is then metabolised to a basic building block, mevalonic acid. This is the source material for a whole host of essential substances, including cholesterol. One stage in the synthesis of mevalonic acid depends on a particular enzyme*, which can be inhibited by any of the statins.

Statins, unfortunately, do not inhibit just the production of cholesterol, but a wide range of other substances which are derived from mevalonic acid. Many of these, such as ubiquinone, dolichol and squalene, have important, even critical, biological functions themselves. Unfortunately, there is no alternative pathway for the synthesis of mevalonic acid. This is probably the reason that the statins, which are highly selective in action, have such broad effects in the body, insidiously over the long term.

\textit{Effect on ubiquinone (aka Co-enzyme Q10 or CoQ10).} This substance plays a major role in the energy-generating system in the powerhouse of the body, the mitochondria. This occurs mainly in the heart and skeletal muscles. Ubiquinone can also be found in substantial amounts in the cell membrane, where it is essential for maintaining structure and activity. Nerve impulses and muscle contraction require much ubiquinone to function properly. Ubiquinone is also necessary for the synthesis of structural proteins, particularly collagen and elastin.

Predictably, lack of ubiquinone results in muscle wasting, muscle pain, especially in the back, heart failure, and inflammation of the tendons and ligaments, and nerve impulse transmission can also be restricted.

This depleting effect is accepted by healthcare providers, who now advise people taking statins to take ubiquinone supplements.

\textit{Effect on dolichol.} This group of substances acts as cell messengers, and plays a very important role in directing newly synthesised proteins to their proper destinations in and out of the cell. Interestingly, they are present at high levels in a part of the brain (the substantia nigra) which is involved in skeletal muscle activity. Many of these proteins are thought to be involved in the expression of emotions, efficient immune system functioning, and passing messages between cells.

\textit{Effect on squalene.} This complex substance is on the same pathway that leads to cholesterol. This too will be reduced by the action of the statins. Reducing the synthesis of squalene could have consequences, as it appears to be implicated in the formation of blood vessels, and to have a role in cancer formation.

\textbf{More unintended consequences of long-term statin usage have been noted:}

\textbf{Adverse effects\textsuperscript{10}.} Many have been reported, including muscle aches (sometimes severe), tingling in the hands and feet, cataracts, memory loss, and liver and pancreas problems.

\textbf{Increased arterial plaque\textsuperscript{11}.} Statin use is linked to an increase in calcified plaque formation in the blood vessels of users. This is a common feature of cardiovascular disease. It increases the risk of a stroke or heart attack.
Increased risk of type 2 diabetes\textsuperscript{12}. Statins significantly increase the risk of this developing, especially in post-menopausal women.

[B] Proton Pump Inhibitors\textsuperscript{13}

\textit{Preamble.}

Proton pump inhibitors (PPIs) such as \textit{Nexium} are the most popular drug globally used to treat digestive disorders such as indigestion, gastric ulcers, inflammation of the oesophagus, gastric reflux and heartburn. They act directly on the acid-forming mechanism in the stomach necessary to digest proteins taken in as food. Although the effect is very specific, the effects of its action are more far-reaching.

Reduced acidity can appear in tissues other than the stomach. A significant increase in disturbances to the heart's normal rhythm has been noted in patients taking PPIs over the long term. It seems that the pharmacological action on heart tissues involves other ions, particularly potassium and calcium, as well as changes in acidity.

Reducing the acid content of the stomach allows some protein to evade digestion. This undigested protein travels down the digestive tract, where some of it may be absorbed into the body. In some people this can lead to food allergies.

A number of other unintended consequences of long-term PPI usage have been noted:

- \textit{Increased risk of bone fracture}\textsuperscript{14} especially of the hip, spine or wrist. This seems to be linked to the effect of PPIs on cells involved in bone building.
- \textit{Increased risk of childhood asthma}\textsuperscript{15} in children from women who received a PPI during pregnancy.
- \textit{Premature ageing of the skin}\textsuperscript{16}. This is due to interference with the acidic environment needed for new skin synthesis and texture.
- \textit{Decrease in vitamin B}_{12} \textit{absorption}\textsuperscript{17} due to reduced acidity in the stomach from long-term PPI usage. The release of this vitamin from the food it comes in is impeded. This applies mainly to elderly patients, convalescents and vegetarians.

[C] Anti-cancer drugs\textsuperscript{18}

\textit{Preamble}

The body is made up of billions of living cells, and these are constantly dividing to reproduce and replace ageing tissues. Different tissue cells divide quicker than others. Normally the process of replacement of old tissue cells by new is under the control of Physis. This switches on the process when necessary, and turns it off when completed.

Cancers are forming continually in the body, due to the effect of natural radiation, toxins and other influences on the body's genetic material. However, the body's immune system, again under the control of Physis, is able to identify, isolate and destroy these renegade cells. Cancers become a health problem when the formation of malignant cells escapes control by Physis for one reason or another. The cell division process carries on uncontrolled and chaotic, and does not stop when it is supposed to. The cell mass continues to grow and grow, ultimately forming a \textit{tumour} (Latin: swelling). If some of the rogue cells break off the tumour and enter the bloodstream, they can travel to distant sites and form a satellite tumour, or \textit{metastasis}. 
Causes of cancer
The basic cause of cancer appears to be damage to DNA, the cell's genetic material. Substances or environmental agents which promote or lead to DNA damage are called carcinogens. These include substances such as arsenic from tap water, chemicals found in cigarette smoke and car exhaust fumes, asbestos in insulation materials, radiation from radioactive gases like radon, and over-exposure to strong sunlight and X-ray diagnosis. Other factors which are linked to the development of cancer are environmental toxins, increasing age and genetic abnormalities.

Essentially, anti-cancer drugs target cells which are reproducing more rapidly than normal healthy cells in the same tissue or organs. Even so, the normal cells themselves are themselves affected, and this shows up as side effects, both immediately and long term.

Chemotherapy
A very wide range of drugs is available to oppose the irregular cell division that is cancer. Collectively this is known as chemotherapy, or "chemo". This is administered with two aims: to prolong life by destroying the cancer, and to improve quality of life by reducing the sufferer's symptoms.

Most chemo drugs act either to interfere with cell division (mitosis) in the affected tissue, or by interfering with DNA synthesis or replication, so causing cell death. The most vulnerable cells are those which reproduce quickly, as in the lung, stomach, breast, lymph glands and white blood cells. Malignant growths which are slow growing tend to be impervious to chemo. Adverse drug reactions such as hair loss and stomach disorders are the consequences of this cell damage, or cytotoxicity. A number of anti-cancer drugs induce premature cell death (apoptosis) in developing tumours.

Many side effects from chemo are themselves treated with yet more drugs, which of course bring their own portfolio of side effects. Nausea, vomiting, pain and ulcers, for example, need their own drug intervention.

Types of chemotherapy
There are a variety of drug classes now available to treat cancers. In effect, most of these are cell poisons, as they are not totally specific for the cancerous cells. The main ones in use are:

a) **Alkylating agents** interfere with the cell's DNA activity. They include the platinum drugs and cyclophosphamide and melphalan. They are used to treat ovaries, breast tumours and malignant melanomas.

b) **Antimetabolites** inhibit normal cell division by interfering with the enzymes involved in DNA synthesis. Examples are fluorouracil and mercaptopurine, which are used to treat leukaemia and breast and digestive tract cancers.

c) **Anthracyclines** are antibiotics isolated from the fungus, and interfere with the synthesis of DNA in malignant cells. Doxorubicin and bleomycin are used for leukaemia and cancers of the breast and bladder.

d) **Alkaloids** include vincristine, vinblastine and the taxanes. The vinca alkaloids interfere with cell division, and the taxanes prevent DNA replication. They are used to treat breast, ovary, prostate, and some lung cancers.
Problems with chemotherapy
Chemotherapy is usually more effective against relatively new cancers, as the normal cell reproduction mechanisms are still in place, so more of the cells are vulnerable to interference by anti-cancer drugs. As the tumour gets bigger, growth becomes uncontrolled and so the cells become less responsive to the cytotoxic drugs, partly because drug penetration is more difficult. Again, in large tumours cell division has virtually ceased, making them unresponsive to mitosis inhibition.

With time, tumours themselves adopt tactics to counteract the impact of chemotherapy. One is to actively pump out the drugs from inside cancerous cells.

The rapid breakdown of cancer cells causes the release of chemicals from the inside of the cells. Following this, high levels of uric acid, potassium, phosphate and calcium are found in the blood. This can lead to kidney and heart damage.

Anti-cancer drugs are usually used in combination, as part of a treatment regimen. Although this is claimed to improve the success rate for treatment, it compounds the number and severity of side effects.

[D] Anti-retroviral drugs

Preamble
Since the HIV & Aids pandemic began, total deaths worldwide have reached 36 million, and a similar number of people are living with the ailment. It is the most common cause of premature death in many sectors of our community, affecting young and old, male and female indiscriminately. The economically active sectors of the population, especially people in the 20 to 30 year age bracket, are particularly badly affected.

HIV & Aids is not a single disease, but a variable complex of signs, symptoms and metabolic disturbances resulting from severe damage to the immune system. This damage is inflicted by a type of virus called a retrovirus. This virus targets the lymphocytes, which are white cells which play a prominent role in the immune system. One major lymphocyte affected is the CD4 lymphocyte.

Management of HIV & Aids
A multifactorial approach is adopted in the treatment of this disease.

1. Prevention of infection, by educational support, encouraging a proper lifestyle, limiting the number of sexual partners, avoidance of contaminated needles, use of condoms, etc.
2. Treatment of infection, by supporting Physis with dietary and lifestyle changes, so boosting the person's immune system.

Common side effects of chemotherapy

<table>
<thead>
<tr>
<th>Short term:</th>
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<tbody>
<tr>
<td>Nausea, vomiting, diarrhoea</td>
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<tr>
<td>Intractable pain, fatigue</td>
</tr>
<tr>
<td>Mouth ulcers / sores, loss of appetite, weight loss</td>
</tr>
<tr>
<td>Anaemia</td>
</tr>
<tr>
<td>Hair loss</td>
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<table>
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<tr>
<th>Longer term:</th>
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<tbody>
<tr>
<td>Immune system depression, more infections from viruses, bacteria and fungi</td>
</tr>
<tr>
<td>Secondary cancers</td>
</tr>
<tr>
<td>Damage to peripheral nerves</td>
</tr>
<tr>
<td>Metabolic disharmony from tissue breakdown, leading to kidney and heart damage</td>
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2. Treatment of infection, by supporting Physis with dietary and lifestyle changes, so boosting the person's immune system.
3. **Anti-infective methods**, including the use of anti-retroviral drugs, drugs used to treat opportunistic infections by other viruses, bacteria and fungi, and cancers, which may develop as a consequence of a crippled immune system.

4. **Palliative treatment**, to deal with the troubling symptoms of the disease, and the unwanted side effects of the drugs used in its primary treatment.

**Anti-retroviral drugs**\(^{20}\)

The conventional drugs used to counteract the effects of this virus are termed anti-retroviral drugs, or ARV drugs.

Most of the anti-retroviral drugs act by inhibiting enzymes which are involved in the penetration, activation and installation of the mechanisms which lead to the production (replication) of more viral particles. The drugs interfere at different stages of the viral replication life cycle. Fusion inhibitors act rather differently, by blocking proteins at the virus entry site.

There are five different types of anti-retroviral drugs available at present:

- **Nucleoside Reverse Transcriptase Inhibitors**: They are better known as *nucleoside analogues*. The HI virus uses an enzyme, *reverse transcriptase*, in order to infect healthy cells and reproduce itself in a person's body. These drugs inhibit this enzyme, so making the virus unable to infect cells and replicate itself.
- **Non-Nucleoside Reverse Transcriptase Inhibitors**: These drugs are often referred to as *non-nucleosides*. They also stop the virus from infecting cells by intervening with the enzyme *transcriptase*, which is needed for virus replication and spread. They bind in a different manner to the nucleoside analogues.
- **Protease Inhibitors**: These inhibit *protease*, an enzyme present in virtually every living cell. Protease is a digestive enzyme, and breaks down protein. It is one of several enzymes that the virus uses to replicate. The protease inhibitors act before the viral protease begins to break down the person's proteins and enzymes. They slow down the duplication of the virus and thus prevent the infection of new cells.
- **Integrase inhibitors**: These act by inhibiting the enzyme *integrase*, an enzyme which helps the person's genetic material to work to produce more viruses. Specifically it helps the virus insert its own DNA into the person's DNA, so diverting production of normal protein into viral protein.
- **Fusion Inhibitors**: These act on proteins present on the virus's surface which let the virus attach itself to and enter into the person's cells. By blocking one of these proteins, fusion inhibitors slow down the reproduction of the virus.

Anti-retroviral drugs are generally used in combination; otherwise resistance to a single drug will invariably be developed by the HI virus. This is known as HAART (highly active anti-retroviral treatment) The likelihood of adverse drug events occurring with this is, not surprisingly, increased.

**Problems with anti-retroviral agents**

The main problem is without doubt the lack of tolerance to the drugs, in the form of severe side effects\(^{21}\). These may be serious enough to lead to discontinuation of treatment or irregular treatment, which can lead to the setting in of drug resistance.
There is also the factor of pill burden, in which the sheer number of pills being consumed, on top of those taken for opportunistic infections and palliative treatment, imposes a huge load on the liver especially, and this at a time when the person's recuperative powers and Physis may be at a low level.

As anti-retroviral treatment is a lifelong course, the chance of side effect-induced tolerance is a major factor in treatment success or failure.

If we take the protease inhibitors as an example of a popular anti-retroviral drug:

All protease inhibitors have a serious side effect – the metabolic syndrome. This shows up as unusual fatty deposits on the body and problems similar to diabetes. Also, all protease inhibitors have a powerful effect on the liver's enzymes. This can have a negative effect on the other drugs being used by the patient.

Discussion

A conventional drug is designed to interfere with a metabolic process in a part of the body thought to be functioning abnormally. Unfortunately, this process often exists in other parts of the body. As a result, the drug will also affect other parts of the body, even those in the non-target areas, which are working normally.

Chemotherapy well illustrates this point. This usually targets enzymes required for cancer growth. However, identical enzymes are present in other tissues such as hair follicles and bone marrow. These are hugely affected by chemo, and many side effects ensue. Avoiding side effects with chemo needs drug targets to be identified in cancerous, but not normal, tissues. This is a major, possibly impossible, challenge.

Modern drugs often claim, with justification, that they are less prone to side effects because they are more specific in their pharmacological actions, and, for example, only affect one enzyme or receptor in one particular tissue or organ. However, most enzymes and receptors have more than one function in the body, and are located in widely different tissues and organs. Many side effects probably occur because of this phenomenon.

In addition, most drugs, especially the more modern ones, are synthetic, new-to-nature chemicals, and these can inflict damage on living cells. General toxic side effects can develop.

So a drug may only affect one enzyme, but if this enzyme is involved in a number of different processes, then all of these processes will be influenced. This could lead to many effects other than the one intended. Unwanted side effects are the result.

The dilemma that conventional drugs face is that the drug may have a specific effect on a particular enzyme involved in the pathology of the disease, but the effects of the inhibition may spread far and wide in the body wherever the enzyme operates. The drug may be highly specific for a particular enzyme (or

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<th>Common side effects of protease inhibitors</th>
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<td><strong>Short term:</strong></td>
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<tr>
<td>• Abdominal pain</td>
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<tr>
<td>• Nausea and vomiting</td>
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<tr>
<td>• Diarrhoea/flatulence</td>
</tr>
<tr>
<td><strong>Medium term</strong></td>
</tr>
<tr>
<td>• Metabolic syndrome</td>
</tr>
<tr>
<td>• Fatigue; weakness</td>
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<tr>
<td><strong>Long term</strong></td>
</tr>
<tr>
<td>• Raised cholesterol</td>
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<tr>
<td>• Rash</td>
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receptor), but the enzyme involved is also used in other metabolic activities, and these will themselves be interfered with.

**Summary**

One aspect of conventional medical treatment is that it is largely based on the extensive use of drugs. Many conventional drugs act upon receptors, which are specialised areas of cell membranes that bind with natural body messengers such as hormones and neurotransmitters. This binding results in changes to the cells' activity, either increasing or decreasing certain aspects of it. Other drugs can influence specific areas of enzymes in the body, resulting in reduced activity. Drugs can therefore exert major changes in the body's wide range of metabolic functions, from energy utilisation to growth, from cardiovascular action to kidney function.

A major problem with conventional drugs is that their action may not be specific. This can take several forms. *First*, a drug may act on a particular receptor in one tissue to bring about the desired effect, but may also inadvertently act on similar receptors in other tissues, which may lead to one or more unwanted responses. *Second*, a drug may affect one type of receptor as the desired effect, but also another type of receptor, to give an unwanted (or unexpected) response. *Third*, if an enzyme is inhibited by a drug, the metabolic pathway(s) it is involved in will slow down. However, there may be repercussions if this same enzyme is part of another pathway which produces vital or essential cell materials.

Many side effects probably occur because of these types of unwanted actions by the drug. There is also the potential for local toxicity brought about by direct contact of the drug, which is in most cases, after all, a synthetic chemical, alien to the body, on sensitive tissues, especially in the digestive system. The possibility of an allergic reaction to the drug is another unintended consequence linked to drug usage.

The benefits of conventional drug treatment are often dissipated by their innate tendency to cause side effects. Many patients discontinue their drug usage because of adverse reactions, especially when in a long-term treatment regimen. In addition, to counteract the side effects of previously prescribed drugs, other drugs may be brought into the treatment schedule. Apart from the cost and inconvenience caused, these drugs themselves often introduce further side effects.

Ideally, a conventional drug should act highly specifically on a single receptor or enzyme to restore the disturbed metabolic situation to normal, without adversely affecting other biological processes. Unfortunately, the search for this therapeutic "silver bullet! has so far proven elusive.

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3. Admissions to hospital. Online at: [http://www.bmj.com/content/329/7456/15](http://www.bmj.com/content/329/7456/15)

Key words:

*How conventional drugs work*

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