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## Drug Use without Border (Administration of Drug without any Adverse Physiological and Biochemical Effect)

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### Abstract

Drug and any agent of therapy have unwanted unintended consequence which may be mild or severe, clinically, physiologic or biochemical effects of drug use most often cause permanent or temporary impairment, the following adverse effect of drug use have been reported, toxicity, adverse drug reaction, side effects, cross drug reaction, accommodation, and time dependent refractoriness, these drawbacks aren't secondary to nimble use of drug with narrow therapeutic index, contraindicated analogues and ban types as well, therefore, it became expedient to formulate a unifying theory of therapy which among others things shows how drug can be use without any of the aforementioned drawbacks, the theory called Boy'o Universal Theory of Therapy(BUTT), by primus inter pares, formulate complex principles, which by any standard make drug use borderless, implicit view, would mean that any drug can be used to treat any sickness irrespective of narrowness or wideness of the drug's therapeutic index.

**Key words:** Drug use adverse effect; Drug use without adverse effect; Therapeutic index impertinence; Unified theory; Boy'o Universal Theory of Therapy (BUTT).

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### Introduction

Drug usage in treatment has led to increase in life expectance, increase in wellness, reduction in burden of certain disease, effective management of outbreak of disease in Urban and Rural area, in past drug use also lead to drastic reduction in mortality rate during outbreak of certain deadly epidemic situation for instance chicken box, small box, tetanus etc. could have assuredly wipeout human beings on the face of the earth were it not for drug treatment that were used during the outbreak, again, the undoing of drug use is that when drug is introduce into the human system beside desired therapeutic effects at normal bioavailability levels, sometime most drug pharmacokinetic profiles cause adverse effects, among them are toxicity, adverse drug reaction, side effects, contraindications, cross drug resistance. Adverse effect of drug may have medium to long term physiobiochemical effects on the body's cells, tissues, and organs, the medical emergence in hospital, urban or rural community may require that drugs with therapeutic index or research drug under trial be used, however, the fears of adverse effect of drug often make experts abandon such attempt, the outcome is massive record of death

per 1000 of populace who need treatment urgently, in addition, efficacious drug with ineffective substitutes had been abandoned due to adverse drug reactions [1], another point worthy of note is debilitating effects or incapacitating effects clinical case of morbidity when wrong diagnosis lead to inappropriate drug treatment [2], also some unintended consequence of metabolic reactivation of secondary metabolites lethal to the body system result in death or permanent disability in patients. Thus in view of the above cogent observation, it becomes expedient to address issues of drawback of drug treatments, this review look at an aspect of ingenious novel theory called Boy'o universal theory of therapy (BUTT) [3], it is a research model which target the signaling medium components of known or anticipated adverse effect in a novel way, the essence is to eliminate adverse effect of drugs and increase efficacy of drug in relation to their pharmacological profile on one hand and biological effects on the other.

### Goodness of drug treatment

Health is wealth is well known age long maxim, for productive capacity of any society at any points in time is dependent on the level of health of the citizens, the deleterious effects of internal

systemic breakdown is aberrant control of the coordinating system, for without latter and good productivity in-day day-out activities is lost and note that, productiveness could be in the following areas; economic, academic, sports, politics, social, and security service to the nation respectively, the stressful effect of modern day life bears on functional integrity of the body system, so that frequent use of drug becomes necessary to sustain maximum level of productiveness which any nation requires to be key players in activities that shape the global world.

The goodness of drug use may be appreciated properly if the medicinal values of drug are asses from the following stand point;

(1) During stressful activity, for instance cognitive and memory retentive ability of CNS, specifically cerebral cortex, could be enhance by moderate intake of legalized drugs during rigorous activities such as security outpost duty, policy analysis by technocrat, and during conduct of comprehensive examination by academic institutions, sick cells patients, patient with disease which cause fatigue, asthmatics and so on, find it hard to cope with stressful academic and research work without regular intake of drug, also blue collar jobs, hard jobs, be they carried out in construction company or in military garrison requires input of pain relievers such as aspirin, indometacine, to ease various body ache preceding completion of work, the social disability of globalize pandemic such as HIV/AIDS, skin infection, diarrhea, hypertension, amyolateral sclerosis (ALS), cancer and recently EVD had been contained effectively, thanks to increase in use of drug adopted as curative and preventive strategies [4], the huge financial returns which in great depth characterize sport and entertainment industry which nowadays makes them lucrative human undertaking can be trace to legalized drug use, legalized drug intake usually enhance performance without which stream of huge income could dry up, research shows that the alarming rate of divorcé and social malady accompanying it, warrant the use of sex enhancer drug, if under performance between couple could bring irreconcilable difference, then the desire for sensual ecstasy of parasympathetic and sympathetic reference input is the delight of any married couple. The leaders in various nation can't in any way cope with huge task of governance, and consequently regular medical checkup and drug use keep them going even when the going seem tough, strenuous farming activities is hard to be conducted regularly without drug intake, food sustainability and fight against hunger and starvation is the desire of UN through it humanitarian agency like the UNDP [5], thus drug could affect general productivity of the world, in a note shell, disease risk factors account for causes of death, epidemiological research have shown that could cause huge burden appanage to diseases account for high rate of motility in 21<sup>st</sup> century, and these also required drug treatment to be effectively contained [6], malaria and other parasitic infection account for millions of death of global populace per annum [7], by drug use, the grave impact of malaria had been curtailed, again these overwhelming effect have accorded mankind abysmal benefits due to their adverse effects, the BUTT theory will control and eschew clinically reported cases of drug undesirable effects, pending BUTT research endeavor will focus on signal transduction pathway (STP) and molecular cross talk (MCT) control and regulation.

(2) Required to restore abnormal body state to normal body functions

Cellular substructure network through which synthetic compound are distributed for normal cell function relies on drug pharmacological mechanism, example lipid distribution from endoplasmic reticulum to other cellular substructure; Mitochondria, golgi apparatus, lysosome etc. [8], similarly insufficient cellular uptake of glucose for energy metabolism in type II diabetes, accumulation of ganglioside in brain and spleen due mainly to absence of lysosomal enzymes or hexosaminidase deficiency in Tay sachs disease [9], faulty cellular regulation of biosynthesis of cholesterol in pathogenesis of atherosclerosis cause huge deposit lipids rich fats in cells lining the blood vessels leading to the following; stroke, hypertension, ischemia of coronary artery, and may precipitate heart attack or paroxysmal left ventricular arrhythmias or dangerous fibrillation and angina [10], and importantly, sudden death have been attributed to these factors, however with drugs their treatment and management have saved countless number of lives, again molecular cargo transporter and intracellular substance traffickers which plays vital roles in uptake of substance, modulation of axonal glutamate reuptake and recycle to utilizable glutamine are implicated in neurodegenerative disease such as Alzheimer's disease [11], also the absence of enzyme in any metabolic pathway which result in accumulation of intermediate could prove detrimental to metabolic integrity require to supply energy needed for biosynthetic of metabolic intermediate. For instance lactose intolerance [12], phenylketonuria [13], lysosomal disease [9], research show are implicated in certain physiological anomalies, also these various diseases or abnormalities can be treated or managed with aid of drug therapy. In clinical cases of pathology wherein infectious and noninfectious disease such as sexually transmitted disease (STD), syphilis, hepatitis, fibroid affect reproductive system adversely, infertility [14], dysfunctional erection [15], amenorrhea, are among the pathophysiological clinical presentation.

In case of infertility, weak spermatocyte in most instance fails to ascend the acidic, muciliated contracting virginal tube, internal OS and fallopian tubes which are localized area of fertilization, failing of which lead to infertility or barrenness [14]. Again normal physiological processes in pathogenic mediated disease particularly viral disease have been investigated, for instance in HIV/AIDS, the HIV virus destroyed CD4, CD8 cells and T cells and thereby lowers their counts and also concomitantly result in manifestation of weaken immune system, occurrence of opportunistic infections and ultimately death, this painful scourge which leave indelible pains in the heart of loved ones are nowadays treated by intake of drug with ability to lower the viral loads. Diarrhea outbreak, Ebola virus disease, measles, hepatitis encompass huge number of diseases treated with drug treatments, it is important to acknowledge that as mentioned, in time past these disease almost wipe out large chunk of global population, fortunately, the goodness of new drug employed in their treatment provided great relief to mankind, a recent epidemiological events is EVD in west Africa in 2014, it has paralyze economic activities of affected nations [16], the worst hit is tourism industry, the physiological symptoms include

bleeding from all facial opening, diarrhea and weakness of the body, drug treatment and isolation offers the only hope of containment, in noninfectious disease, malaria, erythroblastosis fetalis, myeloma, gastrinoma, anorexia nervosa, drugs and physiological treatments were also used to treat the diseases and restore normal body functions, indeed the list is far from being exhaustive, significant number of clinical presentation had been treated, but use of drugs and physioanatomical methods, on the contrary, and notwithstanding the magnitude of the benefits of drug treatment pointed out above, there are treatment drawback which will result in death as well as incapacitating undesirable outcome, this underpin the need for complete elimination of undesirable effects as we shall see latter.

### Drug treatment drawback

Expansive continuum of drug treatment drawback often weigh down on unlimited use of these benefits, few among these drawback are toxicity, side effects, adverse drug reaction, drug refractoriness and contraindication and their consequences. Subsequent section shows how these drawback will, through the parent drug, reactive metabolite of parent drug, or metabolism of the parent drug or interaction of parent drug with other drugs as may be warranted by consequence of action of cytochrome oxidase system on them on one hand and on de novo synthesise cellular products on the other [17], and again given the cell-organ-system destructive effects of drug in therapy, and most time it is wide spread adverse effects, a novel researchable model was advanced and briefly illustrated in section 4 below, disappointing result of finding indicated their presence in spite that high purified forms with low dose and narrow therapeutic index are large proportion of medicament in use, ostensibly, the following drawback encompass challenges for drug discovery, drug development and drug use in finding and application (clinical setting) [18].

### Toxicity

Toxic effects of drug on the processes which occur inside the body structures had been established through research, for instance ototoxicity in use antibiotic drug such as tetracycline and ampiciline [19], Antihypertensive drugs ACES (Anapril) which cause hyperkalemia [20], Ganong (2001) shows that hyperkalemia is secondary to faulty fatal ECG reading of the heart myocardium (Arrhythmia, Heart block and conduction delay), lidocaine, antiarrhythmias drug cause convulsion [21], propranolol, esmolol are B blockers drugs use in treatment of asthma, cough, also some classes of loop diuretics furosemides, ethacrynic acid), potassium sparing diuretic (spironolactone) respectively lead to the following toxicity, hyperkalemic metabolic acidosis and acute renal failure.

Generally speaking, most drug use in treatment are associated with mild to moderate toxicity; few among them are the following; GIT ulceration, liver disease, impotence, paralysis (especially those given by IV route) and cancer drugs which may cause leukemia [22], note that these effects are rarely localized, for in some cases two or more systemic normal functions may be impaired a fact that lead to the evolution of the propounded BUTT

theory, BUTT model is a research milestone capable of eliminating any drug toxicity, especially drugs with narrow therapeutic index, past finding attributes toxicity of drug to formation of active metabolites and pharmacodynamic processes of metabolism of chemical components of drugs involve in conjugation phenomena, in the liver where glucuronidation of the parent drug is carried out prior subsequent elimination [23], besides these active toxic metabolites, the concentration of parent active compound at any given dose necessary to achieve therapeutic bioavailability in hemodynamic time frame distribution could also be toxic, this is true for drugs with low therapeutic index, low rate of elimination from the body depends on extend of elimination and may inflict permanent damage to the body organs.

### Adverse drug reaction

Adverse drug reaction entails unintended, unexpected, unknown harmful pharmacological effect of drug-tissue reactions, usually observed in phase 4 of post clinical trials, at times it is not evident until prolong administration had been carried out, lethal effect of adverse drug reaction includes but not limited to organs hyperplasia, paralysis, fetal death, impaired hemopoiesis and carcinomas, most of which may or may not be reversible unlike drug side effects, again the multi factorial disorder pattern of adverse drug reaction is unlikely to be control in most patient using single or multiple dose, except when therapy is withhold, but even at that incapacitating effects may persist, and importantly, the drug production could be banned leading to waste of money and human resources invested in the drug manufacturing processes, a good number of efficacious and potent drug had been banned owing to unintended consequences of adverse reaction, example chloroquine [24], the BUTT theory main aim is to eschew these drawback, despite their narrow therapeutic index.

### Side effects

Sides effects are also unintended but known mild to acute discomfort associated with drug treatment, discomfort used here do not imply absence of lethal effect, for the manifestation of signs of side effect may have dangerous latent period, however, with mild to tolerable treatment withdrawal, drug treatment side effects have disappeared, in addition, side effects of drug use in treatment of superficially research pathophysiobiochem body condition could result in death of patient, malaria treatment for examples requires hematinics for replenishment of destroyed RBC in a body system infested by plasmodium falciparum parasite, this was discovered through research and treatment experience [25], a reasonable number of cases exist where complex effects of side effects have not been determined, also some drug medicament could accumulate in body tissue with prolong drug use, resulting in side effects which are complex and difficult to treat, for instance concurrent use of Phenyton and prifampin drug and cyclosporine low clearance rate increase the level of caspo fungi and risks which accompany the side effects (FDA, MMS), another diagnostic lethal effect of side effects is false positive result when used in false diagnosis, wrong presentation or wrong treatment may exacerbate complex medical problem at hand and perhaps lead to death, in treatment involving any one of the following drug, metronidazole, vancomycin, gentamycine,

tobramycin, netmicin, aminophylline, ampicillin (>40mg/ml) gives erroneous result in urinalysis for glucose presence using clintest tablets (FDA, MMS), additionally in most drug usage, CNS side effect are confusion, dizziness, headache, nausea, GIT side effects are increase or decrease in appetite, diarrhea and constipation, hematological changes include polycythemia, low RBC count, low hb counts, ESR increase or decrease, increase in musculoskeletal system tremor, change in gait, and muscle palsy, bearing in mind that transient ones are extremely tolerable, acute ones could span days or years (if not treated result in permanent disability).

### Cross drug reaction and refractoriness of drug

Cross drug reaction occurs when two or more drug are given concurrently or together, it has bearing on chemical structures of the drug [26], drug resistance by the body cell or pathogens research shows, could be circumvented by combination therapy, more so, refractoriness simply means absence of expected drug action at site of drug action at a concentration considered normal for bioavailability when refractoriness occurs, alternative use of drug usually restores response, whereas combination therapy may ensure attainment of therapeutic goals, active constituent of drug could be metabolized by various enzymes (CYP 2A3, CYP3C1, CYP2A1) of the cytochrome oxidase system into active dangerous radicals, the processes involve are directed and controlled by signaling mediums and that is why Boy'o Universal Theory of Therapy (BUTT theory) [3] will target critical components of the signal transduction pathways (STP) and molecular cross talk(MCT) that occur between them, STPs are involve in interaction of two or more drugs in the body, drug to drug interaction may alter their pharmacodynamic and pharmacokinetic processes and reactions [23].

### Drug treatment without border

The drawback of multi-faceted effect of drug treatment demands fresh revolutionary model so as to allow use of toxic drugs with narrow therapeutic index in treatment, as mentioned, the novel theory capitalized on signaling medium critical points, like recruiters, modulators, and various adaptor proteins like the SOS, rab or ras family proteins that mediate the final response of STP, the manipulation of the pertinent components will redirect the cascade response in a predetermine way so as to fulfill the BUTT objectives, molecular signaling is at the heart of 98% of systemic processes, they regulate these processes, again drug pharmacological actions depends on STPs regulatory roles to be active, without signaling contributions in both binding and nonbinding actions of drug, biological response will never take place, given that adverse effects of drug due treatments often manifest in two or more location, BUTT divides the body into region, sites and sub-sites, additionally, the molecular signal use utilized derived mathematical equations to fathomed some characters of certain cascade [27], the limitation is nodal point (point at which cascade branched) determination, the branching of cascade down the pathway accounts for many and similar source of STPs response, there are three hypothetical premise, firstly, Boy'o propounded that MCT and STP control CNS and hormonal activities, since neural and hormonal control are the

two main areas through which most, if not all functional aspect of the body; fluid, cell energy utilization, cell secretor processes, tissue aggregation and function etc. are control and regulated, it means that STP and MCT are basic fundamental unit of control and regulation of all body processes genetic, metabolic, physiologic, biochemical and embryologic and so on, also signals occurs in all biochemical synthesis, in secretion, transport and uptake of materials, these processes to a large extend influence, augment or constitute pharmacodynamic or pharmacokinetic activities, they all form the physiological bases of their action, there is therefore point of concordance between drug to drug actions and drug-body cell-tissue interaction, essentially either of these mechanism utilize STP and MCT to moderate and produce positive or negative response of drugs in treatment, example autonomic sympathetic drugs like adrenaline act via G protein pathways, using cAMP, PLC, and other kinase actions along STPs, by these method myosin light chain kinase of myocardium are stimulated, the first hypothetical statement of the propose theory state that all cellular, tissue and systemic physioanotobiochemical processes and their products depend on outcome of STPs and MCT interacting cascades, put in another way, all body processes and their product are function of STPs and MCT responses, obviously the hypothesis 1 depict the cardinal principles of BUTT theory 1, logically therefore, if STP and MCT determines every outcome of all body processes (genetic, physiologic, anatomic, embryologic, biochemic and host of others) then effective control and regulation of their response(s) at relevant sites could eliminate undesirable effect of drugs, and accentuate much needed therapeutic effects, thirdly complex absurd complex intricate many interlinked cascade necessitate the use of concept of locus 1, locus 2, locus 3 per site, per area, per region as mentioned [27], profound research endeavor on this topic is still ongoing, for several hurdles remained to be cross example lack of complete characterization of all protein required for determination of the universal variable was a major bottle neck in investigation involving assessment of roles of STP by mathematical method (Boyo Blossom 2014), another challenge is computation informatics capable of multiple interpretation of data, the goodness of drug use is sine quanone for increase in life expectance, decrease in maternal motility, effective fight against emerging incurable urban and rural disease, cancer, diabetes, hypertension, stress, depression and rural out-break of viral disease, these laudable aims truly are noble goals of UN spearheaded MDGs, imagine a world without drug treatment drawback, beside drug, it can be extended to other areas most lethal compound could be consume without fear of adverse effects, example genetically modified food items could be consumed, as mentioned already, drugs with narrow therapeutic index and high toxicity levels could be safely administered, as an offshoot, the invaluable benefits are treatment of disease of all kinds, in vivo gene manipulation, biotechnological development and the benefit are endless.

## Conclusion and Future Outlook

### Conclusion

It can be concluded that the enormous goodness of drug use warrant the need for complete elimination of drug treatment drawback, adverse drug reaction, toxicity, side effects and

others, the proposed universal theory of therapy need intensive investigation, to test the 3 revolutionary hypothesis, capable of breaking barriers of limitless drug use in all kind of physioanopathobiochemical processes and abnormality, this is possible since STP and MCT found in all cellular, processes regulate and control body processes, their ultimate response actually are manifestation of physioanopathobiochemical machinery of the body.

## Future Outlook

Apparently it is clear that some classical concepts of drug pharmacology may have to be modified in future; especially in final phase of testing the BUTT theory in order to prove the validity of theory and make reality it stated aims and objective. In near future novel revolutionary BUTT principles would enable researchers gather universal parameters required for subsequent

experimentation for BUTT validation, given that the theory covers all aspect of biomedical field, it will alter the course pharmaceutical, biologic, biomedical, medical and health research and treatment endeavors, in that every research or clinical endeavor must employ STP and MCT fundamental concepts. In keeping with principles of BUTT theory, integrated and interrelated multidiscipline approach may be a fundamental skills researchers will need to proof BUTT theory beyond reasonable doubt, The development of experimental procedures of the theory would make available new protocol and new assay and biochemical analysis, leading ultimately to effective control and regulation of normal or abnormal physiologic, biochemical, anatomic, genetic, embryologic, metabolic state of the body, with control of STPs and MCTs responses as the primary targets.

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