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Review Article

Stomach Macrobiotic Digestion and Biotransformation on Dietary Regular Items to Human Wellbeing Suggestions under the Influence of Biochemoinformatics Approach

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Abstract

Diverse mammalian processes, including drug metabolism, are aided by gut microbiota. It's a potential new area for drug targeting, especially for natural compounds found in food like tannins, flavonoids, steroidal glycosides, anthocyanins, lignans, and alkaloids. Through Gut Microbiota Metabolisms (GMMs) and gut Microbiota Biotransformations (GMBTs), the chemical profile and corresponding bioactivities of herbal medicines may be altered and implication to ailments by specific microbiota because the majority of herbal medicines are taken orally. Numerous microbial degraded or fragmented metabolites with their biological significance in rodent based models were produced by briefly introducing the interactions between various categories of natural compounds and gut microbiota in this review. Thousands of molecules are produced, degraded, synthesized, and isolated from natural sources but exploited due to their lack of biological significance in the natural product chemistry division.

Keywords: Microbiota, Microbiota biotransformation, Biochemoinformatics, Gut microbiota

INTRODUCTION

A very dense population of bacteria collectively referred to as the "gut flora" or "microbiota," live in the human gut, where they have a significant impact on drug fate and human biology. Secondary metabolites associated with these interactions have garnered more attention as their underlying mechanisms have become clearer. Gut microbiota produce NPs in two distinct ways. First, dietary components like tryptophan metabolites, 6 short-chain fatty acids, oligosaccharides, and others are used by the gut microbiota to produce the metabolites. Second, the unique Biosynthetic Gene Clusters (BGCs) of the gut microbiota that produce unidentified end products. The discovery of BGC derived natural products derived from the gut microbiota of mammals has made significant progress over the past three decades. These NPs have the potential to perform novel bioactive functions, including those of the protease inhibitors dipeptide aldehydes, the cytotoxic compound tilivalline, the antibiotic microcin M/H47, the genotoxin colibactin, and others. Trillions of microorganisms colonize the human body, fundamental taining homeostasis and altogether impact human wellbeing and illness. The gut microbiota is the collective name for these organisms. It is made up of numerous distinct bacterial species that are dynamic, localized, close to one another, and the host, and they play a crucial role in the progression of numerous diseases (Glenwright AJ, 2017).

Because they are absorbable, these microbes are responsible for the extensive breakdown of the original dietary natural compounds into low-molecular-weight metabolites, which may actually be more to blame for the adverse health effects than the original compounds. There are approximately 500 to 1,000 species in the intestinal microbiota, but interestingly, only a few of the known bacterial phyla have relative (percent) abundance, as shown in. The digestion of complex carbohydrates, colonization resistance against invading pathogens, maturation of the adaptive mucosal immune system, and the production of secondary metabolites like

vitamins are all potential benefits of gut bacteria. Studies of germ-free animal models and our comprehension of the metabolic services provided by the gut microbiota provide evidence for host benefits. GMMs and GMBTs alter the chemical structures of some orally administered NPs to form more than one fragmented metabolites, which have better bioavailability and therapeutic effects than their parent compounds against diseases. Others, despite these NPs' absence of biological significance, persist. The parts of these NPs with respect to unique computational natural screening through BioCheminformatic instruments are less detailed. Natural flavonoids and synthetic indole chalcones were tested for in silico pharmacokinetic properties for validated as drug like nature. Moreover, the analysis of therapeutic target for SARS-CoV-2 and discovery of potential drugs reported by computational methods. In the presented report, efforts have been made to discover and highlight strategies for further exploring the biosynthetic capacity of the human microbiome with distinct NPs. These include indigocarpan, mucronulatol (Wang HY, 2011). In addition, likewise momentarily talks about the potential organic jobs of these metabolites. From the Bio-Chemoinformatics approach, which uses a well-defined ADME protocol and an in silico biological hypothesis to recommend a biopredictive role for all likely degraded NP metabolites caused by the action of the gut microbiota. Finally, we discussed the biology of NPs and the modulation of the gut microbiota in the context of specific biological conditions like cancer, NAFLD, GIP, metabolic, and neurobehavioral disorders. As a result, the NP metabolites predicted by the in silico biological hypothesis were harnessed in this report. This tool safeguards the utilization of degraded metabolites for the Natural Product Chemistry division in a subsequent program for drug discovery innovation (Palmer C, 2007) (Jia W, 2008).

Metabolism of Gut microbiota

The pharmacokinetic and pharmaco dynamic properties of NPs are influenced by metabolic crosstalk between the host and gut micro biota. Both the direct and indirect mechanism of the gut microbiota is well known for its promising effect on pharmacokinetic by participating in the direct metabolism of NPs or by its indirect interaction with the host enzymatic system mechanistically. The production of micro- or mammalian microbial co-metabolites, which either compete for the metabolism of xenobiotic compounds found in our diet, such as NPs, or serve as signaling molecules that influence the host gene expression, facilitates the indirect interaction. A promising yield of microbial metabolites and other derivatives of ellagic acid have been reported for the metabolic fate of ETs molecules with gut microbiota from in vivo cultures. Two species of bacteria, *Gordonibacter urolithinfaciens* and *G.pamelaeae* DSM 19378, can metabolize 1 into the urolithins M5, M6, and UC sequentially. Unknown are the species of microbes that metabolize UA and UB as well as those that are responsible for alternative methods of deoxygenation (Donia MS, 2015).

The main bioactive polyphenols in black tea are theaflavins (TF), theaflavin-3-gallate (TF3G), theaflavin-30-gallate (TF30G), and theaflavin-3, 30-digallate (TFDG). From healthy human volunteers' feces, researchers discovered that TFDG is metabolized into TF, TF3G, and TF30G, gallic acid, and pyrogallol. In addition, the human microbiota metabolizes both TF3G and TF30G into TF, gallic acid, and pyrogallol. *Bacillus subtilis* and *Lactobacillus plantarum* 299v can use to TFDG. Trigonelline essentially diminished degrees of TMAO and was assessed because of Flavin Mono Oxygenase (FMO3) chemical inhibition under ex vivo conditions. Thus, the stomach microbiota in choline digestion and subsequently the creation of metabolites was causing CVD. The Kirby-Bauer disk diffusion susceptibility test was used to measure the growth of the isolated C. freundii strain in the presence and absence of trigonelline. In addition, the isolated liver FMO3 enzyme's in vitro conversion of trimethylamine (TMA) to trimethylamine oxide (TMAO) was examined, and when triglyceride was absent, TMAO was formed (Krishnan S, 2018).

Gut microbial biotransformation

Although the medicinal fungus *G.lucidum* contains a number of triterpenoids, little research has been done on how these triterpenoids are transformed by bacteria. Stomach microbiota biotransformation of ganoderma triterpenoid GA-An and with soil-separated Streptomyces sp. Man-made intelligence 045, making it the main case in which a microorganism was found to biotransform triterpenoid to its 3-O- acetyl subsidiary. The acetylation metabolite 3-O-acetyl GA-A has never before been identified. Despite the fact that *G.lucidum's* numerous triterpenoids have been linked to a variety of biological conditions. Albeit the restorative parasite *G.lucidum* contains various triterpenoids, little examination has been finished on how these triterpenoids are changed by microscopic organisms. Biotransformation of the stomach microbiota using the ganoderma triterpenoid GA-An and soil-separated *Streptomyces sp.* The primary instance in which a microorganism was discovered to biotransform triterpenoid into its 3-O-acetyl subsidiary is man-made intelligence 045. The acetylation metabolite 3-O-acetyl GA-A has until recently never been distinguished. Despite the fact that a wide range of biological conditions have been linked to the numerous triterpenoids found in *G.lucidum (*Milshteyn A, 2018).

Flavanones and flavonols in jumps are principally addressed by subsidiaries of naringenin (flavanone) and quercetin (flavonol), and are exposed to microbial changes in the heterocyclic C ring. Quercetin is converted into 2-protocatechuoylphloroglucinol carboxylic acid through oxygenolytic ring-cleavage, which is catalyzed by flavonol 2, 3- di-oxygenase (quercetinase). Several fungal strains, including *Streptomyces urythermus*, *Aspergillus niger*, *Aspergillus flavus*, *Penicillium olsonii*, and *P. decumbents*, were found to have quercetinase activity *(*Milshteyn A, 2018).

Bacterial enzymes, such as L-rhamnosidase and D-glucosidase, de-glycosylate anthocyanins before cleaving the C-ring at various locations to produce aldehydes from the A-ring and small phenolic acids from the B-ring. According to the findings of this study, *L. plantaurum* and *L. casei's* bacterial biotransformation begins with the production of preliminary small mesotheliotes. Metabolites were identified as protocatechuic acid, catechol, and phenol's decarboxylation and dehydroxylation products. Berberine's main issue was its low oral bioavailability (5 percent) and low plasma concentration, whereas its metabolites were typically maintained at high plasma concentrations. Gut microbiota produced nitro-reductases (90 percent recombinant, expressed in Escherichia coli) was able to transform BBR into dihydroberberine (dhBBR), which had a five-fold higher intestinal absorption rate than BBR. However, prior to final absorption, an unstable form of dhBBR would be oxidized into BBR in the intestines. This sums up the job of the stomach microbiota biotransformation in managing the change retention inversion cycle of BBR in the digestive tract framework. Other metabolites, such as Berberrubine (BRB), Demethyleneberberine (DMB), and Jatrorrhizine (JAT), were found to be produced by rats' anaerobic cultured gut microbiota in another study. BRB, DMB, and JAT were very important for many of BBR's therapeutic activities because they were more lipophilic than BBR (Jia W, 2008).

The exploratory point of view of NP metabolites through computational speculation approach

One of the most important scientific, economic, and social tasks in biomedical research is finding new pharmaceuticals. At numerous stages of the drug discovery process, productivity has increased as a result of advancements in computational biology and bioinformatics. These days these in silico computational approaches assume an essential part in drug revelation improvement of normal items through routine exploratory examination in the lab and in the future to forestall the double-dealing of significant metabolites and atoms.

Hypothesis of Silico biosynthesis

Such techniques have been coordinated way to deal with regular use in the disclosure and streamlining of plant, organism inferred atoms furthermore, metabolites with fondness to an objective, the explanation of stomach muscle-sorption, dissemination, digestion, discharge, harmfulness properties (ADME-PK models), as well as physicochemical and natural portrayal like medication likeliness, natural action range, ligand-receptors based and metabolic forecasts (SOM). So that utility of medication disclosure will become functionalized (Sassone-Corsi M, 2016).

Pharmacokinetics

The current industrial drug discovery paradigm includes these tools for examining the properties of absorption, distribution, metabolism, excretion, and pharmacokinetics (ADME-PK) of New Chemical Entities (NCEs), also known as new metabolites (Sassone-Corsi M, 2016).

Molinspiration

Sub atomic descriptors and medication likeliness properties of metabolites and particles were dissected by the Molinspiration server, in view of Lipinski Rules of five. It states that the majority of molecules that are considered to be "drug-like" must have a log P value of 5, a molecular weight of 500, ten hydrogen bond acceptors, and five hydrogen bond donors. With respect to the respective drug targets (GPCR ligands), kinase inhibitors, ion channel modulators, enzymes, and nuclear receptors, it calculates the molecular properties (LogP, number of hydrogen bond donors, receptors, and polar surface area) and predicts the bioactivity score (Sassone-Corsi M, 2016).

IMPACT ON HUMAN PHYSIOLOGY

Intestinal absorption

A lot of information in regards to HIA has been created quickly by in vivo and in vitro test measures. To predict the HIA-based data, numerous computational classification and correlation models have been developed. The most compelling base examples what's more, metabolites are perceived by a data gain investigation.

Plasma protein binding

Models can also be categorized as ligand and receptor-based models. The qualities of little atoms can be straightforwardly utilized for restricting locales and liking expectation, shaping some ligand-based HSA restricting models (Schluter J, 2012).

Blood brain barrier

The majority of this goal-specific in silico models are predicated on the passive diffusion of compounds across the BBB. A non-linear ionization-specific model based on log P and pKa was used to estimate the negative logarithm of the fraction that is unbound in the brain (log fu, br) in order to account for the influence of brain tissue binding in the development of a straightforward QSAR model for the prediction of log BB. As a result, both internal and external validations showed that the model had good predictive power (Schluter J, 2012).

Metabolic prognosis

Natural compounds found in food, such as polyphenols, triterpenoids, and polysaccharides, interact with the microbiota in the gut, which has a significant impact on human health. The genome-scale metabolic networks and bioinformatic tool predicts novel bioactive metabolites through gut microbiota transformations to solve this complicated category of natural compounds. As a result, the AGORA-based REconstruction for Diet Analysis (AGREDA) approach to analyzing the role of the human gut microbiota in diet metabolism has recently become more acceptable.

Currently, very few scientific measures are reported for the qualitative and quantitative analysis of biomarkers in the context of category of natural compounds vs. gut micro biota, which is a key question for balancing in host health. This revealed degradation pathways for 209 compounds that are present in the human diet, mostly phenolic compounds (Schluter J, 2012).

Significance of gut micro biota vs. natural products in several diseases

Curcumin, a naturally occurring, non-toxic polyphenol, has recently been suggested as a treatment for neurological and neurodegenerative conditions. Blackberry anthocyanins may be able to prevent some of the characteristics of HFD-induced dysbiosis, as demonstrated by the experimental study. These include the PI3K/Akt (Phosphatidylinositol 3-kinase/Protein Kinase B) pathway, the MAPK (Mitogen-Activated Protein Kinase)/Akt pathways, the Akt/Nrf2 (Nuclear factor-E2-related factor 2). Moreover, anthocyanin-prompted changes in the stomach microbiota organization are connected with their enemy of neuro inflammatory properties. Small molecules like rhein, which is the main ingredient in rhubarb, were found to increase the abundance of Lactobacillus and Bifidobacterium in HFD-fed mice, which in turn improved memory and recognition in Alzheimer's disease patients (Haiser HJ, 2013).

CONCLUSION

Ethno pharmacological importance's perspective, customized dietary NPs have been less recorded and utilized for a few clinical issues like asthma, immune modulatory, joint inflammation, Hack, jungle fever, COPD, CVD, diabetes, and malignant growth. Concerns regarding regulation and restoring NPs' aesthetic value appear to be of interest right now, with particular attention paid to the diversity of human gut microbiota populations. Since a particular populace of stomach microbiota and related responses has the type to change ingested NPs to most bioactive metabolites for example inclined to science for explicit diseases, which controls the dysbiosis to eubiosis status of stomach microbiota specialty. Through phase I and II reactions in the gut microbiota, these metabolites are currently the most promising for phytopharmacology considerations with specific animal models. Akkermansia, Bifidobacterium, Lactobacillus, and Faecalibacterium all beneficial to health may be the most important targets for treatment in cases of dysbiosis-related illness. This approach channelizes have physiology with ingested bioactive and effective NPs through controlling stomach microbiota creation and assumes a crucial part in remedial importance in the impending period.

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