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Review

Drosophila melanogaster "a potential model organism" for identification of pharmacological properties of plants/plant-derived components

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ABSTRACT

Plants/plant-derived components have been used from ancient times to treat/cure several human diseases. Plants and their parts possess several chemical components that play the vital role in the improvement of human health and their life expectancy. Allopathic medicines have been playing a key role in the treatment of several diseases. Though allopathic medicines provide fast relief, long time consumption cause serious health concerns such as hyperallergic reactions, liver damage, etc. So, the study of medicinal plants which rarely cause any side effect is very important to mankind. Plants contain many health benefit properties like antioxidant, anti-aging, neuroprotective, anti-genotoxic, anti-mutagenic and bioinsecticidal activity. Thus, identification of pharmacological properties of plants/plant-derived components are of utmost importance to be explored. Several model organisms have been used to identify the pharmacological properties of the different plants or active components therein and *Drosophila* is one of them. *Drosophila melanogaster* "fruit fly" is a well understood, high-throughput model organism being used more than 110 years to study the different biological aspects related to the development and diseases. Most of the developmental and cell signaling pathways and ~75% human disease-related genes are conserved between human and *Drosophila*. Using *Drosophila*, one can easily analyze the pharmacological properties of plants/plant-derived components by performing several assays available with flies such as survivorship, locomotor, antioxidant, cell death, etc. The current review focuses on the potential of *Drosophila melanogaster* for the identification of medicinal/pharmacological properties associated with plants/plant-derived components.

Contents

Abbreviations: CNS, central nervous system; AD, Alzheimer's disease; NFT, neurofibrillary tangles; PD, Parkinson's disease; HD, Huntington's disease; RING, rapid iterative negative geotaxis assay; SOD, superoxide dismutase; CAT, catalase; GPx, glutathione peroxidase; GST, glutathione S transferase; MDA, malonaldehyde; AO, acridine orange; HSP70, heat shock protein 70; JNK, c-Jun N-terminal kinase; BOD, biological oxygen demand; AIDS, acquired immunodeficiency syndrome.

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1. Introduction

Since time immemorial, plants and their different parts have been used by human beings to improve their health and treat several diseases. Plants possess vital ingredients which are used for the synthesis of therapeutic medicines to cure several diseases [1]. Use of traditional medicinal plant is primarily a spiritual and traditional way of curing a disease [2,3]. Plants/plant-derived components are the rich source of several metabolites such as alkaloids, glycosides, coumarins, flavonoids, steroids, anthocyanins, fatty acids, tannins, emodins and leucoanthocyanins, etc. which are responsible for medicinal properties of the plants [4,5]. Several metabolites in particular "secondary metabolites" of medicinal plants have their unique role in the treatment of various diseases like chronic and progressive neurodegenerative diseases, diabetes and cancer [6–8]. Plant-derived medicines promote good human health without any significant side effects and ~80% population in developing countries still depends on plants/plant-derived medicines [9,10].

Previous studies described many advantages of using ayurvedic medicines compared to the use of allopathic medicines. Several reports suggested that allopathic medicines have some side effects and many of them result in strong allergic reactions in an individual [11,12]. Some of the allopathic medicines are known to cause liver and kidney dysfunctions and ulceration in the stomach by producing excess acid [13]. There are many plants that are helpful in the treatment of high fever and in dengue treatment. *Tinospora cordifolia* (Giloy) is an example of one of the medicinal plants which helps in lowering of body temperature and also used for dengue treatment [14]. In the case of dengue without showing any adverse effect on the human body it maintains platelets counts and reduces the body temperature [14,15]. This shows the great potential of ayurvedic medicines to treat several human health problems. Plants are also a rich source of antioxidants and commonly used across the world to treat several diseases related to the production of excessive free radicals [16,17]. Plants and plant-derived components are used from very old times but still there are many plants whose medicinal values are still to be identified or they are under investigation. Thus, to identify the medicinal values of several plants/plant-derived components researchers are using different model organisms to get the details of pharmacological properties of plants/plant-derived components.

2. Model organisms used for medicinal plant research

There are different model organisms that are being used for the identification of medicinal properties associated with different plants i.e. *Mus musculus* [18], *Rat* (*Rattus norvegicus*) [19,20]. *Caenorhabditis elegans* [21], *Drosophila melanogaster* [22], *Nothobranchius furzeri* [23]. Each model organisms has its own advantages and limitations. A comparison of the different model organisms and potential use of *Drosophila* are presented in Table 1.

3. *Drosophila* as a model organism for medicinal plant research

D. melanogaster, commonly known as "fruit fly", has a long history of its use in genetic research (more than 110 years) [24]. This model organism came into the limelight from a pioneer work of Thomas Hunt Morgan, father of *Drosophila* genetics "discovery of X-linked phenomenon in *Drosophila*". Further, in 1933 T.H. Morgan won the Nobel Prize in Physiology or Medicine for his important discoveries that "*chromosome plays a key role in heredity*" [25,26]. Muller in 1920s has shown that mutation rate of genes increases by x-ray radiation to *Drosophila* [25,27]. Christiane Nusslein-Volhard, Eric Wieschaus and Edward B. Lewis won the Nobel prize in Physiology or Medicine in 1995 for their discoveries related to "*pattern formation in Drosophila*" [28].

Use of *Drosophila* in biological research began in the early 20th century [29] and at present, it is one of the most popular, extensively studied and cost effective model organism for biological research [30]. It significantly contributed in several key research like genetics, embryonic development, behavior and disease-related signaling studies [31,32].

The following features of the "fruit flies" make it a promising model for medicinal plant research.

(I) It is a tiny insect (3 mm in size), easy to handle, require small laboratory space thus allowing to culture a large number of flies in laboratories and in the stock centers [33].
(II) It has a short life cycle (~10–12 days at 25 °C) and lifespan of ~90–120 days [33,34]. These features allow the rapid study of the age-depended diseases like neurodegenerative diseases and to detect the effect of the specific plant extract/active component to the several generations of flies in the normal and disease conditions.
(III) It has high fecundity (a single female can lay ~30–50 eggs/day) [35,36] so large scale genetic/drug screening is possible.
(IV) Fly has only 4 pairs of chromosomes and it can be easily genetically manipulated [37].
(V) The fly genome is ~180 Mb in size and is fully sequenced. It encodes ~13,600 protein coding genes as compared to human ~30,000 genes [38–40].
(VI) The genome sequencing of flies revealed that *Drosophila* is an invertebrate model and it possesses ~75% similarity with disease-related genes in human [41,42]. Thus, it has great potential to be used as a human disease model.
(VII) Flies (diseased model) can be easily fed on diet mixed with plants/plant-derived components and the effect of targeted compounds can be examied by observing the phenotypic changes (eye, any anomalies, etc.), developmental changes