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Hypothesis on Novel Bioflavonoid Formulations towards Treating Diabetes Mellitus

Nandhakumar L[1]*, Mohan S[2]
1.Department of Pharmacy, Shri Jagadish Prasad Jhabharmal Tibrewala University, Rajasthan. 333001 India.
2.Faculty of Pharmacy, Karpagam College of Pharmacy, Coimbatore, Tamilnadu 641032 India.

ABSTRACT

Bioflavonoids are the principle component of most of the plant species and are found be abundant. All most all of these flavonoidal components have the potential to control the blood glucose level. There has been limited research works performed on to these flavonoids, because of its low solubility and bioavailability, its utilization is rarely pronounced. However, exploring the areas of utilization of these flavonoids, by enhancing their solubility and bioavailability by suitable method like nanonizing the flavonoids using biodegradable polymers as formulation have the great advantage in treating diabetes. By the way the fullest potential of flavonoids would be explored in treating diabetes safely. We suggest that implementing the nanotechnology to convert the natural bioflavonoids having antidiabetic potential like naringin, hesperidin, rutin, silibinin etc., into nanoparticles using biodegradable polymers would increase the activity of bioflavonoids. It may give the chance of utilizing such nanoformulation clinically to treat and alleviate the problems associated diabetes effectively.

Keywords: Bioflavonoids, biofavonoid formulation, nanonizing, biodegradable polymers, solubility

*Corresponding Author Email: nandhavma@gmail.com
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INTRODUCTION

Diabetes mellitus may be a metabolic disorder consequently affects the carbohydrate, lipid and protein metabolism. It is certainly responsible for the impaired insulin secretion and insulin resistance at the pancreatic cell receptors. As result diabetes would lead to cause various complications at cellular level encompass micro and macro vascular damages (Sabitha et al., 2011 and Modak M et al., 2007)[1,2]. Flavonoids long since it is been known for its medicinal or therapeutic value, and it is a robust solution for most of the diseases and especially in diabetes. Recently there is an increase in demand for the clinical studies on flavonoids and its supporting data to launch these flavonoids as marketed products in diabetic segment. Both in vitro and vivo studies confirm the specific significant activity of flavonoids (Verma et al., 2012 and Raj narayana et al., 2001)[3,4]. So diabetic curing with flavonoids possessing antidiabetic activity may be a better idea for solid control of progression of disease condition, more than ever in hyper-glycemia (Tapas AR et al., 2008 and Thaipong K et al., 2006)[5,6]. Making use of such bioflavonoids are possible by implementing it into the nanotechnology for preparing nanoformulations using biodegradable polymers. For that reason only the scheme of biofavonoid nanoformulation has been given in Figure 1 which paves the way for others researchers to explore.

Highlights

- Bioflavonoids are present in most of the vegetables, fruits and other plant parts.
- Usually, bioflavonoids encompass potential antidiabetic activity along with other beneficial pharmacological activities.
- The factors that limit the use of bioflavonoids are reduced solubility and bioavailability. If solubility problem is tackled effectively by adapting suitable technique, and then it can be used as an antidiabetic agent.
- Exploring the full potential of these flavonoids is possible by novel formulating strategies like nanotechnology.
- Nanonizing bioflavonoids with biodegradable nanocarriers are one such method which discovers the fullest potential for the antidiabetic activity.

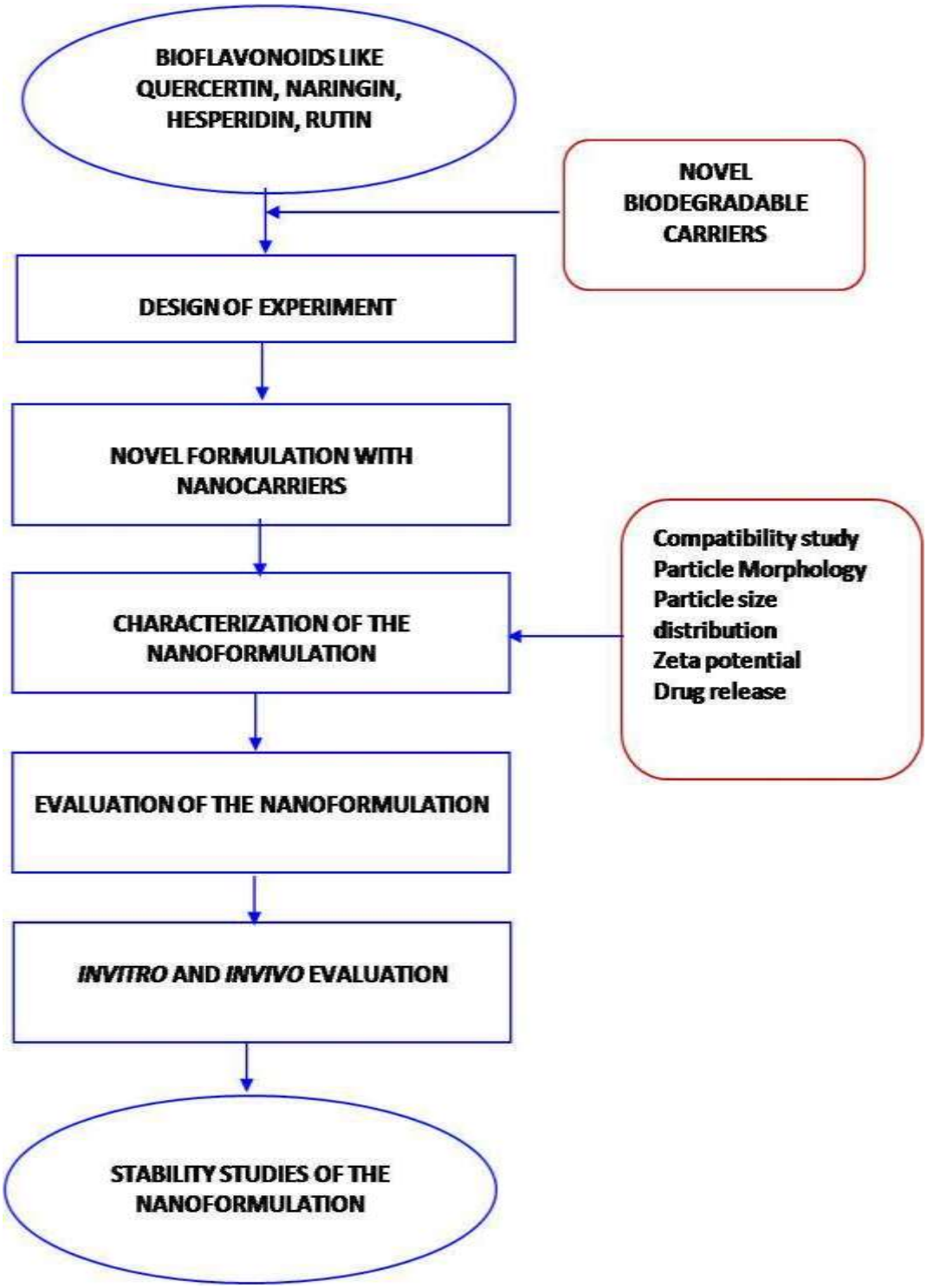

Figure 1: Scheme of novel nanoformulation for bioflavonoids

Role of Bioflavonoids and its scope for nanoformulation

Flavonoids do have hypoglycemic effect, several studies shows that in suitable animal models. Apart from this they also have got free radical scavenging, pain relieving, effective against pathogenic microbes, wound healing activities and so on. This promulgates the exploitation of

flavonoids as tools for curing various diseases and ailments. Such flavonoids presence in enriched diet of routine intake, particularly in house hold items have some awesome plus. This proposes to develop and peep into the research concerning to take advantage of flavonoids in disease management segment.

Consequently flavonoids has many benefits for the management of diabetes and its impediments ant it was expected to exert the action namely pancreatic regeneration of cells present in the pancreas, escalated insulin release from the pancreatic β cells, increased ionic uptake of calcium ions, a remarkable reduction in the aldose redutase (Calderon montano JM et al., 2011)[7]. Flavonoids functions dually in reducing the complications and adverse consequences of reactive oxygen species alongside with the diabetic control. Limitation in usage of polyphenolic moiety is to improvise the solubility, as it determines the bioavailability, which in turn leads to the efficacy of the preparation (Habtemariam S et al., 2011)[8]

Many numbers of novel methods are in hand to improvise the solubility profile of the flavonoid. So that it can be effectively used for the desired action to be delivered. Recent focus on diabetic research platform is vividly relies on nanotechnology for the aforementioned issues.

Nanonizing of the flavonoids using biodegradable polymeric matrix systems play a pivotal role in successful compilation and deliverance of the polyphenolic moieties to the selected site of action with increased bioavailability, bypass of entero-hepatic circulation like efficacy largely (Koyama E et al., 2003 and Amidon GL et al., 1995)[9,10].

Design of Experiment

Designing of the experiment is very essential to identify the significant factors which influence the manufacturing process. By the way we can eliminate the difficulties associated with manufacturing variables which adversely affect the formulation quality and reproducibility. So experimental forecast by utilizing the designing tools always a reliable thing in the long run of research, which possibly eliminates the time, spent on the experiment as well. Critical parameters which control the experimental outcomes are assessed by several experimental designing tools like Plackett-Burman, Taguchi OA, Box-Behnken etc., Hence we suggest that for the designing of nanoformulation containing biofavonoids may be exploited by any of the aforementioned methods (Viveksarathi K et al., 2015)[11].

Nanoformulation of Bioflavonoids with novel carriers

Nearly most flavonoids and its compound groups have observed to be less soluble; one of the main reasons is enhancing the solubility and its resultant bioavailability. So for that reason only, there are diverse ranges of methods by which nanoparticles are generated. Majorly factors

governing for selecting the methods for a particular material are type of drug delivery, drug solubility profile, decomposition trait of candidate and so on (Liu M et al., 2007 and Choi SW et al., 2007)[12,13]. Different methods are available for the nanoformulations as shown in the Figure 2.

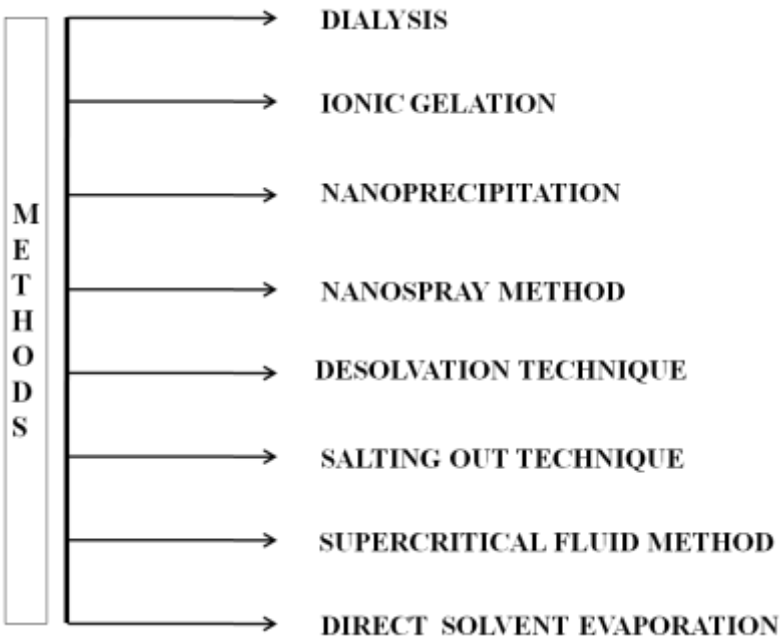

Figure 2: Few important methods to prepare nanoformulations

Characterization of the nanoformulations

The characterization of nanoformulations must be performed in various fronts like measurement of the nanoparticles size and size distribution, zetapotential of the prepared nanoformulation containing bioflavonoids. The assessment of nanoparticles in the formulation is very essential, to assure the good stability of the nanoformulation (Ines N et al., 2012)[14]. To perform those tests wide range of analytical instruments and methods are available like Zetasizer, Fourier Transmission Infrared Spectroscopy, Transmission Electron Microscopy etc., we suggest that characterization of prepared nanoformulations may be performed by the aforementioned analytical instruments and methods.

Evaluation of the nanoformulations

***In-vitro* evaluation**

An assortment of parameters like drug content, entrapment efficiency and release profile of drug contents at various intervals is preformed, by exploiting various analytical instruments including Dissolution apparatus, UV Visible spectrophotometry and HPLC, especially release pattern of drug may be measured (Manoj N et al., 2008)[15].

***In-vivo* evaluation**

Biochemical constituents' activities were assessed using animal model, the number of animals are divided into groups and each group may be given the formulation to be tested and response of activity compared with the reference or standard drug (Nagasamy venkatesh et al., 2015)[16]. Blood samples of the formulation treated animals were collected and tested for the level of glucose present in it.

Stability studies of the formulation

Quite a lot of standards testing protocols are well in place to evaluate the stability of the prepared formulation when on storage at different temperature and relative humidity. The procedure for the stability testing of the nanoformulation has been well given in the ICH (International Conference on Harmonization) guidelines (Rajat S et al., 2011)[17] . To be précised for long-term stability studies $5^0C\pm3^0C$ and $30^0C\pm2^0C$, 65%±5% RH are preferred at the interval of 1^{st}, 3^{rd}, 6^{th}, 9^{th} and 12^{th} month. The accelerated stability study for the formulation $40^0C\pm2^0C$, 70%±5% RH is preferably utilized for the 3^{rd} and 6^{th} month as per the ICH guidelines.

CONCLUSION

With availability of wide range of biochemical constituents from plants holding antidiabetic activity, formulating a component comprising the bioflavonoid as a nano entity would result certainly, into a viable novel nanoformulation at ease. However, by designing such formulations would also escalate the solubility and bioavailability of the encompassed bioflavonoid component. Researchers beget numerous formulations by adopting the newer way that has been discussed in this context. Paramount interest are been shown recent years by various researchers on exploring the real potential of flavonoids, for treating diabetes with newer approaches as novel formulation like nanoparticles. For this reason, we suggest novel bioflavonoid nanoparticles for the effective management of diabetes mellitus and its complications.

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