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REVIEW ARTICLE

Food based phytochemical luteolin their derivatives, sources and medicinal benefits

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ABSTRACT: Luteolin is a type of flavonoid and a 3′, 4′, 5, 7-tetra hydroxyl flavone with a yellow crystalline appearance. Luteolin is widely present in different plant families such as, Lamiacea, Arecaceae, Brassicaceae, Campanulaceae, Asteraceae, Resedaceae and Scrophulariaceae. Luteolin mostly found in edible plants and most important food based phytochemical. Dietary sources of luteolin such as, celery, peppers, carrots, peppermint, olive oil, thyme, oregano and rosemary, etc. On the base of luteolin content among other sources oregano is the better source with 1028.75mg/100g contents. Flavonoids are important component of plants, and widely used in traditional medicine to cure the different type of diseases. Luteolin has different health benefits such as, anti-inflammatory, sun protectant, anti-oxidant, improve heart function, neurological impairments, anti-cancer and many more. Luteolin has many possible mechanisms involved in different biological activities such as, stabilization of p53, modulation of ROS levels, and reduction of NF-kappaB, reduction of AP-1 activity and inhibition of PI3K.
Keywords: Luteolin, Flavonoid, Derivatives, Source, Health benefits.

INTRODUCTION

Luteolin is belonging to the class of flavonoids and yellow crystalline compound of Flavones. Luteolin widely found in plant kingdom, especially in edible plants. It is a 3′, 4′, 5, 7-tetra hydroxyl flavone. Flavonoids play significant role against insects, microorganisms and UV irradiation to defending the plant cells because they are polyphenols in nature (Harborne and Williams, 2000). Flavonoids for animal and human health are beneficial, it is clear and suggested from the previous studies of animal, cell culture, and human population. Flavonoids are common nutrients play an important role as an estrogenic regulators, antioxidants, and antimicrobial agents, because these are present in better amount in foods, such as in fruits, vegetables and medicinal herbs (Birt *et al.,* 2001). Flavonoids are also act as a cancer preventive, it has been noticed from previous study (Knekt *et al.,* 1997; Neuhouser, 2004). During the progression of carcinogenesis flavonoids may block many points, including cell transformation, metastasis, angiogenesis and invasion due to the inhibition of kinases. Flavonoids regulating cell cycle, reducing the transcription factors and also induced apoptotic cell death (Birt *et al.,* 2001).

1.1. Chemical structure of luteolin

Luteolin is flavonoids belonging to the flavone, its structure consist of C_6-C_3-C_6 and also possess two benzene rings. In structure of luteolin third is oxygen containing carbon ring and double bond is present at 2-3 carbon. Luteolin structure also consist of hydroxyl groups at different carbons positions as shown in Figure 1 (Ross and Kasum, 2002). Biological and biochemical activities of luteolin are associated with hydroxyl moieties and the position of 2-3 double bonds present in structure (Chan *et al.,* 2003; Hempel *et al.,* 1999). Some part of luteolin, when passing through intestinal mucosa converted into glucuronides (Shimoi *et al.,* 1998). Luteolin shows better heat stability during cooking, that's why losses of luteolin relatively low (Le-Marchand, 2002).

1.2. Derivate of luteolin

Luteolin is a flavonoid mostly found in plant kingdom. Luteolin mostly found in herbs such as, *Lonicera japonica, Nepeta cateria L, Chrysanthemum morifolium* and *Ajuga decumbens Thunb.* Some previous findings are evident of medicinal benefits, which possesses by luteolin such as anticancer, natural sun protectant, improve heart function, anti- inflammation and antioxidant. According to some previous evident luteolin and some of their important derivatives such as, Luteolin 4'-neohesperidoside, 7-glucuronide-3'-glucoside, 7-sambubioside, 7-galacturonide-4'-glucoside, 7-O-rutinosides, 7, 3'-diglucuronide, 7-gentiobioside, 7-O-glucoside, and many more present in Table 1 with their plant source and their possible structures (Lin *et al.,* 2008).

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3. Source of Luteolin

Luteolin is a significant phytochemical and most commonly found in bunch of vegetables. Fruits and vegetables such as parsley, thyme, celery, olive oil, onion leaves, broccoli, peppermint, peppers, rosemary, oregano, cabbages, carrots, artichoke, chrysanthemum flowers and apple skins are rich source of luteolin (Miean and Mohamed, 2001; Mencherini *et al.,* 2007). According to Table 2 the richest source of luteolin in case of vegetables radicchio and raw Chinese celery in which luteolin is 37.96mg and 34.87mg respectively. In case of herbs most prominent source of luteolin is oregano (1028.75mg) and then juniper berries with 69.05mg. In known plant source, luteolin present in better quantity in fresh sage (16.70mg). In case of fruits, raw lemon without peel contain (1.50mg) better amount of luteolin content. Overall, in case of vegetables, fruits, herbs and plants oregano is best source of luteolin content.

4. Health benefits of luteolin

4.1. Luteolin Fights Cancer

Luteolin is constituent of our daily nutrition but their amount is relatively less than 1mg/day. Inverse correlation is suggested by some epidemiological studies between the risk of some cancer types and luteolin intake (Seelinger *et al.,* 2008). The cancer cells growth block or delayed in vivo and in vitro due to the intake of luteolin in daily nutrition, by tumor cell proliferation inhibition, protection of carcinogenic stimuli, apoptosis induction through the intrinsic signaling and extrinsic signaling pathways and due to the induction cell cycle arrest. When compare the luteolin with other flavonoids, luteolin is most effective one among all of these for the inhibition of tumor cell proliferation. Proliferation of different type of tumor cell effectively subdued with luteolin in vitro about 3 to 50 μM with $IC_{50.}$ Tumor growth effectively inhibited in vivo with the concentration of luteolin 50 molecule to 200ppm in food (Selvendiran *et al.,* 2006) and in application of intragastric 5 to 10 mg/kg (Fang *et al.,* 2007) or 0.1 -0.3 mg/kg/d (Manju *et al.,* 2007). In human skin, luteolin having ability to penetrate and effectively capable for the treatment and prevention of skin cancer (Seelinger *et al.,* 2008). Various types of cancer cells development restricted by luteolin. It inhibits the carcinogens metabolism, inhibit new blood vessels growth inside tumors, stopping the progression of cancer cell cycle and also induced the cell death in cancer cells (Pitot, 1993). Some studies in case of mice are evident, growth of tumor formed due to human skin hepatoma, carcinoma and human ovarian cancer cell effectively restricted by the use of luteolin. Luteolin significantly inhibits the occurrence rate and also reduce the tumors size. Use of luteolin is safe as an anti-cancer agent because their long term treatment at a dose of 30mg/kg in rats did not show any visible toxicity (Hanahan, 2000). Against cancer preventive and therapeutic activities associated with estrogen was found in luteolin through vivo and vitro experiments (Galati *et al.,* 2000).

Luteolin has a chemo-preventive effect on skin cancer induced by ultra violet (UV). Ultraviolet B induced protein-1 activator, cyclooxygenase-2 expression and activity of nuclear factor kappa B (NF-κB) in JB6 P+ cells suppressed by luteolin. Kinase and immunoblot assay data from some studies indicate that luteolin reduce the effect of Src kinase activities, and epsilon (protein kinase Cε (PK Cε)). Afterward, luteolin inhibit the Akt signaling pathway and phosphorylation of MAPK (mitogen-activated protein kinases) induced by ultraviolet B (Byun *et al.,* 2010). Pull-down assays described that in an ATP-competitive manner luteolin directly binds to the protein kinase Cε (PK Cε) and Src. In SKH-1 hairless mice, luteolin suppressed the occurrence of tumor, multiplicity of tumor and their overall size. Some previous evident shows that the skin analysis through immunoblotting and immunohistochemistry indicate that the luteolin cause reduction tumor necrosis factor α (TNFα), cyclooxygenase-2 and proliferating cell nuclear antigen. Luteolin inhibit Src kinase and protein kinase Cε (epsilon) activity. Luteolin cause vigorous chemopreventive activity against skin cancer induced by ultraviolet B by targeting the Src and protein kinase Cε (epsilon) (Byun *et al.,* 2010).

4.2. Luteolin reduce Inflammation

Inflammation that protect over body against heal injury and infection because it is a body defensive mechanism. Results of chronic inflammation some harmful diseases such as arthritis, cancer and arthritis obstructive pulmonary disease (Brody and Spira, 2006; Perwez and Harris, 2007; Karin *et al.,* 2006). Activation of microphages during inflammation by different molecules, such as cytokines and toxins from the host and pathogens respectively. Gram-negative bacteria outer membrane components are Lipopolysaccharide (LPS). Lipopolysaccharide is a common trigger for inflammation and endotoxin. Microphages after their activation produce inflammatory molecule vigorously, such as interleukins (ILs), free radicals and tumor necrosis factor α (TNFα). These are leading toward the recruitment of inflammatory cells, in which lymphocytes and neutrophils for the clearance of pathogens and infection site (Brody and Spira, 2006; Karin *et al.,* 2006). During chronic inflammation continuous production of these molecule may cause cancer like diseases. Luteolin retard the development of these type of cytokines. It is also retard their transduction signal pathways by exerting its anti-inflammatory effects (Xagorari *et al.,* 2001; Chen *et al.,* 2004; Kumazawa *et al.,* 2006). In vivo luteolin suppress the bacteria induced or lipopolysaccharide inflammation in vivo, evident from animals study (Kotanidou *et al.,* 2002; Tormakangas *et al.,* 2005). Luteolin effectively alleviated the high molarity induced by lipopolysaccharide. These lipopolysaccharides release in intercellular adhesion molecule-1 (ICAM-1) and serum expression in the liver and associated with the reduction of lipopolysaccharides stimulated

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tumor necrosis factor α (TNFα) (Kotanidou *et al.,* 2002). Inflammation caused by *Chlamydia pneumoniae* in lungs tissue has been suppressed with the use to luteolin (Tormakangas *et al.,* 2005). Many direct evidence in vitro studies for the anti-inflammatory effect of luteolin's. Release of interleukins-6 (IL-6) and inhibited lipopolysaccharides stimulated tumor necrosis factor α (TNFα) with luteolin and pretreating murine microphage. These are associated with the blockage of MAPK (mitogen-activated protein kinase) family member (JNK, ERK and p38) and activation of NF-κB (nuclear factor kappa B) produced by lipopolysaccharide (Chen *et al.,* 2007; Xagorari *et al.,* 2002).

Two important pathways that include in the activation of MAPK and NF-κB, in responses of stromal cells and epithelial tissue to inflammation mediators (ILs and TNFα) (Karin, 2004). These pathways suppressed due to the use of luteolin underlines the basic mechanism of its inhibitory action on chronic and acute inflammation. On the level of receptor, suppression of inflammatory is partly due to the lipid rafts accumulation. Cytokine induced signaling was blocked with the help of luteolin because it is a crucial point for receptor signaling (Kumazawa *et al.,* 2006). Primary inflammatory stimulators lipopolysaccharides (LPS) and secondary tumor necrosis factor α (TNFα) and interleukins-1 (IL-1) activated the NF-κB. The NF-κB and RelA (p65)/p50 are constituent of heterodimer. These are retained as an inactivated form in cytoplasm due to the association of IκB proteins.

Lipopolysaccharides helpful for the activation of IKK (IκB kinase) due to the binding of TLR-4 (Toll-like receptor 4). Activation of IKK (IκB kinase) turns phosphorylates IκB to start the quick degradation and also permit NF-κB to move into the nucleus. In nucleus activated the targets, such as cytokines and anti-apoptotic properties (IL-1 and TNFα) (Hayden and Ghosh, 2004). Cytokine established the feedback loop for NF-κB by binding the cognate receptors. Inflammatory cytokines convert at IKK (IκB kinase) activation due to the activation of nuclear factor kappa B (NF-κB) pathways by Lipopolysaccharides (Hayden and Ghosh, 2004).
NF-κB pathways are effectively blocked by luteolin. Luteolin can also interferes with the function of primary and secondary inflammatory stimulators through IκB degradation and IKK activation (Chen *et al.,* 2004). Luteolin blocks the upstream steps or directly inhibits IKK activity. Receptor signaling complex formation occur in the IKK activation pathway. On the base of observations, strong antioxidant activities of some flavonoids are ineffective in restricted lipopolysaccharides stimulated tumor necrosis factor α (TNFα) production (Devasagayam *et al.,* 1995). That's why, the luteolin have ability to directly scavenge reactive oxygen species (ROS). Lipopolysaccharides activated nitric oxide production also suppressed by luteolin in activated macrophages (Hu and Kitts, 2004). Luteolin can also useful inhibit inflammation in the colon. Luteolin role as an anti-inflammation also take part as a cancer prevention (Kamata *et al.,* 2005; Karin and Greten, 2005). In anti-inflammatory treatment, luteolin had great success as compare to prednisolone.

4.3. Luteolin as an antioxidant

Most of flavonoids are considered as an antioxidants including luteolin. Reactive oxygen species (ROS) belong to a multiple group of reactive, oxygen containing species such as, hydrogen peroxide (H_2O_2), singlet oxygen ($^1O_2$), hydroxyl radical ($^{\bullet}OH$), superoxide ($O_2^{\bullet-}$) and lipid peroxyl radical ($LOO^{\bullet}$) and short lived. For cellular signaling ROS serve as second messengers (Nimnual *et al.,* 2003). Excessive ROS (reactive oxygen species) production may cause the damage of DNA, protein, lipids and oxidative stress. These are involved is cancer as well as neurodegenerative and cardiovascular diseases. Reactive oxygen species induced Damage of DNA, lipids and protein induced by reactive oxygen species inhibit by luteolin (Robak *et al.,* 1988).

First functions of luteolin as a scavenger of reactive oxygen species through its own oxidation (Lien *et al.,* 1999). Luteolin structure contain 3′, 4′ hydroxylation, double bond at 2nd and 3rd carbons and carbonyl group at carbon number 4. This structure is essential to flavonoids for antioxidant activity (Lien *et al.,* 1999). The hydrogen atom donate to free radicals from an aromatic hydroxyl group. Luteolin as an aromatic compound, around the M-electron system supported unpaired electron. Some studies shows that, luteolin as a scavenger of reactive oxygen species was found in cell free system.

Secondly, luteolin also inhibits or retard the growth of ROS generating oxidase, such as inhibits the superoxide formation y suppressing the activity xanthine oxidase (Nagao *et al.,* 1999). However, in mitochondria luteolin whether effects on ROS generation is unclear in mammalian cells. In leishmanial (parasite) cells it interferes with the electron transport chain of mitochondria (Sen *et al.,* 2006).

Third function of luteolin as an antioxidant, luteolin influence by enhancing or protecting endogenous antioxidants such as superoxide dismutase (SOD), glutathione-S-transferase (GST), catalase (CAT) and glutathione reductase (GR) (Leung *et al.,* 2006; Manju and Nalini, 2005).

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Fourth function of luteolin as an enzymes inhibition, directly inhibit the enzymes activity that catalyze the oxidation of cellular component. Such as luteolin restrict the growth or formation of cyclooxygenase, lipoxygenase and acid-stimulated malonaldehyde in liver lipids (Robak *et al.,* 1988).

Luteolin, last function to cause chelation of transition metal ions. Because due to these ions generation of ROS occur and also control the oxidation of non-transition metal-dependent or inhibit the reaction of lipooxygenase (Ross and Kasum, 2002). In vivo, it should be observed that the luteolin concordant antioxidant mechanism may occur. For example, luteolin inhibit the production of hydroxyl radicals (•OH) in microphages induced by lipopolysaccharides, through scavenging superoxide ($O_2^{\bullet -}$). Also inhibiting the activity of xanthine oxidase (Harris *et al.,* 2006).

4.4. Luteolin is a natural sun protectant

In HaCaT cells, luteolin reduce the ultraviolet B induced (UVB) expression of matrix metalloproteinase (MMP-1) and may cause the direct inhibition or reduce the activity of p90RSK2 (Ribosomal S6 Kinase) and JNK1 (Jun N-terminal kinase). Due to the ultraviolet B (UVB) chronic irradiation in SKH-1 hairless mice, luteolin impaired the wrinkle formation. Intrinsic ageing and extrinsic ageing or photo-ageing are the two basic processes of skin ageing (Chung, 2003). Characterization of intrinsic ageing done by dry, smooth, pale and wrinkle skin. Characterization of photo-ageing by pigmentary changes, deep wrinkles and generally appearing when the face, forearm and neck are sun-exposed (Chung, 2003). Photo-ageing caused by UV radiation but UVB cause the major contribution. *In vivo,* in human dermal epidermis and cultured epidermal keratinocytes, matrix metalloproteinase-1 (MMP-1) expression induced by UV and UVB (Tanaka *et al.,* 2005). Interstitial collagenase matrix metalloproteinase-1 play an essential role for fibrillar collagens by cleaving. The role or function mainly performed to keep skin resilience and elasticity. After cleavage reactions by collagenases including MMP-1, triple-helical fragments (1/4 C-terminal and 3/4 N-terminal) are produced and spontaneously denature at room temperature in gelatin and further degraded into small peptide due to other matrix metalloproteinases (Ala-aho and Kahari, 2005). That's why, the inhibition or prevention of matrix metalloproteinase-1 (MMP-1) overexpression encourage by ultraviolet B could indicate the novel approach to suppress or reduce the photo-ageing (Brennan *et al.,* 2003). Some previous studies described that the naturally occurring compounds, such as luteolin exerts anti-photo ageing effect (Kim *et al.,* 2009; Fisher *et al.,* 1999).

AP-1 (Activator protein-1) produced by ultraviolet B, their activation was inhibited by luteolin. Activation of c-Jun (Jun protein), c-Fos (Fos Protein) and phosphorylation these are major components of AP-1 complex (Angel and Karin, 1991). Activation of c-Fos promoter and phosphorylation of c-Jun induced by UVB (ultraviolet-B). Effect of these are inhibited by the use of luteolin. Upstream kinases, such as JNK (Jun N-terminal kinase), Ribosomal S6 Kinase (RSK) and ESR (extracellular signal-regulated kinase) control the transcription factors c-Jun and c-Fos (Whitmarsh and Davis, 1996; Cesare *et al.,* 1998). In contrast, ultraviolet-B (UVB) induced phosphorylation of ERK, JNK and RSK, which is not suppressed by luteolin treatment. Luteolin after phosphorylation directly inhibiting or suppressing their kinase activity. Results of kinase assay *In vitro* study, show that the significant effects of luteolin on the inhibition of p90RSK2 and JNK1 activity, but not effective against the activity of ERK2 and JNK2. Moreover, luteolin directly bound to JNK1 but not JNK2 in an ATP-competitive manner, indicated by pull-down assays. In an ATP-independent manner luteolin bound the RSK2. Evident form previous studies, clearly indicate that the wrinkle formation in SKH-1 hairless mice, induced by chronic UVB suppressed by luteolin treatment. MMP-13 expression induced by UVB, in a mouse skin lysates effect of rodent interstitial collagenase, significantly suppressed by the use of luteolin.

A well-known transcription factor AP-1, that activates the target genes and binds to the TRE with the consensus sequence TGACTCA (Angel and Karin, 1991; Rittie and Fisher, 2002). Complex of activator protein-1 consist of Fos and Jun family proteins that are regulated by mitogen-activated protein kinases (MAPKs) (Whitmarsh and Davis, 1996).

Phosphorylation of the c-Jun activation domain caused by Jun N-terminal kinase. Upstream kinase of c-Jun activates its transcription activity (Derijard *et al.,* 1994). Expression of c-Fos and c-Jun genes correlates with the activity of AP-1 and is regulated by p38, ERK and p90RSK (Whitmarsh and Davis, 1996; Cesare *et al.,* 1998). From some previous studies, Ultraviolet-B (UVB) irradiation found to induce the activation of c-Fos and phosphorylation of c-Jun, these are suppressed through direct inhibition of their upstream kinases p90RSK2 and JNK1 by the luteolin treatment.

MAPK (Mitogen-activated protein kinases) family members such as JNKs (c-Jun N-terminal kinases) are heavily involved in proliferation, apoptosis and cell survival (Bode and Dong, 2007). Different AP-1 components such as, JunD, c-Jun and activating transcription factor 2 (ATF2) phosphorylated by JNKs. The c-Jun N-terminal kinases can also phosphorylate the c-Myc, Elk1, MLK2, p53, histone H3 and tau (Bode and Dong, 2007). In different cases reported that the c-Jun phosphorylated only by JNKs (Gupta *et al.,*

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1996). In phosphorylation of c-Jun the role of JNKs remains controversial. The role of JNK2 as a negative regulator of c-Jun reported by Sabapathy and Wagner (2004). On the other hand, role of JNK2 as a positive regulator of c-Jun reported by Jaeschke *et al.*, (2006). However, an agreement done about the JNK1, positive regulator of c-Jun (Sabapathy and Wagner, 2004; Jaeschke *et al.,* 2006). Luteolin have a potential to inhibit the wrinkle formation and matrix metalloproteinase (MMP-1) expression induced by ultraviolet-B *in vitro* and *in vivo*. For the inhibition of signal transduction induced by ultraviolet-B, leading to matrix metalloproteinase (MMP-1) up-regulation, p90RSK2 and JNK1 for luteolin are novel molecular targets and a very useful agent for the prevention of skin ageing induced by UVB.

4.5. Luteolin improve heart function

In the biological system, luteolin is known as a free radical scavenger or an antioxidant (Horvathova *et al.,* 2005; Huang *et al.,* 2005). Cardiomyocytes, antioxidant power following Simulated Ischemia/Reperfusion (SI/R) enhanced by luteolin, due to the decrease in subsequent production of malondialdehyde (MDA), lipid peroxidation, production of ROS and increase in the activity of superoxide dismutase (SOD). In pathophysiology ROS play functional role against the myocardial SI/R injury (Tsutsui *et al.,* 2008; Liao *et al.,* 2011). Some earlier studies propose that, the antioxidant activity of luteolin during myocardial SI/R overcome the mass production of free radicals derived from oxygen (Miura and Miki, 2009). The essential proteins and cell membrane lipids interaction with the free radicals derived from oxygen, lead toward the electro-physiologic, metabolic and functional changes of the myocardium. These changes may also induced the potentially myocardial necrosis and lethal ventricular arrhythmia (Hausenloy *et al.,* 2005).

Several previous studies described that the SI/R-induced oxidative damage of cardiomyocytes reduce or suppressed by luteolin. Luteolin shows the protective action to rescue the rat heart tissue against the ischemia/ reperfusion injury (I/R) by suppressing the expression of inducible nitric oxide synthase (Liao *et al.,* 2011). Also the production of nitric oxide reduce, which may prevent from the interaction of superoxide radical with nitric oxide, by that means protect free radical injury. *In vitro* some previous evident indicate that the luteolin effectively protect the myocardium from oxidative injury induced by SI/R.

In cardiomyocytes the NOX2 protein increase, followed by I/R injury. Pretreatment under these conditions with luteolin restrict the NOX2 protein expression and the same results also found for mRNA expression. NOX2 mRNA expression down-regulated by luteolin. According to the analysis of western blot, luteolin through transcription effects the NOX2 expression, which correlates with the change of its protein levels seen in injury in cardiomyocytes induced by SI/R.

Reactive oxygen species (ROS) are better known for the inactivation of anti-oxidative proteases. In the cell, a set of effective anti-oxidative enzymes play an important role as a defense mechanism to secure the organisms from damage induced by reactive oxygen species (ROS). These enzymes such as, SOD, catalase (CAT) and glutathione peroxidase (GSH2Px) and among others. These enzymes suppressing the free radical reaction by causing chemical changes in ROS. Anti-oxidative proteases could be inactivate the explosive increase in reactive oxygen species following SI/R, resulting in protein denaturation, DNA damage and lipid peroxidation. During redox reaction, in the intracellular space reactive oxygen species can also cause changes in the conformation of the macromolecules and structure, because of that in cellular apoptosis regulating the signal transduction. To protect the cardiomyocytes from SI/R induced oxidative damage, luteolin effectively scavenge the reactive oxygen species. In myocardial hypertrophy molecular mechanism, the ROS play an important role or participating for the activation of p38MAPK.

In myocardial protection, the activation of PI3K/Akt pathway play a significant role (Hausenloy *et al.,* 2005). Pretreatment with luteolin may involve the PI3K/Akt survival pathway. The expression level of phosphorylated Akt increased by pretreatment with luteolin and PI3K inhibitor (LY294002) partially inhibit this increase. Phosphorylated Akt could be activate the NOX2 expression and this effect is eliminate to a considerable degree by the PI3K inhibitor (LY294002). Luteolin provide protection to cardiomyocytes by activating the PI3K/Akt signaling pathway, inhibiting oxidative stress and improving cardiomyocyte contractile function from SI/R-induced injury. Phosphorylation of p38MAPK and expression of NOX2 significantly reduced by pretreatment with luteolin, on the other hand luteolin exert cardio-protective effect by enhancing the phosphorylation of Akt.

CONCLUSION

Luteolin widely present in the plant kingdom, mostly in edible plants. Overall the best source of luteolin is oregano with 1028.75mg/100g and followed by Juniper Berries with 69.05mg/100g. Flavonoids are important component of plants, and widely used in traditional medicine to cure the different type of diseases. In some studies on animal luteolin exerts its biological properties *in vivo.* Luteolin has different health benefits such as, anti-inflammatory, sun protectant, anti-oxidant, improve heart function, neurological impairments, anti-cancer and many more.

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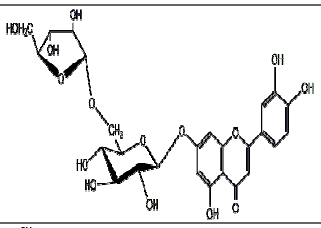
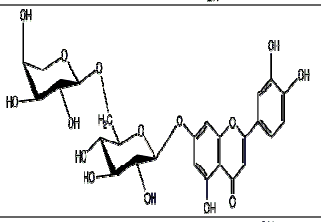
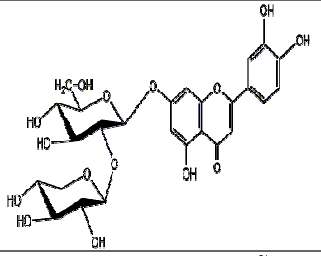
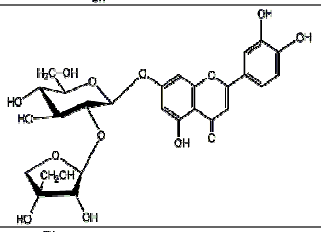
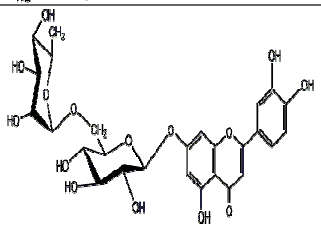
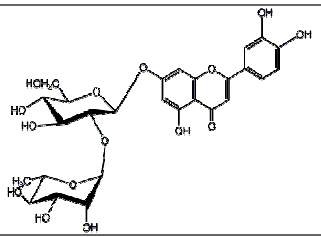
Table 1. Derivatives of luteolin their plant source and structures

Derivatives	Plant class	Plant family	Species	Structure	Refrences
Luteolin 7-arabinofuranosyl-(1->6)-glucoside	Spermatophyta	Podocarpaceae	*Dacrydium spp.*		(Harborne and Baxter, 1999)
Luteolin 7-arabinopyranosyl-(1->6)-glucoside	Spermatophyta, Eudicotyledons	Podocarpaceae, Caryophyllaceae	*Gypsophila repens, Dacrydium spp.*		(Elbandy *et al.*, 2007; Harborne and Baxter, 1999)
Luteolin 7-sambubioside	Asterids	Lamiaceae	*Thymus membrane-ceus*		(Harborne and Baxter, 1999)
Luteolin 7-apiosyl-(1->2)-glucoside	Asterids	Apiaceae, Solanaceae	*Apium graveolens, Petroselinum crism, Capsicum annuum*		(Harborne and Baxter, 1999; Materska *et al.*, 2003)
Luteolin 7-O-rutinoside, Luteolin-7-O-beta-D-rutinoside, Luteolin 7-rutinoside	Asterids, Rosids, Liliopsida	Lamiacea, Arecaceae, Brassicaceae, Campanulaceae, Asteraceae	*Saussurea medusa, Pratia nummularia, Capsella bursa-pastoris, Mentha aquatica L., Phoenix roebelenii*		(Harborne and Baxter, 1999; Lu and Foo, 2002; Xie *et al.*, 2005)
Lonicerin / Luteolin 7-neohesperidoside	Asterids, Euphyllophyta	Poaceae, Asteraceae, Plantaginaceae, Rutaceae	*Cymbopogon citraee, Chrysanthemum morifolium, Saussurea medusa, Veronicastrum sibir-icum, Citrus aurantium*		(Chan, 2005; Harborne and Baxter, 1999; Hayashi *et al.*, 1988)

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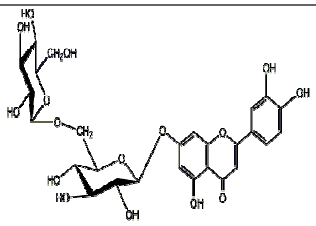
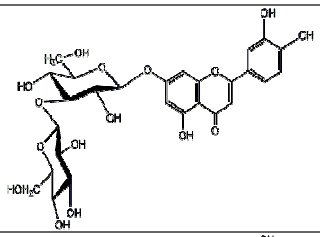
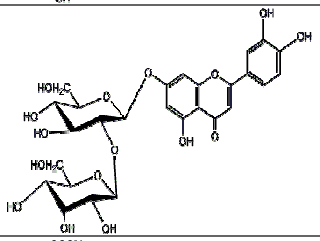
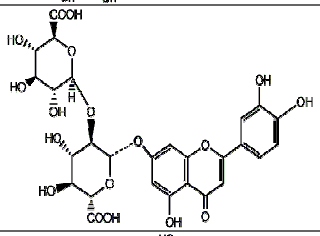
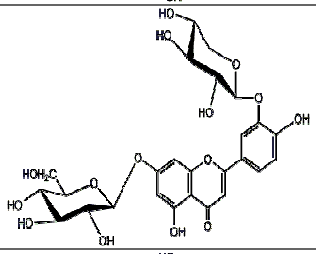
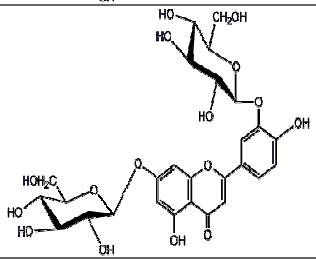
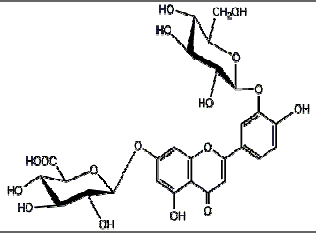
Luteolin 7-gentiobioside	Asterids	Campanulaceae or Lobeliaceae	*Campanula rotundif-olia*		(Harborne and Baxter, 1999)
Luteolin 7-laminaribioside	Liliopsida	Colchicaceae	*Colchicum speciosum*		(Harborne and Baxter, 1999; Markham, 1988)
Luteolin 7-allosyl-(1->2)-glucoside	Asterids	Labiatae	*Sideritis maura*		(Harborne and Baxter, 1999; Markham, 1988)
Luteolin 7-glucuronosyl-(1->2)-glucuronide	Liliopsida	Hydrocharitaceae	*Elodea canadensis*		(Harborne and Baxter, 1999; Mues, 1983)
Luteolin 7-glucoside-3'-xyloside	Spermatophyta	Podocarpaceae	*Podocarpus Nivalis*		(Harborne and Baxter, 1999)
Luteolin 3',7-di-O-beta-glucoside or Luteolin 7,3'-diglucoside	Asterids, Rosids	Asteraceae, Resedaceae, Scrophulariaceae	*Launaea nudicaulis, Reseda luteola, Hebe parviflora*		(Harborne and Baxter, 1999; Mitchell *et al.*, 2001; Mansour *et al.*, 1983)
Luteolin 7-glucuronide-3'-glucoside	Asterids, Embryophyta	Labiatae, Ricciaceae	*Salvia triloba, Riccia fluitans*		(Harborne and Baxter, 1999; Abdalla *et al.*, 1983)

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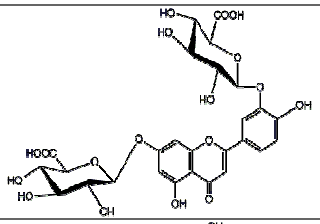
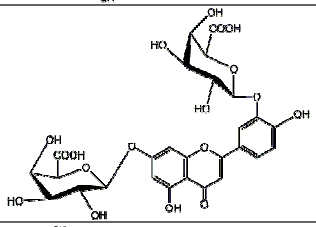
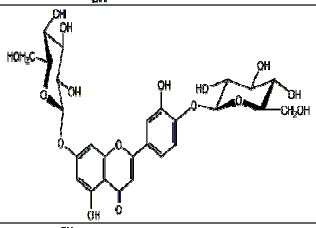
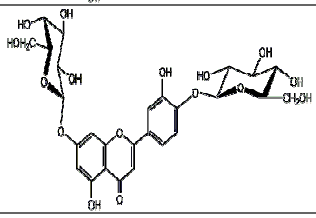
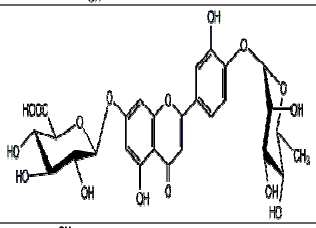
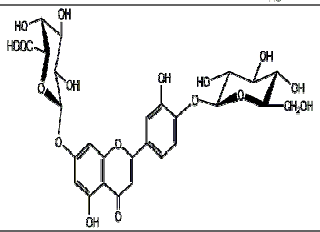
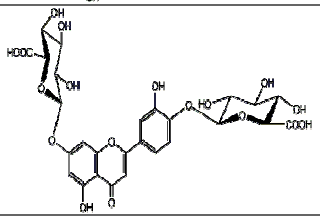
Luteolin 7,3'-diglucuronide	Embryophyta	Marchantiaceae	*Marchantia polymorpha*		(Harborne and Baxter, 1999; Markham and Porter, 1974)
Luteolin 7,3'-digalacturonide	Embryophyta	Marchantiaceae	*Marchantia berteroana*		(Markham and Porter, 1975)
Luteolin 7,4'-diglucoside	Asterids, Embryophyta, Rosids	Asteraceae, Fabaceae, Jubulaceae	*Launaea nudicaulis, Vicia balansae, Frullania dilatata*		(Harborne and Baxter, 1999; Mansour *et al.*, 1983)
Luteolin 7-galactoside-4'-glucoside	Asterids	Asteraceae	*Vernonia baldwinii, Vernonia greggii, Vernonia texana*		(Harborne and Baxter, 1999)
Luteolin 7-glucuronide-4'-rhamnoside	Embryophyta	Conocephalaceae	*Conocephalum Coicum*		(Harborne and Baxter, 1999)
Luteolin 7-galacturonide-4'-glucoside	Asterids	Apiaceae	*Cuminum cyminum*		(Harborne and Baxter, 1999; EI-Negoumy and Mansour, 1989)
Luteolin 7,4'-diglucuronide	Embryophyta	Marchantiaceae	*Marchantia polymorpha*		(Harborne and Baxter, 1999; Markham and Porter, 1974)

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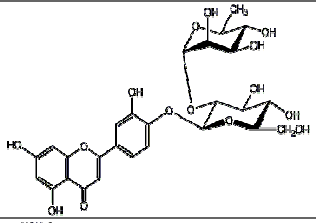
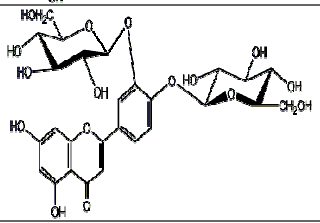
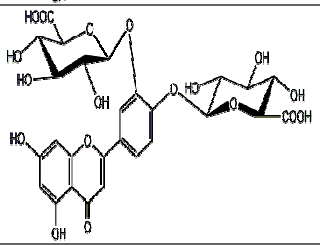
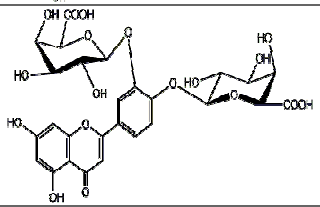
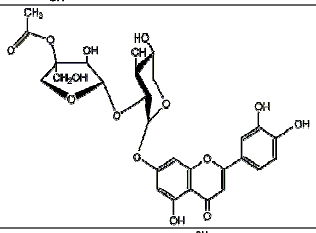
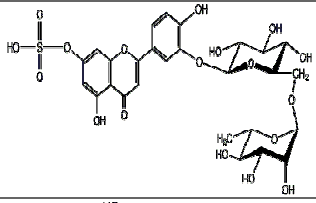
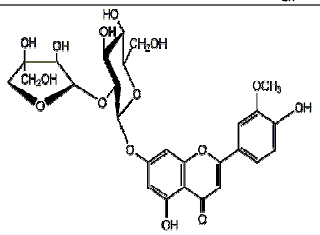
Luteolin 4'-neohesperidoside	Asterids	Apocynaceae	*Caralluma tuberculata*		(Brown *et al.*, 1990)
Luteolin 3',4'-diglucoside	Liliopsida	Orchidaceae	*Listera ovata*		(Williams, 1979)
Luteolin 3',4'-diglucuronide	Embryophyta	Ophioglossaceae	*Lunularia cruciata*		(Harborne and Baxter, 1999; Markham and Porter, 1974)
Luteolin 3',4'-digalacturonide	Embryophyta	Marchantiaceae	*Marchantia berteroana*		(Harborne and Baxter, 1999; Markham and Porter, 1974)
Luteolin 7-(3'''-acetylapiosyl-(1->2)-xyloside)	Asterids	Campanulaceae or Lobeliaceae	*Campanula patula*		(Harborne and Baxter, 1999)
Luteolin 7-sulfate-3'-rutinoside	Liliopsida	Arecaceae	*Opsiandra maya*		(Harborne and Baxter, 1999)
Luteolin 3'-methyl ether 7-apiosyl-(1->2)-glucoside	Rosids, Asterids	Apiaceae, Fabaceae	*Apium graveolens, Dalbergia monetarya*		(Harborne and Baxter, 1999)

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Table 2: Luteolin content (mg/100g) in different sources

	Food Source	Luteolin Contents		Food Source	Luteolin Contents
Vegetables	Radicchio	37.96mg	Vegetables	Raw cauliflower	0.08mg
	Raw Chinese Celery	34.87mg		Raw red cabbage	0.06mg
	Dried spices, parsley	19.75 mg		Raw lettuce iceberg	0.06mg
	Dried Parsley	19.75mg		Raw cabbage Chinese	0.06mg
	Peppermint fresh	11.33mg		Raw Cabbage	0.04mg
	Raw green peppers (hot chili)	5.11mg	Herbs	Oregano	1028.75mg
	Raw pepper Serrano	4.14mg		Juniper Berries	69.05mg
	Raw peppers, jalapeno	1.34mg		Thyme, fresh	51.00mg
	Raw Celery	1.31mg		Fresh Mexican Oregano	25.10mg
	Raw Kohlrabi	1.30mg	Plants	Fresh sage	16.70mg
	Raw Parsley	1.24mg		Fresh Rosemary	4.00mg
	Raw Spinach	1.11mg		Raw Chives	0.15mg
	Raw green sweet peppers	0.69mg		Raw Dishcloth Gourd	0.01mg
	Raw red sweet peppers	0.63mg	Fruits	Raw Lemons without peel	1.50mg
	Raw Beets	0.37mg		Raw Sweet potato leaves	0.20mg
	Raw Brussels sprouts	0.34mg			

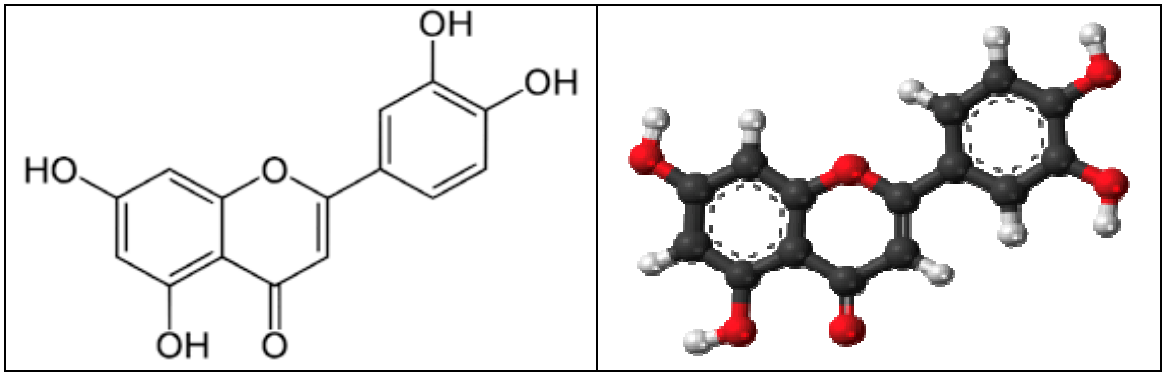

Figure 1. Chemical structures of Luteolin

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CONFLICTS OF INTEREST
"The authors declare no conflict of interest".