2. REVIEW OF LITERATURE

Rizos E C et al (2012)\textsuperscript{6} conducted clinical trial on combination therapies of DPP4 inhibitors and GLP1 analogues with insulin in Type 2 Diabetic Patients and found incretin-based therapies combined with basal insulin are able to reduce HbA1c by 0.5-0.7%. DPP4 inhibitors have no significant effect on weight, whereas GLP1 analogues reduced weight by 1-2 kg.

Upreti VV et al (2012)\textsuperscript{7} studied the effect of saxagliptin on the Pka of the active components of a Combined Oral Contraceptives (COC) in an open-label, randomized, 2-way crossover study in 20 healthy female subjects. They concluded coadministration of both generally well tolerated and so can be co-prescribed.

Bolton et al (2011)\textsuperscript{8} carried out bioequivalence of saxagliptin/Metformin XR fixed dose combination tablets and single component saxagliptin and metformin XR tablets in healthy adult subjects and found tolerability of combined dosage comparable to that of individual components.

Mohammad Abdul et al (2012)\textsuperscript{9} developed a validated RP-HPLC method for simultaneous determination of two new gliptins (saxagliptin & vildagliptin) in their binary mixtures with metformin using a mobile phase of potassium dihydrogen phosphate buffer pH (4.6)-acetonitrile (15:85 v/v) at a flow rate of 1 ml per min at UV detection 208 nm. They found Vildagliptin, saxagliptin and metformin in the range of 5-200, 0.5-20 and 50-2000µg/ml, respectively.

Narendra et al (2012)\textsuperscript{10} developed a validated UV-Vis spectroscopy method for simultaneous estimation of saxagliptin HCl and Metformin HCl in active pharmaceutical ingredient at λmax 274 & 231 nm; respectively in concentration range of 50-90 µg and 2-10 µg respectively.

R. Kalaichelvi et al (2011)\textsuperscript{11} developed a validated spectroscopic method for estimation of saxagliptin in pure and from tablet formulation at 208 nm in methanol at linear concentration range of 5-40 µg per ml (r2=0.999)

Srikant et al (2011)\textsuperscript{12} has carried out LC determination of saxagliptin and pure bulk and pharmaceutical dosage forms at 220 nm using (0.02M sodium dihydrogen phosphate, pH-3 adjusted with ortho phosphoric acid): methanol: acetonitrile inn ratio of 45:20:35 at flow rate 1.0 ml per min.
The method was found linear in the concentration range of 10-100µg/ml for saxagliptin in 8.20 min. RT.

R. Pravin Cumar et al (2012)\textsuperscript{13} estimated saxagliptin and metformin by a validated RP-HPLC method simultaneously in tablets on C18 (5 µm, 25 cm X 4.6mm, i.d) column at 225 nm using phosphate buffer (pH 5.0), acetonitrile, and methanol (75:15:10) mobile phase and the retention time was found 5.65. and 6.20 min for metformin and saxagliptin, respectively.

Patil Prafulla et al (2012)\textsuperscript{14} estimated Metformin and Saxagliptin at 248 nm on Zodiac C18 column (150mmX 4.6 mm; 5µ) using mobile phase mixture of phosphate buffer pH 6.8, acetonitrile (94:6) in concentration range of 12.5-75 µg/ml for metformin and 0.125-0.75 µg/ml for saxagliptin.

M. Sarat et al (2012)\textsuperscript{15} analyzed saxagliptin and pioglitazone using validated HPLC method on a C18 column utilizing mobile phase acetonitrile: phosphate buffer (60:40, pH 7.0) at flow rate of 0.8 ml per min with UV detection 260 nm. The method was linear in the range of 20-8- µg/ml for saxagliptin and 10-70µg/ml for pioglitazone, respectively.

Hiren et al (2012)\textsuperscript{16} developed spectrofluorometric method to determine sitagliptin phosphate in bulk, pharmaceutical formulation and human urine at wavelength of 297 nm in a linearity range of 0.6-10 µg/ml.

Kavitha K Y et al (2012)\textsuperscript{17} has developed and validated stability indicating RP-HPLC method for the simultaneous estimation of sitagliptin and simvastatin using C18 (250X4.6mm, 5µm) G column, mobile phase consisting of water:acetonitrile (30:70 v/v) at 236 nm using photodiode array detector. The method was linear in the range of 40-400 µg/ml for sitagliptin and 10-50 µg/ml for simvastatin, respectively.

Sumitra et al (2012)\textsuperscript{18} has developed and validated RP-HPLC method for simultaneous estimation of sitagliptin and metformin using C18 column with a mobile phase phosphate buffer (pH 4) and acetonitrile (60:40) at 260 nm. The method was linear in the range of 2-12µg/ml for sitagliptin and 20-120 µg/ml for metformin, respectively.

Govindasamy et al (2012)\textsuperscript{19} has estimated simultaneously sitagliptin phosphate monohydrate and metformin hydrochloride in bulk and pharmaceutical formulation by RP-HPLC method on C18 column.
at 252 nm using 0.02M potassium dihydrogen phosphate and acetonitrile (55:45) at pH 4.3. The method was linear for sitagliptin 4-20g/ml & 10-5- µg/ml for metformin, respectively.

Bhende et al (2012) has estimated sitagliptin phosphate and metformin hydrochloride in combined tablet dosage forms on an XTerraC8 (4.6X100mm, 3 µm) column using a mobile phase pH 9 phosphate buffer: acetonitrile: methanol (35:45:20) at 260 nm. Linearity of sitagliptin and metformin were found in the range of 50 to 150 ppm.

Dubala et al (2012) has developed and validated bioanalytical RP-HPLC method for sitagliptin phosphate in human plasma by protein precipitation technique on a phenomenex C18 (250X4.6mm, 5µ) column at 267 nm using mobile phase 0.5% v/v of triethylamine solution (pH 6.8) and acetonitrile (77:23) with a linearity range of 10-1000ng/ml.

Amruta B. Loni et al (2012) developed UV spectrophotometric method for estimation of Sitagliptin phosphate and Metformin hydrochloride in bulk and tablet dosage form based on absorption maxima at 266 and 232 nm, respectively and linear response was found for sitagliptin 25-225 µg/ml and 2-12 µg/ml for metformin, respectively.

Lakshmana Rao et al (2012) validated RP-HPLC method for simultaneous estimation of Metformin hydrochloride and Sitagliptin phosphate in bulk drug and pharmaceutical formulation using Xterra Symmetry C8 column (100X4.6mm, 5 µ) using mobile phase methanol: acetonitrile: phosphate buffer (pH 8) in ratio of 20:35:45 v/v/v at 254 nm. The linear response was found in the concentration range of 100-300 µg/ml for metformin hydrochloride and 10-30 µg/ml for sitagliptin phosphate.

Monila et al (2012) developed two spectrophotometric methods for determination of Sitagliptin phosphate in bulk and in pharmaceutical formulations based on complexation of the drug with Bromo Thymol Blue and Bromo Cresol Green, extracted with chloroform, showing absorbance maxima at 412 nm and 419 nm and Beer’s law is obeyed from 25-125 µg/ml & 10-50 µg/ml respectively.

Shyamala et al (2011) has developed and validated RP-HPLC method for simultaneous estimation of Sitagliptin phosphate and Metformin hydrochloride in tablet dosage forms on Hypersil (250X4 mm, 5 µ) column, using mobile phase acetonitril and phosphate buffer in the ratio of 45:55 at wavelength 260 nm with a concentration range of 20-120 µg/ml and 2-12 µg/ml, respectively.
Kashid et al (2012) has developed and validated RP-HPLC method for Sitagliptin in Human plasma using mobile phase acetonitrile: methanol: buffer (2:3:5 v/v) at pH 4.0. The extracted analyte was injected into an Inertsil C18 column (150X4.6mm, 5 µ) and monitored at 267 nm. The response was linear in the range of 25-125 µg/ml.

Pharne A. B. et al (2012) has developed a simple, selective, rapid, precise and economical RP-HPLC method for Vildagliptin with UV detection on HPLC system at a flow rate of 1.0 ml/min at 210 nm using 50mM ammonium bicarbonate (pH 7.8) and acetonitrile. The method was tested for linearity range of 10-120 µg/ml.

Malakar A et al (2012) developed and validated a RP-HPLC method for estimation of Vildagliptin in pharmaceutical dosage forms on Xterra Waters C18 (150X4.6mm, 5 µm) column at 210 nm using buffer ph 9.5 and methanol (60:40 v/v). The developed method was linear from 5-200 µg/ml.

Verma P. N. et al (2013) has simultaneously determined metformin and vildagliptin in solid dosage forms by stability indicating RP-HPLC method using phosphate buffer and acetonitrile (60:40 v/v) at a flow rate of 1.0 ml/min and the effluent was monitored at 263 nm. Linearity was in the range of 1000.6-3001.8 µg/ml for metformin & 100.2-300.6 µg/ml for vildagliptin, respectively.

Sultana R et al (2013) has developed and validated stability indicating assay method of vildagliptin in bulk and tablet dosage form by RP-HPLC method on C18 column using buffer:acetonitrile (50:50 v/v) at a flow rate of 1.0 ml/min. The method was linear from 10-60 µg/ml.

Shrikrishna B et al (2013) has simultaneously estimated vildagliptin and metformin in bulk and tablet dosage form using 0.1 N NaOH using measurement of absorbance at the wavelength of maximum. They found linear response from 30-7-µg/ml for vildagliptin & 5-25 µg/ml for metformin.

El-Bagary R et al (2011) has determined vildagliptin and sitagliptin simultaneously in bulk and dosage forms based on the charge transfer complexes with DDQ, TCNQ and p-chloranil. Beer’s law was obeyed in the range of 50-300 μg/ml, 20-120 µg/ml & 100-900 µg/ml with DDQ, TCNQ and p-chloranil.
**Gundala u et al (2013)** has simultaneously estimated vildagliptin and metformin in bulk and pharmaceutical formulations by UV spectrophotometry by multi-wavelength technique at 217 nm and 234 nm over the concentration ranges of 0.7-7 µg/ml. The method was validated in accordance of ICH guidelines.

**Gueler I et al (2013)** has studied effects of Vildagliptin in patients with type 2 diabetes mellitus after heart transplantation and compare with control patients for matched pairs analysis. Mean glycated hemoglobin (HbA1c) and significant reduction in mean blood glucose studied and did not show any negative effects on lipid profile or body weight.

**El-baggary et al (2011)** has determined vildagliptin simultaneously with pioglitazone hydrochloride and metformin hydrochloride on a symmetry C18 column (150mmX4.6mm, 5µm) at a flow rate of 1 ml/min with UV detection at 210 nm and found linear response over the concentration range of 5-200 µg/ml, 0.5-3 µg/ml and 10-150 µg/ml for vildagliptin, pioglitazone and metformin, respectively.